Quantitative evaluation of fetal ventricular function by speckle tracking echocardiography

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Conflict of interest: none

Authorship roles: All authors have made substantial contributions to following: (1) the conception and design of the study, acquisition of data, or analysis and interpretation of data; (2) drafting the article or revising it critically for important intellectual content; and (3) final approval of the version to be submitted.

Abstract

Methods

The study included 59 patients with normal fetal heart structure, blood flow, and heart rhythm (fetal abnormality-negative group) and 50 patients with abnormal fetal heart structure, blood flow, and/or heart rhythm (fetal abnormality-positive group). aCMQ was performed in both groups to obtain left and right ventricular endocardial global longitudinal strain (GLSendo), mid-myocardial global longitudinal strain (GLSmid), and epicardial global longitudinal strain (GLSepi). Parameters between the two groups were compared and correlation analyses performed. A deformation analysis was performed by two trained observers, and reproducibility was assessed.

Results

The fetal left ventricular and right ventricular global longitudinal strain (LV-GLS and RV-GLS, respectively) decreased in a gradient from the endocardium to the epicardium. LV-GLS and RV-GLS of all myocardial layers were lower in the fetal abnormality-positive than -negative group (all $P<0.05$). Correlation analysis showed that neither LV-GLS nor RV-GLS was significantly correlated with gestational age in the fetal abnormality-negative group (all $P>0.05$), whereas left ventricular GLSendo, GLSmid, and GLSepi were negatively correlated with gestational age in the fetal abnormality-positive group ($r=-0.39$ to -0.44, all $P<0.05$). Repeatability testing showed that the inter-observer and intra-observer intraclass correlation coefficients for LV-GLS and RV-GLS in each myocardial layer were >0.75 (all $P<0.001$).

Conclusions

As a new speckle tracking echocardiography tool, aCMQ has feasibility and repeatability in evaluating myocardial deformation of the fetal ventricle. This technique might provide helpful information on ventricular myocardial deformation in fetal hearts with abnormal structure or rhythm for clinical guidance in pregnancy.

Key words

Speckle tracking echocardiography; Automated Cardiac Motion Quantification; fetal; myocardium; strain

1. Introduction

The fetal heart is markedly different from the adult heart and has unique hemodynamic characteristics. The opening of the foramen ovale and ductus arteriosus during the fetal period results in a close relationship between the left and right cardiac systems in the fetus. Therefore, abnormalities in any fetal system may affect the cardiac function of the fetus. During the prenatal diagnosis period, conventional echocardiography focuses on the evaluation of fetal heart structural malformations. However, with the development of medicine, more attention is being paid to the evaluation of fetal heart function. Many studies have shown that the evaluation of fetal heart function has important clinical value in the management and prognosis of gestational hypertension, gestational diabetes, and fetal congenital heart disease[1].

Speckle tracking echocardiography (STE) technology can automatically track speckle motion and obtain myocardial deformation parameters such as longitudinal, radial, and circumferential strain and the rotation angle to evaluate myocardial function. Automated Cardiac Motion Quantification (aCMQ), a new STE tool, determines the cardiac cycle by identifying the opening and closing of the atrioventricular valve without the need for an electrocardiogram. In addition, aCMQ can quantitatively evaluate the deformation parameters of each layer of the myocardium by tracking the speckle motion of the endocardium, mid-myocardium, and epicardium. Thus, aCMQ

can theoretically evaluate the changes in myocardial deformation and function more accurately. The purpose of this study was to explore the clinical feasibility and value of aCMQ in evaluating fetal ventricular myocardial strain.

2. Material and Methods

2.1 Study population

This study involved 109 randomly selected women in the mid-second or third trimesters of pregnancy who underwent fetal echocardiography at West China Second University Hospital of Sichuan University from July 2020 to December 2020 (gestational age: mean ± standard deviation, 28.0±3.5 weeks; range, 21.6–36.6 weeks). All were singleton pregnancies. Of these women, 59 had normal fetal heart morphology, blood flow, and heart rhythm (fetal abnormality-negative group) and 50 had abnormal fetal heart structure, blood flow, and/or heart rhythm (fetal abnormality-positive group). The fetal abnormality-positive group comprised 10 cases of pulmonary stenosis and tricuspid regurgitation; 1 case of pulmonary stenosis and pulmonary regurgitation; 1 case of pulmonary stenosis and aortic stenosis; 8 cases of ventricular septal defect; 2 cases of ventricular septal defect and aortic stenosis; 3 cases of tetralogy of Fallot; 3 cases of atrioventricular septal defect; 1 case of double-outlet right ventricle, pulmonary stenosis, and absence of ductus arteriosus; 2 cases of interrupted aortic arch and ventricular septal defect; 1 case of bicuspid aortic valve and aortic stenosis; 4 cases of coarctation of the aorta; 2 cases of coarctation of the aorta and ventricular septal defect; 1 case of aortic hypoplasia and atrial septal aneurysm; 3 cases of atrioventricular block; 1 case of premature beats and tricuspid regurgitation; 2 cases of increased cardiothoracic ratio and atrioventricular valve regurgitation; and 5 cases of moderate and severe tricuspid regurgitation. The inclusion criteria were pregnant women with no history of hypertension, diabetes, or congenital heart disease as well as a gestational age consistent with the ultrasound-determined gestational age. Women in whom the four-chamber cardiac view of the fetus could not be clearly obtained because of maternal abdominal wall fat thickness and/or

placental factors were excluded. This study was approved by the ethics committee of West China Second University Hospital of Sichuan University.

2.2 Study protocol

Imaging was performed with a Philips EPIQ 7C color Doppler ultrasound diagnostic apparatus equipped with C5-1 probe, machine configuration aCMQ software, and image post-processing workstation QLAB 10.8. The dynamic images of the fetal four-chamber view at frame rates of >80/s were collected and stored when no obvious fetal movement was observed. To achieve a high frame rate, the field of view was optimized by reductions in the sector width and depth and appropriate use of zoom.

The stored dynamic images were imported into the QLAB 10.8 image post-processing workstation for analysis. The cardiac cycle was determined by identifying the opening and closing activity of the atrioventricular valve with the naked eye. The start frame (start) was defined as the frame before the mitral valve closure in the four-chamber section, and the end frame (end) was set as the frame immediately before the next mitral valve closure. The trace region of interest was selected and the software set to automatically track and obtain the longitudinal strain curve of each layer of myocardium.

The left and right ventricular endocardial global longitudinal strain (GLSendo), mid-myocardial global longitudinal strain (GLSmid), and epicardial global longitudinal strain (GLSepi) were recorded. The average values of two consecutive cardiac cycles were analyzed.

To verify the inter-observer measurement variability, 10 patients were randomly selected and the fetal ventricular strain parameters were obtained by two separate observers according to the above analysis method. To obtain the intra-observer variability, the above data were re-analyzed and compared after 2 weeks.

2.3 Statistical analysis

SPSS 19.0 (IBM Corp., Armonk, NY, USA) was used for statistical analysis, and all measurement data were tested for homogeneity of variance and normality. Normally distributed

quantitative data are presented as mean ± standard deviation. Analysis of variance was used for multi-group comparisons, and the independent-samples t-test was used for inter-group comparisons. Pearson correlation analysis was used for simple linear correlation between variables. Non-normally distributed quantitative data are presented as median. The Kruskal–Wallis test was used for multi-group comparisons, the Wilcoxon test was used for inter-group comparisons, and rank correlation curves were used to analyze the correlation between variables. The inter- and intra-observer repeatability test results are expressed as intraclass correlation coefficients (ICCs); an ICC of >0.75 indicates good repeatability of the data. A *P* value of <0.05 was considered statistically significant.

3. Results

3.1 Changes in myocardial deformation parameters in each layer of left and right ventricles

The left ventricular global longitudinal strain (LV-GLS) of 109 fetal hearts showed a gradient decrease from the endocardium to the epicardium. The right ventricular global longitudinal strain (RV-GLS) also showed a gradient decrease from the endocardium to epicardium (Table 1).

3.2 Comparison of myocardial deformation parameters in fetal abnormality-positive and -negative groups

The LV-GLS of all myocardial layers was lower in the fetal abnormality-positive than -negative group (all $P<0.05$) (Table 2, Figure 1). Similarly, the RV-GLS of all myocardial layers was also lower in the fetal abnormality-positive than -negative group (all $P<0.05$) (Table 3, Figure 2).

3.3 Correlation analysis

The LV-GLS of each myocardial layer in the fetal abnormality-negative group was not significantly correlated with the age of the pregnant woman or the gestational age ((|r|=0.01–0.18, all $P>0.05$). The LV-GLS of each myocardial layer in the fetal abnormality-positive group was not

significantly correlated with the age of the pregnant woman (|r|=0.02–0.05, all P>0.05). However, in contrast to the fetal abnormality-negative group, the left ventricular GLSendo, GLSmid, and GLSepi were significantly negatively correlated with the gestational age in the fetal abnormality-positive group (r=−0.39 to −0.44, all P<0.05) (Figure 3).

No correlation was observed between the RV-GLS and the age of the pregnant woman or the gestational age in any myocardial layer in either the fetal abnormality-positive or -negative group (all P>0.05).

3.4 Repeatability test

The inter-observer and intra-observer ICCs for LV-GLS and RV-GLS in each myocardial layer were all >0.75 (all P<0.001) (Table 4), indicating that the data had good repeatability and reliability.

4. Discussion

The ventricle has a unique and complex myocardial fiber structure that determines its mechanical movement. Compared with conventional echocardiography, STE technology can more sensitively evaluate the changes in cardiac function in adults and children by acquiring myocardial deformation parameters[2,3]. With the development of ultrasound imaging technology, focus has moved to the analysis of fetal myocardial mechanics and proving that the assessment of fetal myocardial strain is feasible and repeatable[4-6].

The global longitudinal strain parameters of the fetal heart obtained from the fetal four-chamber view are reportedly the most reliable deformation parameters that reflect fetal heart function[7]. Therefore, in this study, the four-chamber view of the fetus was selected for aCMQ to obtain longitudinal strain-related parameters and explore their clinical value. We showed that randomly selected fetal heart images with the clear four-chamber heart view can be successfully analyzed using aCMQ technology.

In this study, the aCMQ tool of QLAB10.8 software automatically tracked and obtained strain curves for the endocardium, mid-myocardium, and epicardium. LV-GLS values of the fetal

heart showed a gradient decrease from endocardium to epicardium. This is likely because of the arrangement of myocardial fibers and heterogeneity of the myocardium resulting in the deformation amplitude of the endocardium being significantly higher than that of the epicardium. In recent years, studies have shown the feasibility of using STE to analyze the myocardial deformation of different layers of the left ventricle in adults[8-9], and the results have been consistent with respect to the transmural heterogeneity of myocardial deformation. However, these previous studies focused on adults; there are no reports on layer-specific strain analysis of the fetal heart. In this study, we show for the first time that the left ventricular myocardial deformation of fetal heart has transmural heterogeneity using aCMQ.

In addition, the longitudinal strain parameters of the fetal right ventricle were analyzed by aCMQ. RV-GLS values of the fetal heart also showed a gradient decrease from the endocardium to epicardium. This is consistent with strain analysis of the right ventricle by Erley et al.[10], who also showed that the deformation amplitude of the right ventricular endocardium is larger than the deformation in the epicardium in adults. However, there is currently no layer-specific strain analysis of the fetal right ventricle, and more studies are needed to explore and confirm its clinical value.

Our study showed that the myocardial strain values of all layers of the left and right ventricles were significantly lower in the fetal abnormality-positive than -negative group. The fetal abnormality-positive group included abnormalities of cardiac morphology, blood flow, and/or heart rhythm, among which fetal congenital heart disease and arrhythmia were most commonly seen. Abnormalities in morphology, structure, and/or blood flow will affect the normal fetal circulatory shunt system, leading to changes in cardiac preload and/or afterload. Abnormal load conditions can cause damage to the function of myocardial cells and lead to a decrease in myocardial deformation and thus function[11,12]. In recent years, several studies have shown that the ventricular global longitudinal strain of the fetus decreases when the fetus has congenital heart disease[11,13], which is consistent with our results. In addition, previous reports using vector velocity imaging technology to analyze the structural and mechanical changes of myocardial structure in fetuses with arrhythmia have shown that the shortening of fetal diastole can lead to

myocardial ischemia and functional impairment, and the strain and strain rate can be used to evaluate the early impairment of cardiac function in fetuses with arrhythmia[14]. Therefore, the analysis of myocardial deformation by STE and aCMQ can be used to assess the early impaired ventricular function in the event of fetal cardiac structure or rhythm abnormalities. It should be noted that because of the limited sample size in this study, there was no detailed grouping in the fetal abnormality-positive group, and further studies with increased sample sizes are needed to fully assess this. In addition, there are differences in the design and use of equipment among available reports on fetal myocardial mechanics, and a large-scale cohort study is needed to confirm the potential clinical value of fetal myocardial mechanics analysis and standardize its clinical application.

Finally, the correlation analysis showed that the LV-GLS and RV-GLS of all myocardial layers in the fetal abnormality-negative group had no significant correlation with the age of the pregnant woman or the gestational age. This is consistent with previous studies showing that the LV-GLS and RV-GLS of normal fetuses during pregnancy are constant[4,15-17]. According to a fetal myocardial development hypothesis[18], the growth of the heart is the result of cardiomyocyte hypertrophy, and the number of cardiomyocytes per unit volume of the ventricle is constant. Because longitudinal strain is the relative change in the length of the myocardial segment relative to its original length, it is likely to remain stable from the moment a stable number of cardiomyocytes is obtained. Conversely, in the present study, the LV-GLS of each layer in the fetal abnormality-positive group decreased as gestational age increased. The presence of cardiac morphology and/or rhythm abnormalities in the fetus will lead to disturbances in cardiac hemodynamics. Over time, the persistent abnormal hemodynamic changes will continue to affect the fetal ventricular preload and afterload, which may lead to corresponding changes in myocardial deformation. However, there was no significant correlation between the RV-GLS and gestational age in the fetal abnormality-positive group in this study, and a sampling error caused by the small sample size cannot be ruled out. Additionally, the number of cases in the fetal abnormality-positive group was limited; therefore, we cannot guarantee absolute consistency between the research findings and the real-world situation.

In summary, as a new STE technique, aCMQ has feasibility and repeatability in assessing the myocardial deformation of the fetal ventricle. Quantitative evaluation of the changes in ventricular myocardial deformation of abnormal fetal heart structure and/or heart rhythm may provide further information for clinical guidance in pregnancy. However, large-scale cohort studies are still needed to further confirm the potential clinical value of fetal myocardial mechanics analysis and standardize its clinical application.

Acknowledgments

This study was supported by the National Key R&D Program of China (2017YFC0211705), the Key R&D Program of Science and Technology Department of Sichuan Province (2019YFS0403, 2019YFS0037), and the Popularization and Application Project of the Sichuan Health and Family Planning Commission (17PJ41). The authors are very grateful to the patients who contributed the images in this article. We also thank Hanne Gadeberg, PhD and Angela Morben, DVM, from Liwen Bianji, Edanz Editing China (www.liwenbianji.cn/ac), for editing the English text of a draft of this manuscript.

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Table 1. Comparison of related deformation parameters of myocardium in each layer of left ventricle and right ventricle

Varible	N	LV-GLS	RV-GLS
GLSendo(%)	109	-19.9±1.5	-18.9±1.5
GLSmid(%)	109	-18.5±1.4	-17.0±1.4
GLSepi (%)	109	-17.0±1.2	-15.4±1.3
F		63.4	91.1
P		<0.001	<0.001

Table 2. Comparison of related deformation parameters of left ventricular myocardium in fetal abnormality-positive and -negative groups

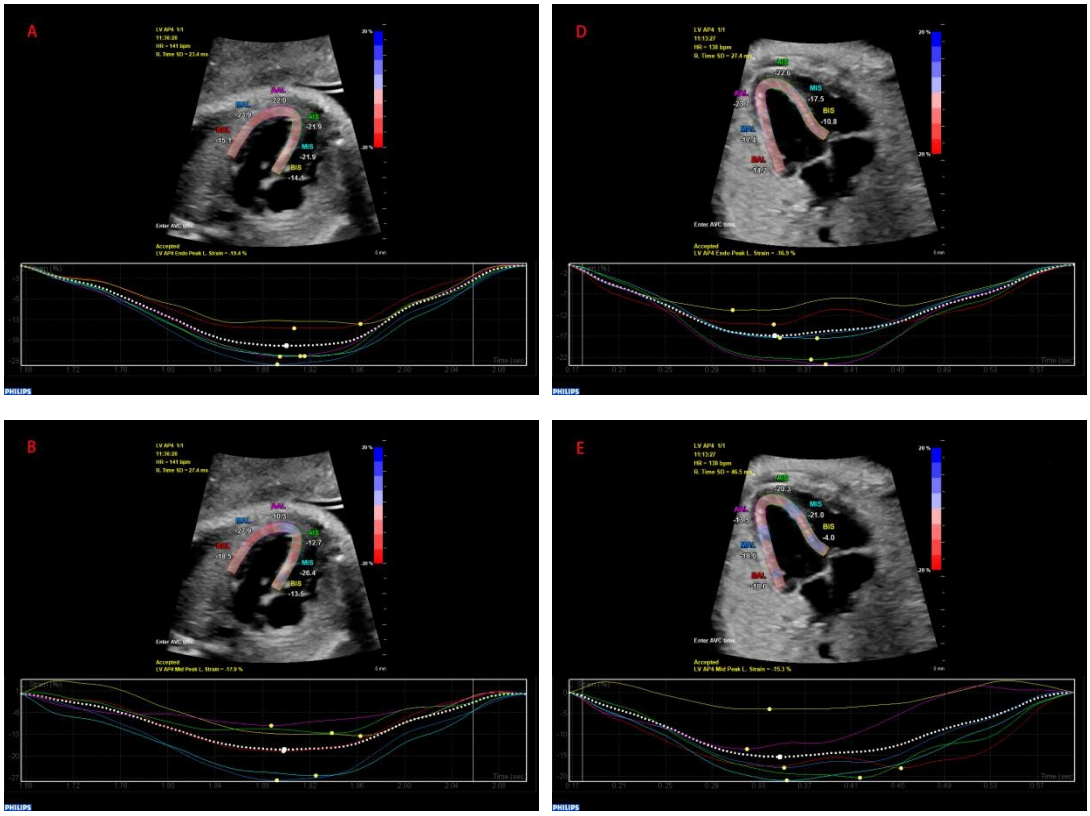
Varible	positive group(50)	negative group(59)	*t*	*P*
LV-GLSendo(%)	-17.1±2.3	-19.8±1.5	7.2	<0.001
LV-GLSmid(%)	-16.1±2.3	-18.5±1.4	6.7	<0.001
LV-GLSepi (%)	-14.7±2.3	-17.0±1.2	6.4	<0.001

Table 3. Comparison of related deformation parameters of right ventricular myocardium in fetal abnormality-positive and -negative groups

Varible	positive group(50)	negative group(59)	*t*	*P*
RV-GLSendo(%)	-15.5±3.2	-18.9±1.5	6.8	<0.001
RV-GLSmid(%)	-14.8±3.0	-17.0±1.4	7.0	<0.001
RV-GLSepi (%)	-12.3±2.8	-15.4±1.3	7.2	<0.001

Table 4. Repeatability test of related deformation parameters of myocardium in each layer of ventricle

parameters	ICC of intra-observer	ICC of inter-observer	*P*
LV-GLSendo(%)	0.94	0.91	<0.001
LV-GLSmid(%)	0.98	0.93	<0.001
LV-GLSepi(%)	0.97	0.86	<0.001
RV-GLSendo(%)	0.90	0.83	<0.001
RV-GLSmid(%)	0.92	0.89	<0.001
RV-GLSepi(%)	0.79	0.76	<0.001



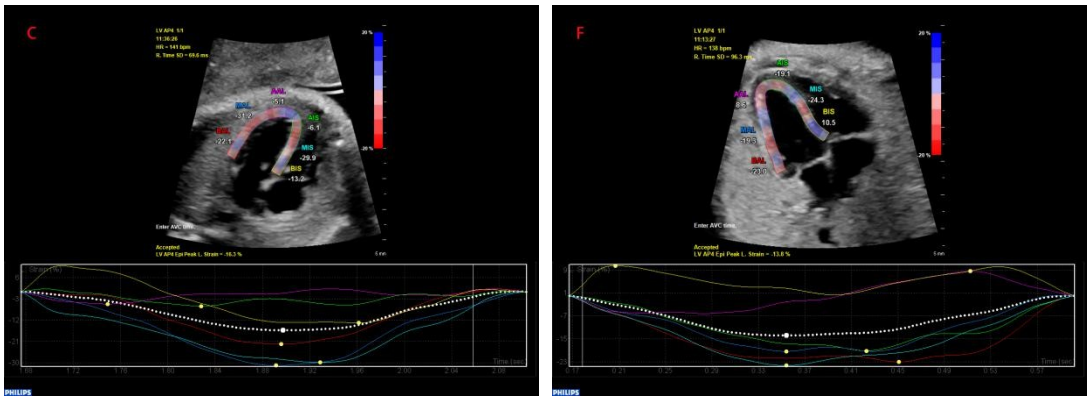
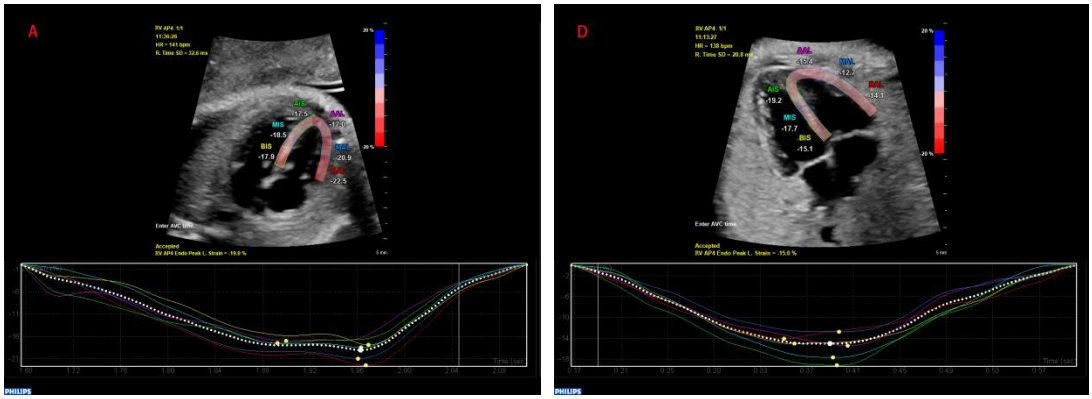


Figure 1. (A–C) LV-GLS values from endocardial myocardium to epicardial myocardium in the fetal abnormality-negative group in turn. (D–F) LV-GLS values from endocardial myocardium to epicardial myocardium in the fetal abnormality-positive group in turn.



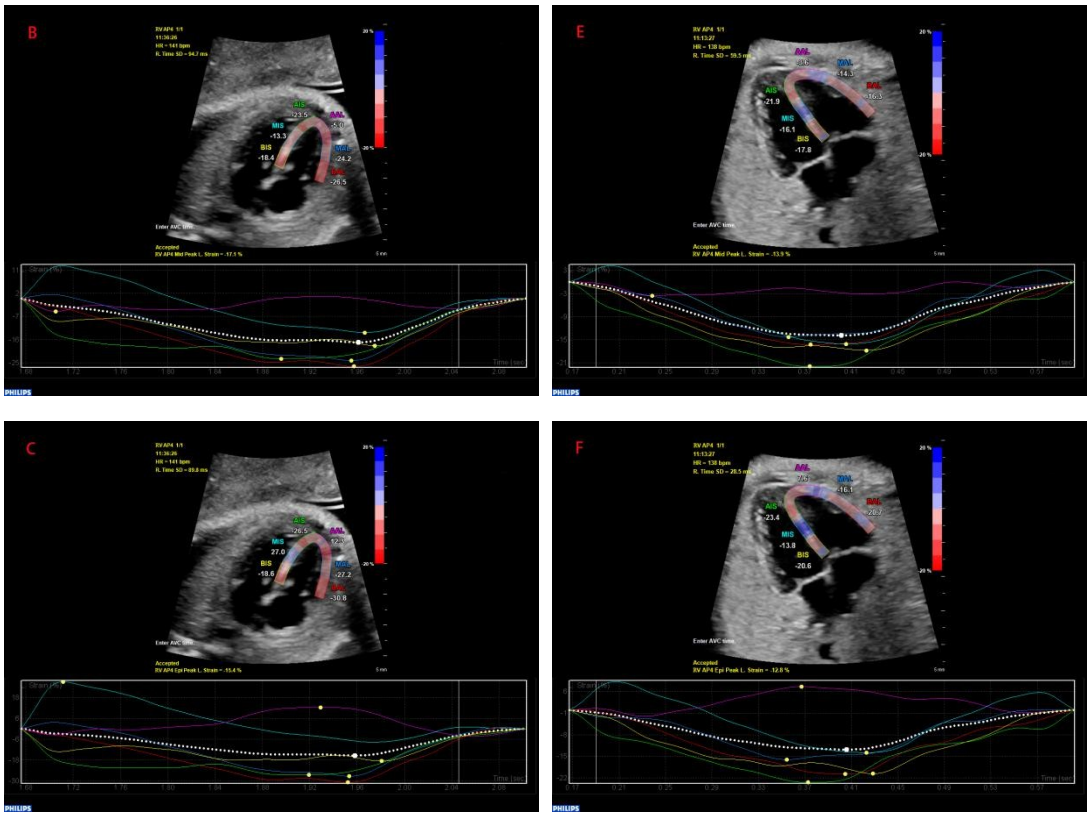


Figure 2. (A–C) RV-GLS values from endocardial myocardium to epicardial myocardium in the fetal abnormality-negative group in turn (D–F) RV-GLS values from endocardial myocardium to epicardial myocardium in the fetal abnormality-positive group in turn.

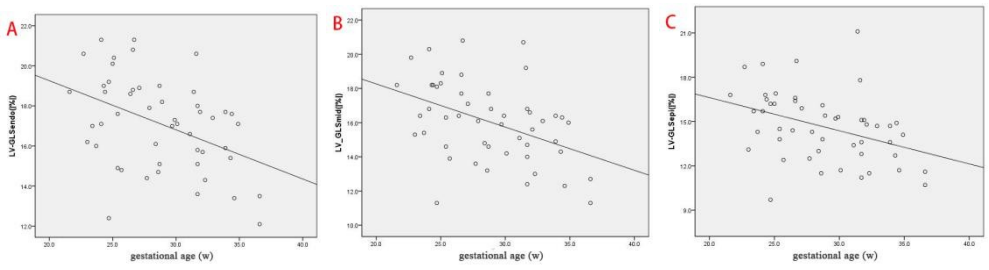


Figure 3. (A–C) Correlation between the LV-GLS values of each myocardial layer in the fetal abnormality-positive group and the gestational age in turn.