Clinical value of isolated intracardiac echogenic focus in the fetal heart: A retrospective study in Chinese women

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Summary

Purpose: To assess the resolution of intracardiac echogenic focus in gestation and to evaluate its association with fetal cardiac structural defects. Materials and Methods: Retrospective data of fetal echocardiography from January 2014 to December 2016 in low-risk pregnancies were collected. The study variables included observation resolution data of fetuses with intracardiac echogenic foci detected in the second-trimester, and follow-up data in the third-trimester. The Chi-square test was used to determine the association between intracardiac echogenic foci and fetal cardiac defects. Additionally, several statistical measures of performance for the foci as predictive markers were calculated. Results: The authors examined 8,120 fetuses. Among 531 fetuses with intracardiac echogenic foci, the overall incidence rate was 6.5% on a sonogram at 22–28 gestational weeks. The left ventricle was the most common site. Significant differences were observed between the locations and features of changes in the foci ($\chi^2=18.68, p=0.0009$). No significant associations were found between the foci locations and fetal cardiac structural defects ($P_{\text{fisher}}=0.28$), or between the foci and cardiac defects ($\chi^2=0.91, p=0.34, OR = 0.72$ with 95% confidence interval $(0.40, 1.30)$). Conclusions: In most cases, isolated intracardiac echogenic focus was a transient sonographic marker during the gestational period. However, foci in the right ventricle were more stable than in the other locations. Intracardiac echogenic foci were not associated with cardiac defects, despite persistence in the third trimester.

Key words: Echocardiography; Intracardiac echogenic focus; Low-risk pregnancy; Structural heart defects.

Introduction

Fetal echocardiography is performed to detect structural cardiac anomalies. Intracardiac echogenic focus may be observed in the four-chamber view. It was first described by Schechter et al. in 1987. These small discrete structures were considered to be incomplete fenestrations or mineralizations of the chordae tendineae and/or the papillary muscles [1, 2]. Numerous reports have discussed this finding and its possible associations in cross-sectional populations, but the significance of this marker is still debated. Clinically, this finding increases maternal and family anxiety, and is the reason behind referrals from doctors or requests from patients for fetal echocardiography examination.

The present authors are aware that the benign nature of this marker can be best confirmed by pregnancy in prolonged time. Reports regarding the resolution of cardiac echogenic focuses are varied. Some series on neonatal echocardiography demonstrated persistence of intracardiac echogenic focus [3, 4], while others reported resolution of the focus in 20–90% of cases [5-7].

The purpose of current study was to provide updated information regarding echogenic focus within fetal heart in the Chinese population, thereby minimizing the variability in the interpretation of this marker in clinical practice. The outcomes of the study would be useful for the counseling of patients with an isolated intracardiac echogenic focus and for adjusting the patient’s risk to undergo further tests.

Materials and Methods

This study was a retrospective analysis (from January 2014 to December 2016) of fetal echocardiography data collected from the two of prenatal screening center of Shaanxi, China. Study protocol was approved by the ethics committee of Xi’an Jiaotong University.

Patients were categorized as low-risk pregnancy based on the following criteria: (1) pregnant women aged < 35 years with singleton pregnancies, (2) normal results of maternal aneuploid serum “triple screen”, (3) fetuses with isolated intracardiac echogenic focus (i.e. without other associated sonographic markers or anomalies), and (4) women without prior history of congenital heart disease or aneuploid offspring. All patients had undergone targeted fetal anatomic survey before being referred for fetal echocardiography. Referral was made by medical doctors or by patients’ independently. A database search was taken to identify presence or absence of cardiac echogenic focus and its locations (left, right, or bilateral ventricles), number (solitary or
Table 1. — Locations and numbers of echogenic focus with fetal heart structural defects detected by echocardiography in the second trimester.

<table>
<thead>
<tr>
<th>Cardiac echogenic focus locations</th>
<th>No. of fetuses with cardiac echogenic focus (%)</th>
<th>Heart structural defects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left ventricle</td>
<td>455</td>
<td>5 ventricular septal defects</td>
</tr>
<tr>
<td>Solitary</td>
<td>437 (82.3)</td>
<td>1 atrioventricular septal defect</td>
</tr>
<tr>
<td>Multiple</td>
<td>18 (3.4)</td>
<td>1 narrow aorta, ventricular septal defect*</td>
</tr>
<tr>
<td>Right ventricle</td>
<td>29</td>
<td>1 pulmonary stenosis, 1 left superior vena cava</td>
</tr>
<tr>
<td>Solitary</td>
<td>26 (4.9)</td>
<td>1 ventricular septal defect</td>
</tr>
<tr>
<td>Multiple</td>
<td>3 (0.6)</td>
<td>1 narrow aorta, ventricular septal defect*</td>
</tr>
<tr>
<td>Bi-ventricle</td>
<td>47</td>
<td>1 ventricular septal defect</td>
</tr>
<tr>
<td>One Left ventricle</td>
<td>41 (7.7)</td>
<td>1 double outlet right ventricle*</td>
</tr>
<tr>
<td>One Right ventricle</td>
<td>6 (1.1)</td>
<td>1 narrow aorta, ventricular septal defect*</td>
</tr>
<tr>
<td>Multiple</td>
<td>3 (0.6)</td>
<td>1 narrow aorta, ventricular septal defect*</td>
</tr>
</tbody>
</table>

*Multiple cardiac echogenic focus.

Results

Cardiac echogenic focus was identified in 531 fetuses among 8,120 (6.5%) low-risk pregnant women in the second-trimester during the study period. The mean maternal age was 25.7 ± 3.6 years. The mean gestational age at referral during the second-trimester was 22.8 ± 3.2 weeks, and the third-trimester follow-up was at 31.2 ± 2.8 weeks. The mean size of the fetal echogenic focus at the initial diagnosis was 2.6 ± 1.1 mm. Structural cardiac defects were diagnosed in 3.0% (247 of 8,120 cases) of the overall population. Likewise, structural defects of the fetal heart were detected in nine of 455 fetuses with left-sided ventricular echogenic focus, 29 with right ventricular echogenic focus, and two of 47 with both-sided intracardiac echogenic focus (P_fisher = 0.28). The distribution of fetal cardiac echogenic focus locations, number, and structural heart defects in the second trimester are shown in Table 1.

Serial follow-up features of echogenic focus in the fetal heart changes were collected in the third trimester, and the resolutions were compared (Table 2). Significant differences were identified between features of echogenic focus changes and its locations (χ²=18.68; p = 0.0009). A higher portion of cardiac echogenic focus located in the right ventricle remained unchanged (34%) compared to the echogenic focus located in the left ventricle (11%) or in both ventricles (13%).

Overall, 12 (2.3%) fetuses with isolated intracardiac echogenic focus developed cardiac defects. The total number of cardiac defects in each group is shown in Table 3. The sensitivity and specificity of an isolated cardiac echogenic focus as a screening marker of fetal heart structural defects was 4.86% (95% CI 2.54% to 8.33%) and 93.41% (95% CI 92.83% to 93.94%), respectively. The positive predictive value and negative predictive value were 2.26% (95% CI 1.31% to 3.88%) and 96.90% (95% CI 96.81% to 96.99%), respectively. No significant association was identified between echogenic focus within fetal heart and cardiac defects [χ² = 0.91, p = 0.34, OR = 0.72 with 95% CI (0.40, 1.30)].

Discussion

Advanced ultrasound technology has been widely used in obstetrical practice; thus, the detection rate of fetal heart defects and cardiac echogenic focus has been continuously rising. The prevalence of echogenic focus in the fetal heart is reported to be 2.3–9.6% [5, 8, 9] in low-risk populations. In the present study, it was found to be 6.5% (531 of 8,120 cases), which was within the reported range. Left ventricular echogenic focus was reported to be the most common site, ranging between 60–100% in previous studies [5, 10], which was similar to the present findings (85.7%). This can be explained by the large size of the left papillary muscle...
or the large mass of the chordae tissue. The second most common location for the detection of echogenic focus in this study was biventricular (8.8%), with previously reported rates ranging between 4–25% [11, 12]. In contrast, the least frequent site of echogenic focus was the right ventricle at 5.5% and the previously reported rates were 0–25% [13, 14].

Understanding the natural course of intracardiac echogenic focus and its effects on the fetal heart are directly related to the decision-making process in pregnant women. The origin of intracardiac echogenic focus still remains unclear. Schechter et al. [2] suggested that the cardiac echogenic focus may be incomplete fenestrations of the fetal papillary muscle and chordae tendineae, and develops as processes of endocardiac tissue. Others suggested that the abnormal development of the microvasculature may lead to early ischemic changes in the papillary muscle [15].

In general, intracardiac echogenic focus is mostly solitary and is connected to the papillary muscles or chordae tendineae. These structures typically measure 1–4 mm in diameter but are not larger than 6 mm [10]. In the present study, as the gestational weeks progressed, most of the left ventricular or biventricular echogenic focus gradually weakened or disappeared, whereas an isolated echogenic focus in the right ventricular remained stable over time, which was statistically significant.

Previous reports concluded that the appearance of echogenic focus in different fetal organs frequently signals associated pathological findings or diseases during prenatal sonogram examination [16, 17]. Multiple echogenic foci or diffuse echogenicity in the fetal heart, especially when the right ventricle is also involved, has been described in association with other pathologies and may signal poor prognosis [18]. Therefore, the present authors have attempted to describe the risk of echogenic focus in the fetal heart. The incidence of right-sided echogenic foci was much lower than left-sided foci. Moreover, the authors speculated whether these foci are normal variants of the development of the atrioventricular apparatus. The current evidence suggests that no relationship was found with structural anomalies of the heart and this may be due to the small sample size. However, the present authors believe it is interesting to know whether echogenic foci are benign transitory prenatal changes or related to poor prognosis. Particularly the special characteristic of right-sided echogenic focus changes during pregnancy. Thus, more studies are warranted for further investigation.

There have been some reports that have differently described the serial evaluation of features of cardiac echogenic focus through the progress of pregnancy. In 1994, Petrikovsky et al. [3] re-examined serial echocardiography at 26–28 weeks and 34–36 weeks for fetuses with intracardiac echogenic focus (41 of 1,139 fetuses). The results showed that the cardiac echogenic focus remained unchanged, decreased in size, and increased in size in 51%, 12%, and 36% cases, respectively. In addition, Achiron et al. [14] reported that echogenic focus in the fetal heart detected between 13 and 16 weeks in 163 out of 2,214 pregnancies, disappeared in 60% of fetuses re-examined at 20–22 weeks. These findings are in contrast to other studies, such as that by Degani et al. who found that the echogenic foci appeared by 22–24 weeks of gestation in eight of 48 cases (17%). Neonatal echocardiography was performed in 39 infants of the study group; persistent cardiac echogenic focus was demonstrated in 38 infants at the level of the chordae or papillary muscles, but no cardiac defects existed [19]. Similar results were reported by Bradley et al. who stated that the intracardiac echogenic focus noted at the second trimester scan persisted throughout gestation and did not resolve on subsequent evaluation [20]. These differences might be explained by the gestational age at the time of examination, the condition of the pregnant woman itself, the composition of the research object, the resolution of the instrument, and the experience of the doctors conducting the tests.

Some scholars have cast doubts regarding the association of intracardiac echogenic focus with the cardiac structure in low-risk populations. Some studies considered echogenic focus within the fetal heart to be associated with fetal cardiac defects but others refuted it [12, 21]. The present study found no association between location of isolated fetal intracardiac focus and cardiac defects in the subjects. Importantly, the present study found no association between location of isolated fetal intracardiac focus and cardiac defects in the subjects. Importantly, the present study}
tantly, low sensitivity of cardiac echogenic focus at 4.86% was detected in the present study, which was higher than the value of 1.5% as reported by Barsoom et al. in 2001 [22]. This may be attributable to the use of ultrasound equipment with higher resolution since the year 2000 worldwide, which might have increased the detection rate. The results of these studies were consistent in the observation that isolated intracardiac echogenic focus might not be a predictive marker for fetal cardiac defects, and its efficiency as a screening tool for fetal echocardiography in low-risk pregnancies was low [4, 7, 12]. Therefore, the presence of cardiac echogenic focus did not increase the risk of congenital heart defects.

There are some potential limitations of this study. First, this study had a relatively small sample population in a low-risk population, and although fetal echocardiography was carried out in the second-trimester of pregnancy (22–28 weeks of gestation) and late pregnancy (29–36 weeks of gestation), it is necessary to evaluate more cases to demonstrate the characteristics of intracardiac echogenic focus. Moreover, the results may not be sufficient to determine whether a similar conclusion can be reached in a high-risk group. Prior studies have demonstrated that the possibility of fetal cardiac malformation and chromosomal abnormalities will increase if it is at high risk [23]. Another limitation is that the present authors did not perform echo-cardiography in the neonatal period to follow-up the cases with intracardiac echogenic focus. The present authors hypothesize that this could have improved the ascertainment of the present case. Lastly, the authors only studied Chinese population in single center; hence, the results may not be reflective of the findings in the general population. Notably, there is a controversy regarding the association of cardiac echogenic focus with race and ethnicity with particular prevalence in fetuses of Asian women [9, 24]. Nevertheless, the present authors believe the present report provides data that warrant further clinical investigation to assess the significance of cardiac echogenic focus in fetuses.

In conclusion, intracardiac echogenic focus can be considered as a benign variance in low-risk pregnancies, and serial antenatal echocardiography is unnecessary. However, larger studies that can assess the pathological nature of the echogenic focus are awaited, especially those that assess the right-sided echogenic focus. It could be interesting to discover if there are any consequences affecting fetuses in such cases.

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References


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