Original Article

Evaluation of fetal cardiac morphology and function by fetal heart quantification technique in the normal second and third trimesters

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Background: The study of fetal heart is receiving increasing attention. Fetal heart quantification (Fetal HQ) technology is a new speckle tracking technology that can analyze the 24-segment morphology and function of fetal ventricles. This study aims to use Fetal HQ to assess the changes in the structure and function of the fetal heart in normal mid to late pregnancy, providing a foundation for the clinical application of fetal cardiac speckle tracking technology.

Methods: The heart size, global sphericity index (GSI), left ventricular [stroke volume (SV)], cardiac output (CO), ejection fraction (EF), global longitudinal strain (GLS), fractional area change (FAC), 24-segment end-diastolic diameter (EDD), sphericity index (SI) and fractional shortening (FS) of the two ventricles of 500 normal pregnant fetuses were evaluated by Fetal HQ. The subjects were divided into 5 groups according to gestational weeks (GA), and the changes of fetal heart morphology and function were observed. $P<0.05$ indicated the statistically significant difference.

Results: The fetal heart rate decreased gradually with the increase of GA ($P<0.05$). The size parameters of the fetal heart and two ventricles gradually increased with increasing GA ($P<0.05$). The 24 segments EDD of both ventricles increased with increasing GA ($P<0.05$), while the EDD increased first and then decreased from the ventricle base to the apex. The GSI and the 24 segments SI of two ventricles were basically not significantly different among the groups ($P>0.05$). The EF, GLS, FAC of the left ventricle and the GLS, FAC of the right ventricle decreased with the increase of GA ($P<0.05$), and SV and CO increased with increasing GA ($P<0.05$). The 24 segments FS of the left ventricle showed a downward trend with the increase of GA and gradually increased from the base to the apex. The FS of most segments of the right ventricle decreased with the increase of the GA and increased first and then decreased from the base to the apex.

Conclusions: The whole and segmental size parameters of fetal heart can quantitatively evaluate the growth and development of fetal heart; the GSI and segmental SI are reliable morphological indexes for evaluating fetal heart; fetal ventricular function parameters EF, FAC, GLS and segmental FS can evaluate fetal cardiac function. The Fetal HQ technique can help us to evaluate the heart growth and development of normal fetuses in the second and third trimester of pregnancy.

Keywords: Fetal heart quantification technology; 24 segments; antenatal examination

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Introduction

Background

Prenatal fetal monitoring is crucial within perinatal medicine, with ultrasound imaging serving as a cornerstone in assessing fetal well-being. Particularly, the advancement in ultrasound technology has revolutionized prenatal fetal heart examination, significantly enhancing its accuracy and clinical utility (1). In recent years, there has been a growing emphasis on evaluating fetal cardiac function during prenatal ultrasound examinations (2). Research has demonstrated that fetal cardiac function serves as a pivotal clinical marker in assessing various fetal conditions, including congenital heart disease, intrauterine growth restriction, and twin-to-twin transfusion syndrome (3-5).

One of the innovative technologies in this field is two-dimensional speckle tracking imaging (2D-STI), which originated in 2004 for assessing adult cardiac function (6). Fetal heart quantification (Fetal HQ) technology represents a more recent development, introduced by Professor Devore. This technique utilizes a 24-segment speckle tracking method, offering simplicity in operation, minimal time requirement, and excellent repeatability (7,8). Previous research has utilized Fetal HQ to investigate fetal heart function abnormalities associated with conditions such as severe tricuspid regurgitation and maternal gestational diabetes (9,10).

Rationale and knowledge gap

Fetal HQ has pioneered a more detailed segmentation of the fetal left and right ventricles, dividing them into 24 segments from the base to the apex. This segmentation allows for the extraction of morphological and functional parameters of the fetal heart as a whole and of each individual segment. Since the introduction of Fetal HQ, a surge of related studies has emerged both domestically and internationally. The efficacy of Fetal HQ in assessing cardiac morphology and function has been evaluated in conditions such as gestational diabetes, fetal growth restriction, and congenital ventricular aneurysm, yielding positive results (11-13).

In recent years, the European Association of Cardiovascular Imaging (EACVI) and the American Society of Echocardiography (ASE) have incorporated the assessment of global longitudinal strain (GLS), based on 2D-STI, into their guidelines and consensus documents as a recommended parameter for cardiac evaluation. GLS is considered one of the most promising indicators for assessing cardiac function, following ejection fraction (EF) (14,15).

As the fetal heart undergoes continuous growth and development, there is still much to understand about this physiological process. The morphology and function of the fetal heart may evolve differently at each stage of pregnancy. Currently, there remains a lack of consensus on the application of 2D-STI for fetal cardiac evaluation, both domestically and internationally.

Objective

This study aims to utilize Fetal HQ to conduct cardiac speckle tracking analysis on a large sample of mid- and late-gestation fetuses. The goal is to assess changes in fetal cardiac morphological and functional parameters with gestational age (GA), providing a research foundation and reference range for the clinical implementation of fetal speckle tracking technology. We present this article in accordance

Highlight box

Key findings
- The Fetal heart quantification (Fetal HQ) technique can evaluate the heart growth and development of normal fetuses in the second and third trimester of pregnancy.

What is known and what is new?
- The fetal heart grows and develops with increasing gestational weeks and has different changes in its form and function.
- The global sphericity index (GSI) and segmental sphericity index (SI) are reliable morphological indexes for evaluating fetal heart; the parameters ejection fraction (EF), fractional area change (FAC), global longitudinal strain (GLS) and segmental fractional shortening (FS) can evaluate fetal cardiac function.

What is the implication, and what should change now?
- Ultrasound can evaluate the subtle changes of fetal heart structure and function, and is an important research direction in the field of prenatal diagnosis in the future.

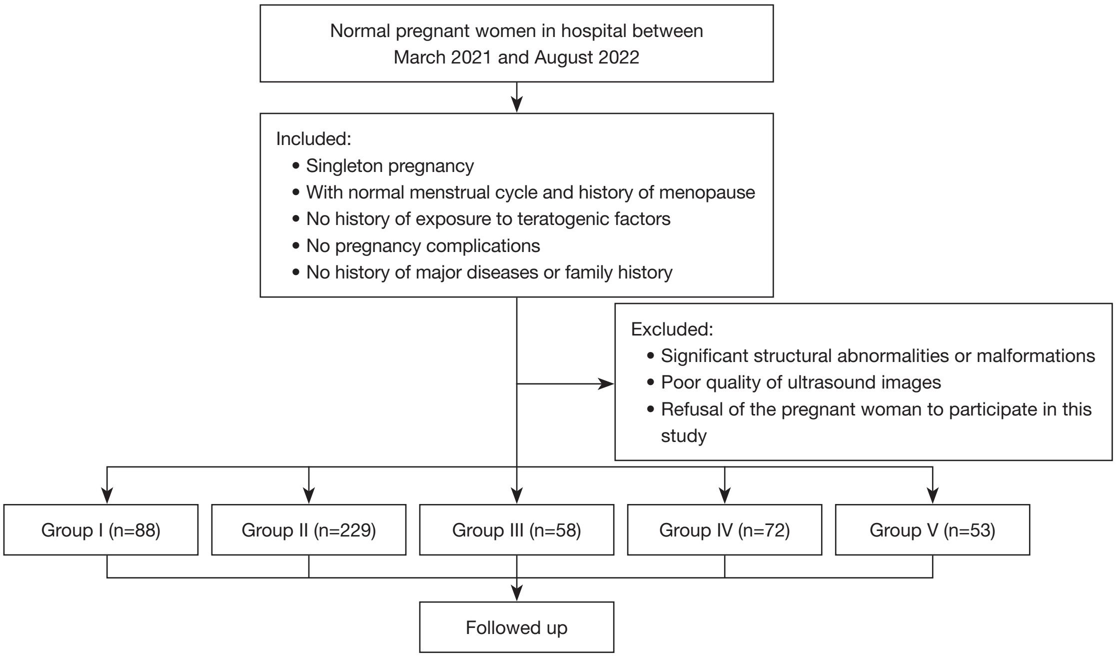

Figure 1 Flowchart of the study process. The study subjects were divided into five groups with gestational weeks: $20–23^{+6}$ weeks (Group I), $24–27^{+6}$ weeks (Group II), $28–31^{+6}$ weeks (Group III), $32–36^{+6}$ weeks (Group IV), $37–40^{+6}$ week (Group V).

with the STROBE reporting checklist (available at https://tp.amegroups.com/article/view/10.21037/tp-24-123/rc).

Methods

General information

In this cross-sectional study, normal pregnant women who underwent prenatal examinations at the First Affiliated Hospital of Soochow University from March 2021 to August 2022 were randomly selected as the research subjects. General information and fetal echocardiography were obtained, and quantitative analysis of the fetal hearts was conducted. This study was approved by the Ethics Committee of the First Affiliated Hospital of Soochow University (No. [2022]241), and all pregnant women signed an informed consent form for voluntary participation in this study. There was no obvious selection bias in the data. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Inclusion criteria and exclusion criteria

Inclusion criteria: (I) singleton pregnancy; (II) pregnant women with normal menstrual cycle and history of menopause; (III) no history of exposure to teratogenic factors in early pregnancy; (IV) no pregnancy complications such as gestational hypertension; (V) no history of major diseases or family history in the pregnant women themselves. Exclusion criteria: (I) multiple pregnancies; (II) significant structural abnormalities or malformations of the fetus found during the obstetric examination; (III) poor quality of ultrasound images due to excessive fat in the abdominal wall of the pregnant woman; (IV) refusal of the pregnant woman to participate in this study.

Grouping

A total of 500 pregnant women with normal pregnancy were included. In order to analyze the specific situation of fetal heart growth and development at different gestational weeks, we divided the study subjects into five groups with gestational weeks: $20–23^{+6}$ weeks (Group I), $24–27^{+6}$ weeks (Group II), $28-31^{+6}$ weeks (Group III), $32–36^{+6}$ weeks (Group IV), $37–40^{+6}$ week (Group V), and each group contains 88, 229, 58, 72 and 53 study subjects respectively. The week of gestation was calculated according to the last menstrual period or the crown-rump length measured by ultrasound during early pregnancy (*Figure 1*).

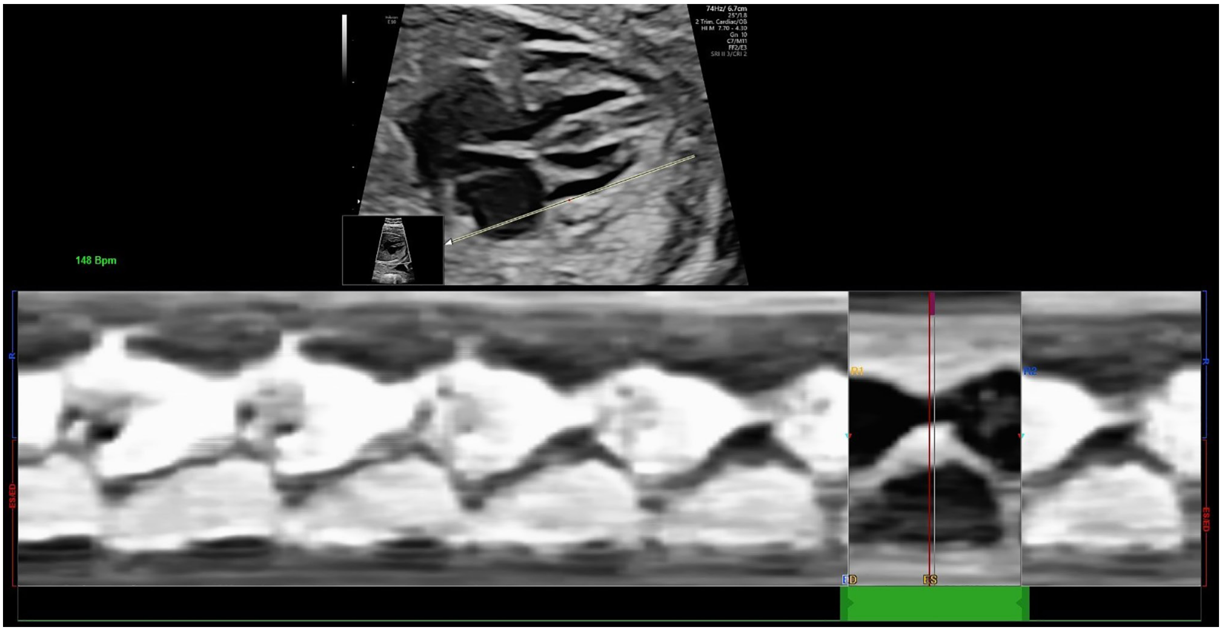

Figure 2 Select the cardiac cycle. Draw a sampling line on the two-dimensional image, combined with two-dimensional and M-mode ultrasound to select the appropriate cardiac cycle.

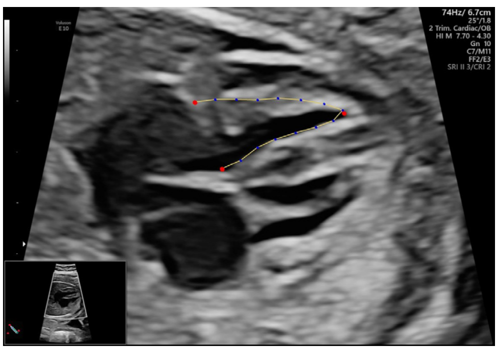

Figure 3 The speckle tracking process. The software semi-automatically tracks endocardial motion through three localization points: the mitral septal attachment point, the lateral mitral wall attachment point, and the apex.

Clinical data collection

General clinical data such as maternal age and gestational week (GA) were recorded. In this study, A GE Voluson E10 color Doppler ultrasound system was used, equipped with C1-6-D//RM6C transducers and the Fetal HQ software package. Fetal growth and developmental parameters such as biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC), femur length (FL) were measured. Dynamic videos of standard four-chamber view of the fetal heart were retained for quantitative assessment using the Fetal HQ to obtain morphological and functional parameters (*Figures 2-4*). All image acquisition was performed by senior ultrasound physicians with extensive experience. The analysis of Fetal HQ includes measurements of end-diastolic heart size and morphology, as well as speckle tracking analysis of 24 segments of the two ventricles. The former measurements were averaged over three times, while the latter were measured once. Twenty cases were randomly selected and tracing analyses were independently conducted by the author and another senior ultrasound physician. After one month, the author analyzed the selected cases again. The reproducibility of these analyses was then examined.

Statistical analysis

Using the statistical analysis software SPSS 26.0, continuous data were expressed as $\bar{x}\pm s$. For multiple group comparisons that met the assumptions of normal distribution and homogeneity of variance, one-way analysis of variance (ANOVA) was used. If the assumptions were not met, the Kruskal-Wallis test was employed. Further pairwise comparisons were conducted using the Bonferroni method. Each parameter was subjected to univariate linear regression analysis with GA, and differences were

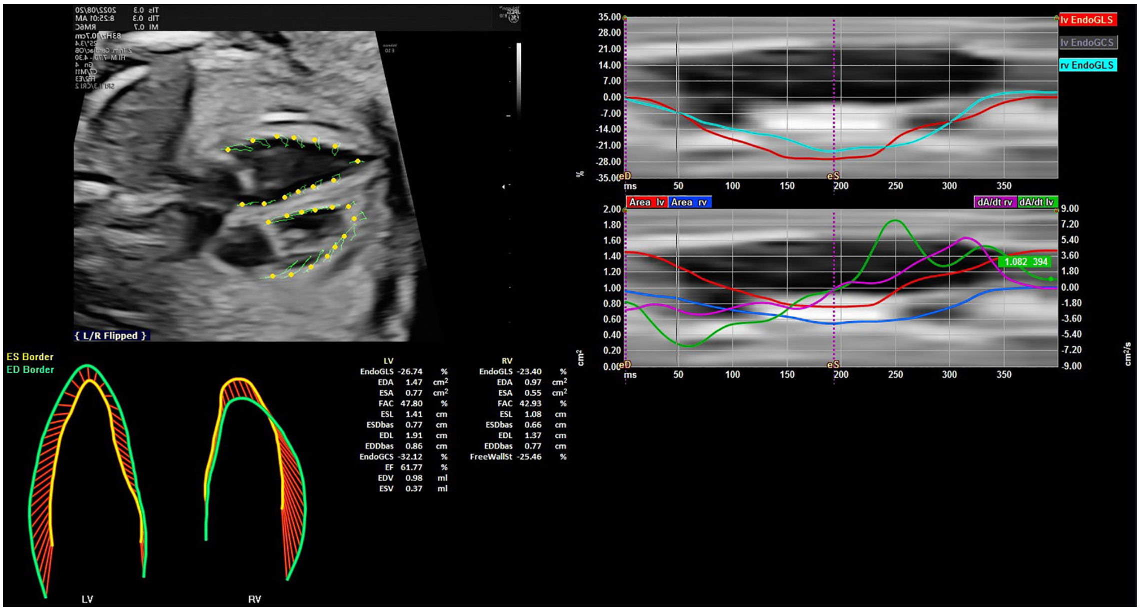

Figure 4 The results interface of speckle tracking. The motion trajectories and measurement parameters of the left and right ventricles can be seen. LV, left ventricle; RV, right ventricle; EndoGLS, endocardial global longitudinal strain; EDA, end-diastolic area; ESA, end-systolic area; FAC, fractional area change; ESL, end-systolic length; ESDbas, end-systolic displacement of basal; EDL, end-diastolic length; EDDbas, end diastolic diameter-basal; EF, ejection fraction; EDV, end-diastolic volume; ESV, end-systolic volume.

considered statistically significant when P<0.05. The inter-rater and intra-rater reliability tests were assessed using the intraclass correlation coefficient (ICC), with ICC values below 0.4 indicating poor reproducibility and values above 0.75 indicating good reproducibility.

Results

General information of the study population

Five hundred normal pregnant women, aged 18 to 41 years, with a mean of 29.6±3.7 years, with gestational weeks of 22^{+3} to 40^{+5} weeks, were included in this study. No statistically significant differences were found between the age, gestation and delivery of the pregnant women in each group (P>0.05), and the fetal heart rate (FHR) gradually decreased with increasing gestational weeks in each group (P<0.05), as shown in *Table 1*.

Comparison of fetal heart-related parameters

Comparison of overall fetal heart size and morphological parameters

The long diameter, wide diameter and area of the fetal heart at the end of diastole gradually increased with increasing gestational weeks, and the difference was statistically significant (P<0.05). However, there were no significant differences in the results between 32 to 36^{+6} weeks and 28 to 31^{+6} weeks, and between 37 to 40^{+6} weeks and 32 to 36^{+6} weeks. There was no significant difference in the morphological parameters of the fetal heart global sphericity index (GSI) between the two groups (P>0.05), as shown in *Table 2*.

Comparison of the overall size and morphological parameters of the fetal both ventricles

The area and length diameter of the left and right ventricles at end-diastole increased with increasing gestational weeks (P<0.05), consistent with the overall cardiac size and morphological parameters, as shown in *Table 3*.

Comparison of overall fetal both ventricular functional parameters

Left ventricular EF, GLS, fractional area change (FAC) and right ventricular GLS, FAC tended to decrease with increasing gestational weeks (P<0.05), and stroke volume (SV) and cardiac output (CO) increased with increasing gestational weeks (P<0.05), as shown in *Table 4*.

Table 1 General clinical information

Characteristic	20–23^{+6} weeks	24–27^{+6} weeks	28–31^{+6} weeks	32–36^{+6} weeks	37–40^{+6} weeks	P
Age (years)	30.13±4.15	29.40±3.57	29.68±3.13	29.80±3.46	28.80±3.88	0.29
Gravidity	1.61±0.84	1.66±0.84	2.33±0.94	1.85±1.10	1.91±1.13	0.55
Parity	0.25±0.51	0.38±0.54	0.33±0.51	0.40±0.57	0.23±0.54	0.09
Fatal heart rate	148.50±8.14	147.92±7.45	145.67±8.71	143.71±8.27	140.11±9.43	<0.01

Values are presented as mean ± standard deviation. Age represents the age of the pregnant woman, and Gravidity and Parity represent the number of pregnancies and deliveries, respectively; they did not differ between groups. Fetal heart rate was expressed in beats per minute.

Table 2 Comparison of overall heart size and morphologic parameters between groups

Parameter	20–23^{+6} weeks	24–27^{+6} weeks	28–31^{+6} weeks	32–36^{+6} weeks	37–40^{+6} weeks	P
Length ED (mm)	28.97±2.02	30.36±2.37	38.05±3.54	44.21±3.68	48.44±3.14	<0.01[a]
Width ED (mm)	25.13±1.66	26.49±1.99	33.75±2.80	39.23±3.20	42.83±2.76	<0.01[a]
Area ED (mm^2)	573.50±71.17	634.32±92.19	1,014.74±172.06	1,369.39±210.96	1,634.39±191.66	<0.01[a]
GSI	1.15±0.06	1.15±0.07	1.13±0.06	1.13±0.06	1.13±0.06	0.02[b]

Values are presented as mean ± standard deviation. [a], indicates two comparisons between groups III-IV and IV-V, P>0.05; [b], indicates no difference between the results of both comparisons. ED, end diastolic; Length, long cardiac diameter; Width, wide cardiac diameter; Area, heart area; GSI, global spherical index.

Table 3 Comparison of morphologic parameters of overall ventricular size

Parameter	20–23^{+6} weeks	24–27^{+6} weeks	28–31^{+6} weeks	32–36^{+6} weeks	37–40^{+6} weeks	P
LV ED area (mm^2)	1.15±0.19	1.27±0.24	1.93±0.38	2.66±0.60	2.93±0.58	<0.01[a]
LV ED length (mm)	1.78±0.18	1.84±0.22	2.24±0.30	2.67±0.38	2.76±0.32	<0.01[a]
RV ED area (mm^2)	0.91±0.17	1.02±0.23	1.73±0.39	2.36±0.55	2.81±0.56	<0.01[a]
RV ED length (mm)	1.42±0.14	1.48±0.19	1.86±0.22	2.17±0.29	2.38±0.29	<0.01[a]

Values are presented as mean ± standard deviation. [a], indicates two-way comparison, P<0.05. LV, left ventricle; RV, right ventricle; ED, end diastolic; Length, long diameter; Area, heart area.

Comparison of fetal both ventricular segmental size parameters

The end-diastolic diameter (EDD) of both left and right ventricular segments at 24 segments increased with increasing gestational weeks (P<0.05). The EDD of both left and right ventricles increased and then decreased from segment 1 to segment 24, with the maximum value of the left ventricle at segment 5/6 and the maximum value of the right ventricle at segment 6/7, as shown in *Figures 5,6*.

Comparison of morphological parameters of the fetal left and right ventricular segments

There was almost no statistical difference (P>0.05) when comparing the 24-segment SI of the left and right ventricles in each group. The SI of the left and right ventricles decreased and then increased from segment 1 to segment 24, with the minimum value of the left ventricle at segment 5/6 and the minimum value of the right ventricle at segment 6/7, as shown in *Figures 7,8*.

Comparison of the functional parameters of the fetal left and right ventricular segments

The fractional shortening (FS) of the left ventricular segment 24 showed a decreasing trend with increasing gestational weeks, and the decreasing trend of the FS of the right ventricular segment 1–12 with increasing

Table 4 Comparison of overall ventricular function parameters between groups

Parameter	20–23^{+6} weeks	24–27^{+6} weeks	28–31^{+6} weeks	32–36^{+6} weeks	37–40^{+6} weeks	P
Left ventricle						
SV (mL)	0.40±0.11	0.45±0.13	0.82±0.26	1.33±0.53	1.47±0.49	<0.01[a]
CO (mL/min)	57.70±15.19	64.73±19.36	116.07±33.84	186.37±72.24	200.22±63.26	<0.01[a]
EF (%)	61.19±6.45	58.03±8.19[b]	57.13±7.08[b]	56.04±7.77[b]	52.93±8.37[b, c]	<0.01
GLS_L (%)	–24.04±4.91	–23.19±5.54	–21.44±4.16[b]	–20.25±4.26[b, c]	–19.44±3.57[b, c]	<0.01
FAC_L (%)	46.81±5.88	44.53±7.22	42.90±5.72[b]	41.93±6.36[b, c]	39.31±6.42[b, c]	<0.01
Right ventricle						
GLS_R (%)	–22.72±4.01	–22.07±4.14	–21.10±4.87	–20.18±3.53[b, c]	–21.80±4.52	<0.01
FAC_R (%)	41.64±6.07	40.24±5.87	38.05±6.62[b]	36.61±5.84[b, c]	38.84±6.54	<0.01

Values are presented as mean ± standard deviation. [a], indicates a two-by-two comparison except for groups I-II and IV-V, P<0.05; [b], indicates a comparison with group I, P<0.05; [c], indicates a comparison with group II, P<0.05. SV, stroke volume; CO, cardiac output; EF, ejection fraction; GLS, global longitudinal strain; FAC, fraction of area change.

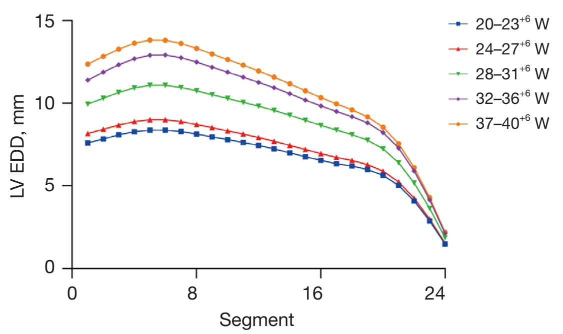

Figure 5 Illustration of changes in the EDD of the 24 segments of the LV with gestational week. EDD, end-diastolic diameter; LV, left ventricle.

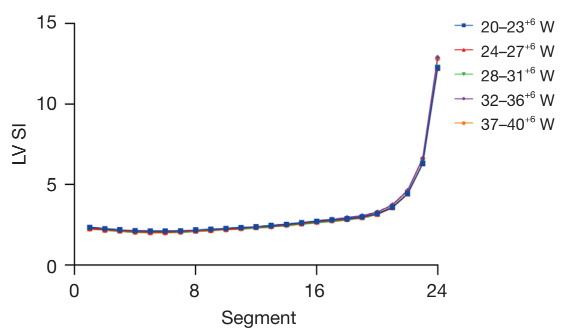

Figure 7 Illustration of changes in the SI of the 24 segments of the LV with gestational week. SI, sphericity index; LV, left ventricle.

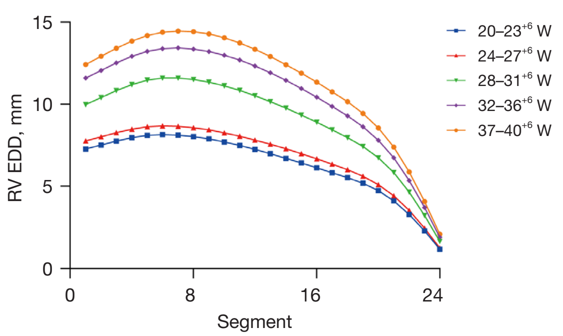

Figure 6 Illustration of changes in the EDD of the 24 segments of the RV with gestational week. EDD, end-diastolic diameter; RV, right ventricle.

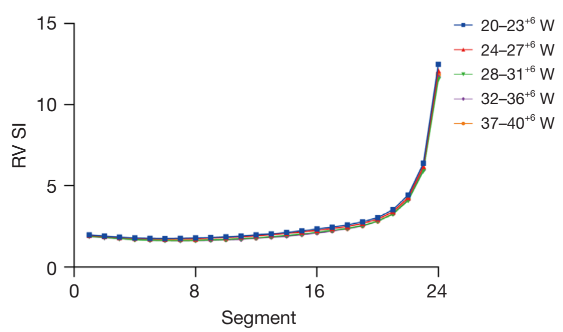

Figure 8 Illustration of changes in the SI of the 24 segments of the RV with gestational week. SI, sphericity index; RV, right ventricle.

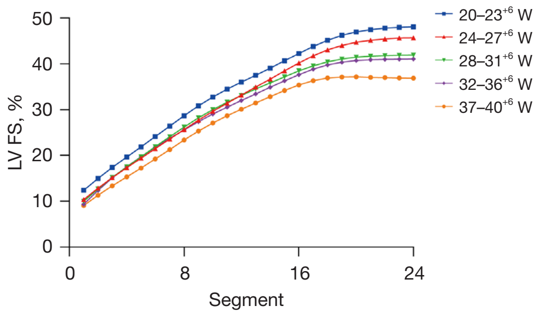

Figure 9 Illustration of changes in the FS of the 24 segments of the LV with gestational week. FS, fractional shortening; LV, left ventricle.

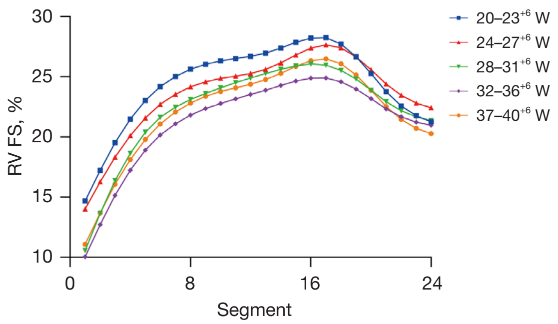

Figure 10 Illustration of changes in the FS of the 24 segments of the RV with gestational week. FS, fractional shortening; RV, right ventricle.

gestational weeks was more pronounced than that of the other segments. The FS of the left ventricle gradually increased from segment 1 to segment 24 in each group, and the FS of the right ventricle first increased and then decreased from segment 1 to segment 24 in each group, as shown in *Figures 9,10*.

Linear regression analysis

A one-dimensional linear regression analysis of each continuous fetal variable and gestational week yielded the following results: (I) heart end-diastolic length, width and area were positively linearly correlated with gestational week, heart rate was negatively linearly correlated with gestational week, and GSI was not significantly correlated with gestational week; (II) left and right ventricular end-diastolic length and area were positively linearly correlated with gestational week, left ventricular SV and CO were positively linearly correlated with gestational week, left ventricular EF and both The left ventricular SV and CO were positively and linearly correlated with gestational week, and the left ventricular EF and both ventricular GLS and FAC were negatively and linearly correlated with gestational week (see Table S1); (III) the left and right ventricular 24-segment EDD were positively and linearly correlated with gestational week (see Tables S2,S3); (IV) the left ventricular 20–24-segment was positively and linearly correlated with gestational week, and the right ventricular 2–23-segment SI was negatively and linearly correlated with gestational week (see Tables S4,S5); (V) linear correlations (see Tables S6,S7).

Repeatability evaluation

Repeatability tests were performed for the parameters related to this study, and the overall fetal heart parameters had good repeatability, as shown in Table S8 and Figure S1.

95% reference value range

The 95% medical reference value range of each indicator was calculated, and the normality test was performed on the measurement data, and the normally distributed data were calculated by the normal distribution method with a range of $\bar{x}$±1.96s; the skewed data were calculated by the percentile method with a range of $P_{2.5}$ to $P_{97.5}$, and the results are shown in Tables S9-S15.

Discussion

Based on Fetal HQ, this study evaluated the fetal heart in the mid to late stages of normal pregnancy and identified the changing patterns of various parameters with GA. The findings demonstrate that Fetal HQ can effectively assess the fetal heart in the mid to late stages of normal pregnancy, providing a clinical basis for fetal cardiac assessment. Fetal HQ is a two-dimensional speckle tracking technology that comprehensively analyzes fetal cardiac structure and function (8,16). Its clinical advantages lie in its simple operation, low requirement for fetal position, requiring only dynamic data of 3–5 cardiac cycles in fetal rest state, and marking the endocardial surfaces of the left and right ventricles at end-systole and end-diastole, respectively, to obtain relevant parameters of fetal cardiac morphology and function. Moreover, determining the fetal cardiac cycle accurately is an important condition to ensure the accuracy of speckle tracking parameters (17). This technology determines the starting point of the cardiac cycle through both two-dimensional and M-mode images, compensating for the inability to monitor fetal electrocardiograms. Lastly, this technology can interpret the overall fetal cardiac and ventricular segment, aiding ultrasound physicians in comprehensively evaluating fetal cardiac conditions.

The results of this study indicate a negative correlation between FHR and GA, which is consistent with previous domestic and international study (18). The rhythm of the cardiac cycle is governed by both the sympathetic and parasympathetic nervous systems. Most scholars (19) believe that the sympathetic nervous system develops early in fetuses, while the parasympathetic nervous system accelerates its development from second trimester onwards. Therefore, the FHR is faster in early gestation, but as GA increases, the dominance of the parasympathetic nervous system leads to a gradual decrease in FHR.

The fetal cardiac morphology parameters in this study include the end-diastolic length, width, area, and GSI; end-diastolic length and area of both ventricles; EDD and sphericity index (SI) of 24 segments of both ventricles. The increase in cardiac length, width, and area intuitively reflects the process of fetal cardiac growth and development. The parameters at 37–40^{+6} weeks were significantly larger than those at 32–36^{+6} weeks, but there was no significant difference between 32–36^{+6} weeks and 28–31^{+6} weeks or between 37–40^{+6} weeks and 32–36^{+6} weeks. This may suggest that fetal cardiac growth and development are faster before 32 weeks, with significant changes in size, while after 32 weeks of late gestation, fetal heart size tends to mature, with changes in size but not significant. The EDD results of the 24 segments of both ventricles suggest a decrease in the EDD of the left ventricle from segments 5–24, which basically forms a triangular shape, while segments 1–4 at the base have slightly smaller EDDs, possibly due to the traction effect near the valve insertion point, resulting in locally smaller diameters. The EDD of the right ventricle increased from the base to the apex and then decreases. The scatter plot showed a more significant change in EDD compared to the left ventricle, and the curve is smoother, with a crescent shape. SI is a reliable index for measuring cardiac morphology, and previous study (8) have suggested that GSI and SI of each segment of both ventricles are independent of GA and ultrasound measurements of fetal growth. In this study, there was no significant correlation between GSI and GA, and there was almost no significant difference in SI among the groups, which is consistent with other domestic and international research results. The difference between this study and previous research results lies in the weak positive correlation between some segments of SI of the left ventricle and GA, and the weak negative correlation between most segments of SI of the right ventricle and GA. This suggests that with increasing GA, fetal cardiac development gradually matures, and the increase in cardiovascular circulation and placental maturity leads to an increase in cardiac load in late gestation, especially in the right ventricle. The fetal heart may undergo adaptive changes in response to hemodynamic changes, leading to some segments of the right ventricle becoming closer to spherical at a smaller GA (20).

The functional parameters of fetal cardiac in this study include SV, CO, EF, GLS, FAC, and FS of 24 segments of both ventricles. In this study, SV and CO increased with GA, with a faster growth in mid-to-late pregnancy, and the rate of increase slowed down after 37 weeks of gestation, reflecting the process of CO increasing with fetal growth and development, enabling quantitative assessment of cardiac function. Left ventricular EF, GLS, and FAC, as well as right ventricular GLS, showed a decreasing trend with GA, with a significant decline after 28 weeks for left ventricular EF, GLS, and FAC; right ventricular GLS and FAC also showed a decreasing trend, but increased after 37 weeks of gestation. These changes indicate that as fetal cardiac growth and development progress, cardiac function tends to mature. Although the degree of ventricular contraction relatively decreases, the CO still increases, suggesting that with increasing GA, the reserve capacity of fetal cardiac function also increases, and the compensatory ability to intrauterine environmental changes gradually improves. Previous studies have shown inconsistent results regarding the left ventricular GLS with some showing no significant changes with GA (21-26), some indicating a significant decrease with GA (27-30), and others suggesting an increase with GA (31). Regarding the research results on right ventricular GLS, there is also some inconsistency. The study subjects span different gestational weeks, showing either a stable (23,25,31,32), decreasing (21,24,28,30,33,34), or increasing (31,35) trend in right ventricular GLS with GA. For instance, in the study by Ye *et al.* (21), where 50 normal pregnant women were sequentially evaluated for fetal cardiac function at 24 weeks, 32 weeks, and 37 weeks, it was found that left ventricular GLS remained unchanged throughout gestation while right ventricular GLS showed a decreasing trend. Kapusta *et al.* (24), in their study involving 49 pregnant women examined at 20–24 weeks and 30–34 weeks, found a moderate decrease in overall strain of the right ventricle, but no significant decrease in the left ventricle. Kim *et al.* (25) conducted cardiac examinations on 122 fetuses at 19–36 weeks and found no significant correlation between systolic strain of both ventricles and GA. Alsolai *et al.* (28) conducted fetal cardiac examinations every two weeks from 36 weeks to delivery on 276 fetuses, and observed a gradual decrease in both left and right ventricular GLS. Matsui *et al.* (29) analyzed fetal myocardial strain in 144 fetuses from 14^{+1} to 39^{+1} weeks and found a decrease in strain of both ventricles with pregnancy under high frame rate conditions, while under low frame rate conditions, the decrease in strain couldn't be captured. van Oostrum *et al.* (27) conducted cardiac evaluations every 4 weeks from enrollment to delivery on 124 healthy pregnant fetuses, and found a significant decrease in GLS of both ventricles with GA. The discrepancies between previous studies and the current one could be due to differences in the ultrasound diagnostic equipment used, as well as the speckle tracking software. Studies indicate that a low image frame rate significantly impacts the evaluation results because of the small size and fast FHR, which requires a much higher frame rate than that for adult heart speckle tracking. In this study, efforts were made to ensure a frame rate ≥80 Hz when collecting dynamic fetal cardiac videos, providing a better basis for speckle tracking annotation. Furthermore, previous studies mostly selected specific gestational weeks or smaller gestational week intervals for cardiac evaluation, which may not fully reflect the dynamic changes in fetal cardiac function. Moreover, compared to previous studies, the advantage of this study lies in its larger sample size, resulting in higher reliability of the reference ranges for various fetal cardiac parameters.

This study obtained FS for each of the 24 segments of both ventricles. The FS of the left ventricle gradually increased from the basal to apical segments, which is related to the shape of the left ventricle with a wide base and narrow apex, ensuring relatively coordinated ejection capability of each segment of the left ventricle. The FS of each segment of the left ventricle showed a negative linear relationship with GA, consistent with the changes in overall functional parameters with GA. The FS of the right ventricle increased gradually from the basal to mid segments but decreased gradually in the apical segment. The FS of segments 1–20 of the right ventricle showed a negative correlation with GA, but there was an increasing trend in FS in the $37–40^{+6}$ week group. This may be due to an increase in placental maturity and gradual closure of the arterial duct in late pregnancy leading to an increase in right ventricular afterload, prompting compensatory increase in right ventricular contractility to maintain ejection volume.

Fetal growth and development are continuous processes, and fetal cardiac abnormalities caused by pregnancy complications can occur at any GA. Therefore, evaluating fetal hearts by subdividing GA intervals helps in early detection of morphological or functional abnormalities, aiding in understanding the changes in hemodynamics of different diseases and enabling timely intervention to improve prognosis. With the development of speckle tracking imaging technology and the development of machine-independent software, DICOM files can now be obtained from almost any ultrasound machine used for fetal imaging, and machine-independent software can be used to analyze fetal cardiac strain (36). Different speckle tracking technologies have their own advantages and disadvantages. 2D-STI technologies like Fetal HQ divide the ventricle into different segments, track endocardial motion, improve accuracy and repeatability through semi-automatic analysis, and are angle-independent. However, they require high frame rates (37,38). Velocity vector imaging (VVI), based on 2D-STI, evaluates myocardial tissue motion and velocity in a vector manner, generating parameters such as velocity, strain, and strain rate of myocardial motion, providing a more accurate assessment of local myocardial motion. However, image quality and frame rate significantly impact the measurement results (39). Three/four-dimensional speckle tracking technology (3D/4D-STI) automatically tracks tissue acoustic speckles in three-dimensional space throughout the cardiac cycle, overcoming the limitations of 2D-STI in inter-plane tracking and providing more strain parameters. However, data acquisition is time-consuming and highly dependent on image quality and temporal resolution (40). Different speckle tracking technologies have their own advantages and limitations, making it crucial to establish standardized examination methods. We believe that the relevant data on normal mid-to-late pregnancy provided by this study can serve as valuable references for the future clinical application of fetal speckle tracking technology.

The innovations of this study include: (I) fetal cardiac quantitative analysis technology is a relatively new speckle tracking technology, which analyzes the morphology and function of fetal ventricles in 24 segments, thus enhancing the level of fetal cardiac evaluation during pregnancy. (II) Currently, there is a lack of application standards for fetal cardiac speckle tracking in China. This study measured and statistically analyzed 500 cases of normal pregnant fetuses, describing the changes in fetal cardiac morphology and function at different gestational weeks, thus providing a certain basis and reference for the clinical application of this technology. Limitations of this study include: (I) although a large sample size was included, all data were from a single-center cross-sectional study, and no multicenter cohort studies were conducted. (II) Clinical data collected were limited, and multivariate regression analysis was not conducted on other variables that may affect fetal cardiac function.

The results of this study differ somewhat from previous research, which may be due to differences in the distribution of pregnant women, GA intervals of fetuses, ultrasound imaging equipment, speckle tracking software, speckle tracking algorithms, and image frame rates. In the future, we will continue to expand the sample size, eliminate possible biases, and collect more clinical data to conduct more in-depth research.

Conclusions

The overall and segmental size parameters of the fetal heart can quantitatively assess the growth and development of the fetal heart; the GSI of the fetal heart and the SI of each segment are reliable morphological indicators for assessing the fetal heart; the fetal ventricular function parameters EF, FAC, GLS and FS of each segment can assess the fetal heart function. The technique of quantitative fetal heart analysis can help us to assess the heart growth and development of the fetus in normal mid to late term pregnancy.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://tp.amegroups.com/article/view/10.21037/tp-24-123/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tp.amegroups.com/article/view/10.21037/tp-24-123/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Committee of the First Affiliated Hospital of Soochow University (No. [2022]241). Informed consent was taken from all the participants for this study.

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