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The assessment of the fetal heart function using two-dimensional speckle tracking with a high frame rate☆

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ABSTRACT

Background: Two-dimensional (2D) speckle tracking echography (STE) is a new diagnostic modality that allows for the assessment of myocardial deformation. The present study assessed the feasibility of fetal 2D-STE at a high frame rate and determined the reference values for left ventricular (LV)- and right ventricular (RV)- global longitudinal strain (GLS).

Methods: In this prospective study, 109 fetuses with gestational ages ranging from 18 to 38 weeks underwent 2D echocardiography between August 2018 and December 2019. All recordings were performed using the Aplio i800 (CANON Medical Systems Corporation, Tochigi, Japan) and a convex probe (4 MHz) for fetuses.

Results: Longitudinal peak systolic strain measurements were obtained in 98 of 109 healthy fetuses (90%). All ultrasound videos were recorded with a median frame rate of 172 (range, 100–274) frames/s. The LV-GLS was almost constant, regardless of the number of weeks since the second trimester ($r = -0.0087$, p = ns). The RV-GLS decreased significantly with gestational age ($r = 0.39$, $p < 0.01$).

Conclusions: STE may be useful for quantifying the systolic myocardial function in a fetus.

1. Introduction

Echocardiographic evaluations of the fetal cardiac function have been limited because of difficulty with imaging such a small heart. Two-dimensional (2D) speckle tracking echography (STE) is a new diagnostic modality that allow for the assessment of myocardial deformation. This new method is not angle-dependent and is expected to have a higher feasibility than tissue Doppler imaging. However, the speckle tracking method has not been clinically applied for the evaluation of the fetal heart function because the ideal frame rate for 2D imaging for the fast heart rate of fetuses, differences in devices among venders, and the optimum image resolution are unknown.

We herein report our examination of the feasibility of fetal 2D-STE at a high frame rate.

2. Methods

2.1. Study population

In this prospective study, 109 fetuses with gestational ages ranging from 18 to 38 weeks underwent 2D echocardiography in the Department of Obstetrics and Gynecology, Okayama University Graduate School of Medicine between August 2018 and December 2019.

Monochorionic twins and all fetuses with malformations, chromosomal abnormalities, cardiac defects or failure, fetal growth restriction, or arrhythmia were excluded from the study.

The local ethics committee approved the study protocol and informed consent was obtained from each mother.

2.2. Analyses of 2D images

All recordings were performed by a single experienced examiner using the Aplio i800 (CANON Medical Systems Corporation, Tochigi, Japan) and a convex probe (4 MHz) for fetuses.

For each fetal examination, digital loops containing at least 5 heart cycles in a B-Mode apical 4-chamber-projection were acquired in high 2D-quality and at frame rates ranging from 100/s to 274/s (median 172 frames/s).

Myocardial strain was analyzed offline using the 2D Wall Motion

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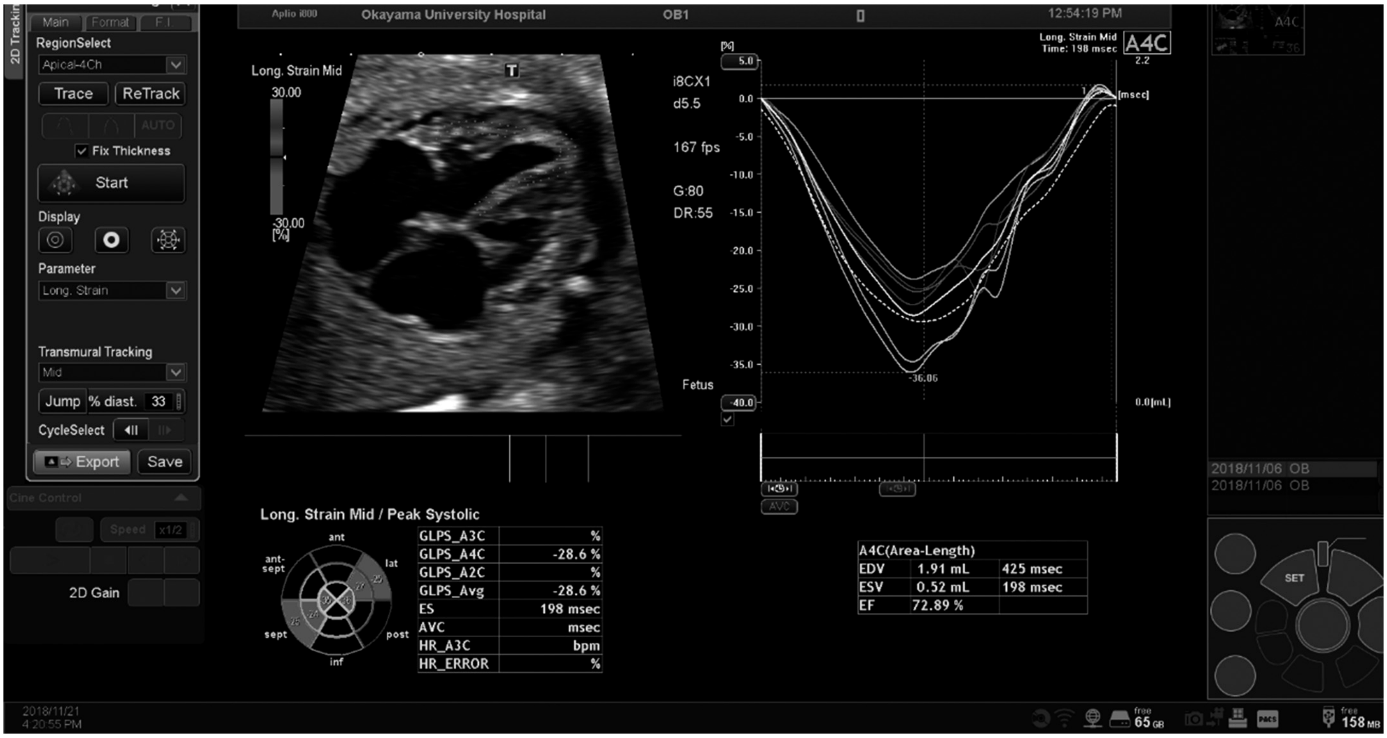

Fig. 1. A regional longitudinal strain analysis in a healthy fetus at 30 weeks' gestation. The software program automatically segmented the left ventricle into six equidistant segments (basal septal, mid septal, apical septal, apical lateral, mid lateral, septal lateral) and conducted segmental and global analyses of deformation parameters. Using the area length method, we were also able to measure the left ventricular EF.
GLPS: global longitudinal peak strain, EDV: end-diastolic volume, ESV: end-systolic volume, EF: ejection fraction.

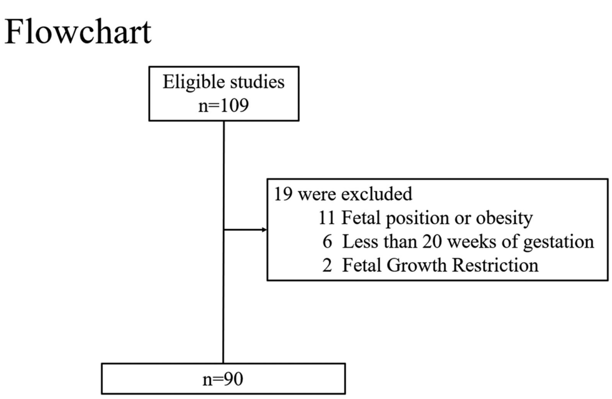

Fig. 2. Flowchart for prospective study.

Tracking software program (CANON Medical Systems). The reader needed to select one fetal heart cycle from the end-diastolic frame to the next end-diastolic frame. The ventricular epicardial border was manually traced on the four-chamber view. The software algorithm discriminated the endocardial border, but the reader could manually adjust the endocardial border and myocardial thickness if necessary. The end-diastole phase was automatically defined by the estimated ventricular size.

By performing STE, it was feasible to measure the global longitudinal strain (GLS). Using the area length method, we were also able to measure the left ventricular ejection fraction (LVEF) (Fig. 1).

2.3. Statistical analyses

Data were analyzed using BellCurve for Excel statistical software program (Social Survey Research Information Co., Ltd., Tokyo, Japan). Statistical significance was defined as a p value 0.05. Study variables are expressed as the mean ± standard deviation (SD). Ninety percent reference ranges (5th-percentile and 95th-percentile values) and their respective 95% confidence intervals (CIs) were calculated for global strain.

The intra-and interobserver variability were assessed using the intraclass correlation coefficients (ICCs), with a 95% CI. The intraobserver ICC by one-way classification was assessed using 10 random samples on 5 separate occasions by the same reader. To assess the interobserver ICC by the two-way random model, 10 random samples were measured on 5 separate occasions by 2 different readers. Observers/readers were not blinded to gestational weeks during the image analysis.

3. Results

The longitudinal peak systolic strain measurements were obtained in 98 of 109 healthy fetuses (90%). The fetal heart could not be visualized in 11 cases because of difficulties related to fetal position or obesity. Six fetuses under 20 weeks of gestation were excluded due to intraobserver variability. Two fetuses were excluded because of fetal growth restriction (Fig. 2). The median gestational age was 25 (range, 20–38) weeks. All ultrasound videos were recorded with a median frame rate of 172 (range, 100–274) frames/s (Table 1). The intraobserver ICC was 0.98 (95% CI: 0.97–0.99), and the interobserver ICC was 0.97 (95% CI: 0.88–0.99).

The left ventricular (LV)-GLS was almost constant, regardless of the number of weeks since the second trimester ($r = -0.0087$, p = ns). The right ventricular (RV)-GLS decreased significantly with gestational age ($r = 0.39$, $p < 0.01$). The left ventricular ejection fraction (LVEF) was constant ($r = -0.07$, p = ns) (Fig. 3). The average LV-GLS was −24.0% ± 5.3%, and that of the RV-GLS was −20.5% ± 4.8%. In addition, 32 (36%) of the 90 subjects were measured at least twice in different weeks. The average LV-GLS was −22.68% ± 5.46% and −22.97% ± 4.56% at the first and second time (paired t-test,

Table 1
Baseline characteristics of the 90 fetuses.

Maternal age	35 ± 6
Gestational age	25w2d (20w0d~38w0d)
EFBW (g)	929 ± 597
SD	0.26 ± 0.77
Frame rate	169 ± 37
CTAR (%)	24.0 ± 4.0

Data are expressed as numbers (n), average ± SD, median (range), or percentage (%).
EFBW: estimated fetal body weight, SD: standard deviation, CTAR: cardio thoracic area ratio.

p = 0.83), respectively, and the average LV-GLS was −21.17% ± 3.80% and −18.70% ± 3.09% at the first and second time (paired t-test, p = 0.02), respectively. The LV-GLS value remained constant regardless of the number of weeks, while the RV-GLS value showed a decreasing trend with the number of weeks.

4. Discussion

In this study, we made two important clinical observations. First, our analysis at a high frame rate showed that the LV-GLS and LVEF did not markedly differ depending on the gestational age since the second trimester. Second, the RV-GLS decreased significantly with gestational age and was higher than that of the left ventricle.

Until 2010, there were many reports that the strain was constant after the second trimester [1–4]. However, Willruth et al. reported that

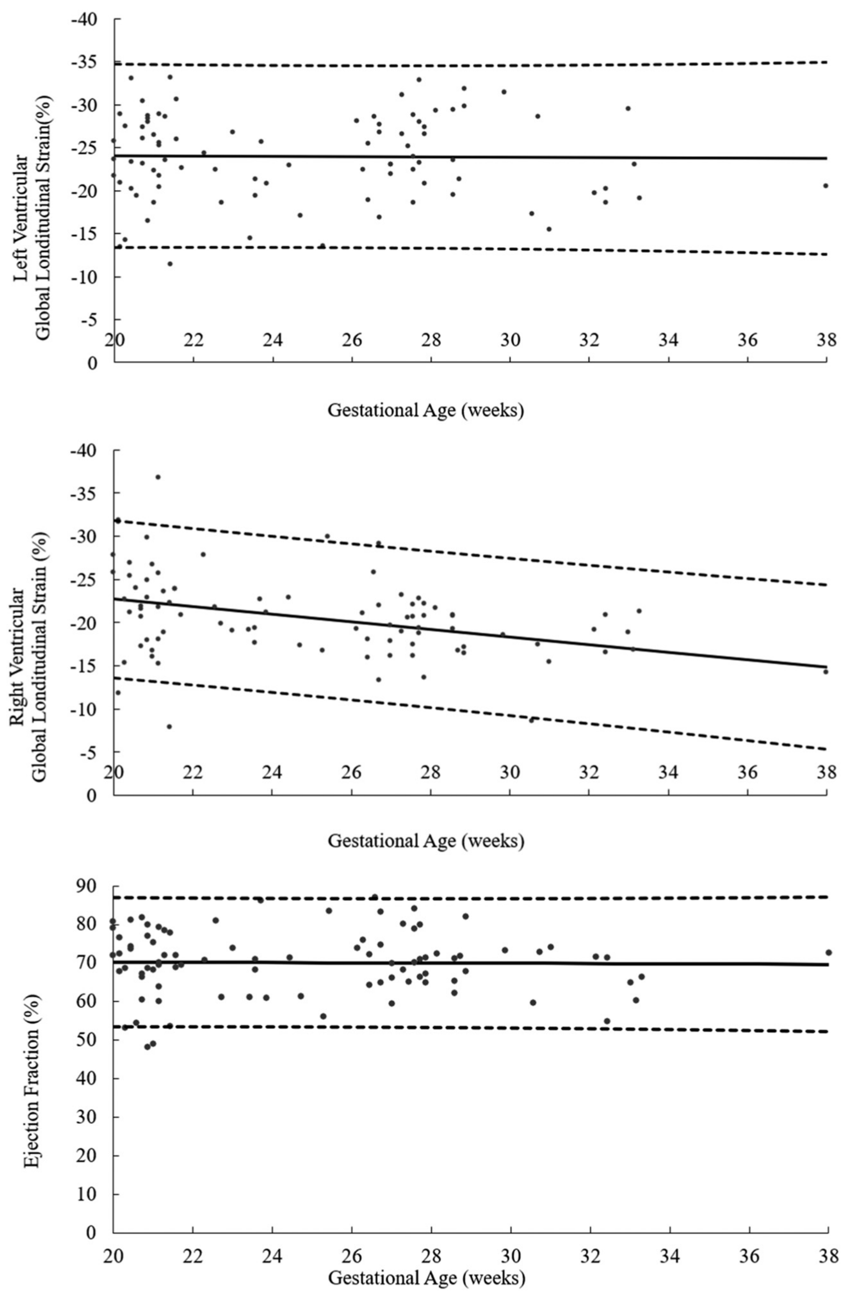

Fig. 3. Global left and right ventricle myocardial longitudinal systolic peak strain and left ventricular ejection fraction plotted against gestational age, showing the regression line and 90% confidence intervals: (1) left ventricular global longitudinal strain, (2) right ventricular global longitudinal strain, and (3) left ventricular ejection fraction.

the LV strain was constant, while the RV strain showed a decreasing trend after the second trimester [5]. In addition, Kapusa et al. studied 44 normal fetuses in the second trimester (20–24 weeks gestation) and third trimester (30–34 weeks gestation) [6]. In their study, from the second to the third trimester, the strain tended to decrease only in the right ventricle. The fetal heart mainly grows through myocyte hyperplasia rather than hypertrophy in early gestation [7], whereas in mid- and late gestation [8,9], and especially in the postnatal period, cardiac growth is mainly characterized by progressive myocardial hypertrophy. Therefore the cardiac muscle consists of an increased number of myocytes, whereas the number of cardiomyocytes per volume remains stable throughout pregnancy [7]. This results in increasing velocities during cardiac contraction but a relatively constant strain and strain rate [5,7].

In our study, the LV-GLS was found to be constant, regardless of the number of weeks since the second trimester. In contrast, the RV-GLS decreased significantly with gestational age. This observation could be explained by the increasing afterload throughout gestation related to the increase in systolic blood pressure caused by a progressive increase in placental impedance associated with placental maturational changes [10,11].

The LVEF was constant throughout gestation in our study. Few papers have measured the fetal LVEF. Uittenbogaard et al. reported that the mean LVEF and RVEF remained constant with increasing gestational age [12]. If the EF during the fetal period is indeed almost constant, then EF measurement using the 2D-speckle tracking method may be useful for evaluating the fetal heart function. On examining the difference in the strain between ventricles, the RV-GLS was found to be higher than the LV-GLS. Willruth et al. similarly reported that the right ventricle strain was higher than that of the left ventricle [5].

4.1. Study limitations

There have been many reports on STE so far, but there are still few reports using venders with high frame rates. At least 60–110 frames/s are recommended when imaging the adult heart [13], and even higher rates are desirable to provide enough frames per heart beat in a fetus [14]. The present report used a high frame rate in a relatively large population. In addition, the left and right ventricles have different anatomical structures and contraction directions. STE in the right ventricle was more difficult to measure correctly than that in the left ventricle due to the moderator band. It is also necessary to further examine whether or not these evaluations can be performed using only the longitudinal strain. Radial and circumferential parameters were not examined because of the difficulty of such examinations and the strong error between these models in the JUSTICE STUDY [15]. Furthermore, the six equidistant segments were not examined. While independent subjects were evaluated each week, changes in the same subject will need to be addressed due to the small number of cases. These issues will need to be addressed in the future. Studies on normal strain values in adults have been extensive [15], but the fetal strain values remain unclear. When the ultrasound machine and analysis software program are different, even for the same object, it is pointed out that the strain values are different. Future studies should consider the difference in the strain value due to differences between venders.

5. Conclusion

STE may be useful for quantifying the systolic myocardial function in a fetus. Further studies are needed to evaluate the performance using only the changes in the longitudinal strain. The evaluation of the fetal heart function in cases of cardiac heart disease is also an issue for further examination.

CRediT authorship contribution statement

Akiko Ohira: Conceptualization, Methodology, Formal analysis, Writing - original draft. **Kei Hayata:** Conceptualization, Methodology, Writing - review & editing. **Sakurako Mishima:** Investigation. **Kazumasa Tani:** Investigation. **Jota Maki:** Methodology, Investigation. **Takashi Mitsui:** Investigation. **Eriko Eto:** Investigation. **Hisashi Masuyama:** Methodology, Writing - review & editing, Supervision.

Declaration of competing interest

The authors declare that there are no conflicts of interest.

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