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ORIGINAL ARTICLE—OBSTETRICS & GYNECOLOGY

Feasibility of automated fetal fractional shortening measurement with two-dimensional tracking and construction of a reference range for normal fetuses

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Abstract

Purpose To assess the feasibility of an automated fractional shortening (Auto FS) measurement method using two-dimensional tracking and to construct a reference range for normal fetuses.

Methods This study was conducted from May 2017 to March 2018. First, cardiac motion in the four-chamber view was recorded in the B-mode. Subsequently, the region of interest was set on the edge of the ventricular septum or ventricular muscle at a point one-third away from the atrioventricular valve toward the cardiac apex. Tracking was automatically performed. Values measured between the ventricular septum and right ventricle were defined as R-Auto FS, whereas those measured between the ventricular septum and left ventricle were defined as L-Auto FS. Those on each ventricular muscle were defined as Combined-Auto FS.

Results Data were obtained from 131 singleton fetuses. R-Auto FS significantly decreased with an increase in the number of gestational weeks, and L-Auto FS and Combined-Auto FS showed the same tendency (Spearman's correlation analysis: $p = -.528$, $p = -.351$, and $p = -.636$, respectively).

Conclusion We succeeded in defining a reference Auto FS value for normal singleton pregnancies. Auto FS was negatively correlated with gestational age. This novel technique can assess fetal heart contractility.

Keywords Auto FS · Fractional shortening · Two-dimensional tracking method · Fetal cardiac function

Introduction

Previously, fractional shortening (FS) calculated using M-mode echocardiography was reported for measuring fetal cardiac contraction rate using the ultrasound technique [1–3]. Although other methods using the M-mode have also been considered [4], the M-mode is currently the main method used for calculation of FS to evaluate fetal cardiac function [5–7]. However, the previously used M-mode was inaccurate as intra-class correlation coefficient (ICC) errors were large [8]. The two-dimensional tracking (2DT) method is used to set the region of interest (ROI) at an arbitrary site on the B-mode image and track the ROI automatically. We believed that we could measure the cardiac contraction rate more easily and precisely by tracking the fetal heart muscle automatically. Recently, we developed an automated FS (Auto FS) measuring method that uses the 2DT method for tracking fetal heart motion, wherein the Auto FS can be calculated automatically. However, it is unclear whether this novel technique can be used in daily clinical practice. The aim of this study was to assess Auto FS measurement using the 2DT method and to construct a reference range for normal fetuses. To the best of our knowledge, this is the first report on Auto FS measurement using the 2DT method, which provides reference values for normal fetuses. Furthermore, this study provides information regarding both L-Auto FS and R-Auto FS. In addition, the combined systolic function of both ventricles, Combined-Auto FS, was also analyzed.

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Materials and methods

Study population

This prospective study included normal singleton pregnancies, in which fetal echocardiographic examinations were performed between 16 and 41 weeks of gestation between May 2017 and January 2018 at our institution. In all pregnancies, the gestational age was corrected by the crown-rump length at the first trimester. The exclusion criteria were obstetric complications, multiple pregnancies, fetal malformation, fetal chromosomal abnormality, small-for-gestational age fetuses, and large-for-gestational age fetuses. This study was approved by the ethical committee of our institution (ID number A16047), and written informed consent was obtained from all participants.

Echocardiography

All echocardiographic examinations were performed using an ARIETTA 70 ultrasound machine with a C35 convex transducer with a frequency range of 2–8 MHz (Hitachi, Ltd., Tokyo, Japan). Measurements were performed once for each patient. First, the fetal heart movements were recorded utilizing the four-chamber view for several seconds under the fetal heart mode, which is suitable for observing quick fetal heart movements. Recording was paused during the ventricular end-diastolic phase to set the ROI on the edge of the cardiac muscle at a point one-third away from each valve toward the cardiac apex. The calculation of FS was automatically started, according to the following formula: Auto FS (%) = (diastolic dimension − systolic dimension)/diastolic dimension × 100.

Among the values obtained, the three most stable consecutive heartbeats were used to calculate the average. We defined the value measured in the right ventricle as R-Auto FS, and in the left ventricle as L-Auto FS. Furthermore, the value measured in both the right and the left ventricles was defined as Combined-Auto FS. At the time of measurement, the displacement of the fetal heart due to fetal movement and maternal breathing was disregarded by template matching processing and destination automatic correction processing mounted on the Arietta 70, and the 2DT method was performed. Thereby the accuracy of the 2DT method for the fetal heart increased. We measured FS using the traditional method in a few cases at the same time to compare traditional FS measurement with Auto FS measurement.

Statistical analysis

The normality of the distribution of the data was determined by the Shapiro–Wilk test. A non-parametric test was used for analysis because the obtained data were not normally distributed. We referred to previous reports that reported a reference value according to the number of gestational weeks [9–11]. Spearman's correlation coefficient was used to evaluate the association between the number of gestational weeks and each Auto FS measurement. A linear regression model was created using the high R^2 values based on a scatter plot. The residual error was calculated as the difference in value from the predicted value for each week using the measured values and a linear regression model, and a scaled residual error was calculated. The absolute value of the scaled residual error was defined as the scaled absolute residual value. We evaluated the association between the scaled absolute residual value and the number of gestational weeks. The linear regression equation with the high R^2 value was defined as SD. The predicted value + 1.96 SD was defined as + 1.96 SD, and the predicted value − 1.96 SD was defined as − 1.96 SD. The Z score was calculated using the following equation: (measured value − predicted value)/SD. The ICC and 95% confidence interval (CI) were calculated for evaluation of the inter- and intra-subject reproducibility for each Auto FS measurement. To determine the intra-subject concordance rate, 20 subjects were randomly selected, and the Auto FS was measured two times by one operator (S.N.). To determine the inter-subject concordance rate, 10 subjects were randomly selected, and the Auto FS was measured two times by two operators, from among S.N., M.N., K.U., and M.T. Bland–Altman analysis was performed to compare FS calculated by the two methods (i.e., the 2DT method and the M-mode). SPSS software version 23.0 (SPSS Inc., Chicago, IL, USA) was used for all the statistical analyses. A statistically significant difference was defined as $p < 0.05$.

Results

One hundred and seventy-one singleton pregnancies were included in this study. In 31 cases, a four-chamber view was not obtained within a few minutes because of the fetal position. Therefore, we attempted the Auto FS measurement in 140 singleton pregnancies. The Auto FS method with the 2DT method was successfully used in 131 of the 140 pregnancies when the four-chamber view was visualized clearly during a few heartbeats (Figs. 1, 2). It was impossible to measure in a few cases, even though the

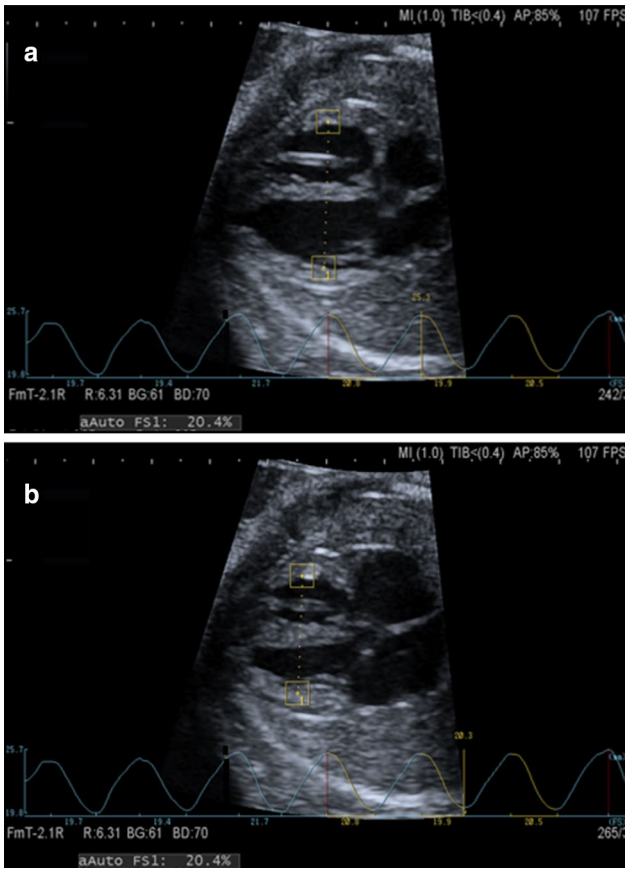

Fig. 1 Combined-Auto FS measurement. Combined-Auto FS in this case was 20.4%. **a** Indicates the diastolic phase, and **b** indicates the contraction phase. The ROI includes the contraction of the myocardium along the minor and major axes

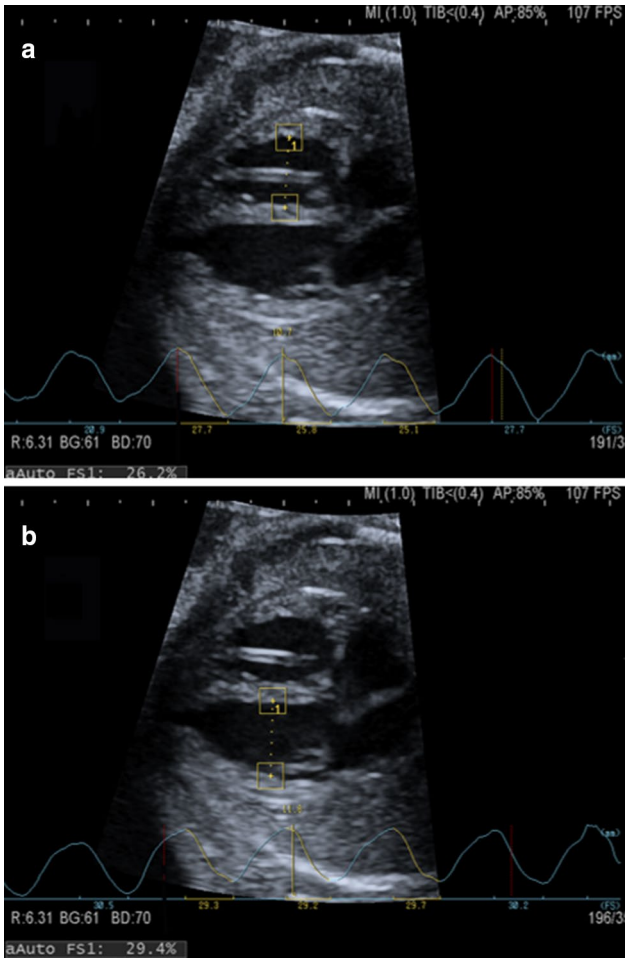

Fig. 2 **a** R-Auto FS was 26.2%. **b** L-Auto FS was 29.4%

four-chamber view was obtained, and the main reason was that the fetal heart was very small, especially at an early gestational age, or the mother's body mass index was high. Consequently, we could measure Auto FS from 16 weeks and 0 days to 40 weeks and 3 days, and when the mother's body mass index was from 19.5 to 29.4. Of the 131 cases, four cases with ventricular septal defects after birth were excluded. Clinical characteristics and pregnancy outcomes of patients are shown in Table 1. R-Auto FS decreased significantly with the gestational age, and L-Auto FS showed a similar tendency (Spearman's correlation analysis: $p = -.528$ and $p = -.351$, respectively). Combined-Auto FS showed a similar decline as the gestational age increased ($p = -.636$). Scatter plots, regression curves, and the SD (+1.96 SD, −1.96 SD) for each Auto FS measurement are shown in Table 2 and Fig. 3. Intra-observer ICCs for R-Auto FS, L-Auto FS, and Combined-Auto FS were 0.874 (95% CI 0.627–0.942), 0.896 (95% CI 0.740–0.961), and 0.949 (95% CI 0.866–0.981), respectively. Inter-observer ICCs for R-Auto FS, L-Auto FS, and Combined-Auto FS were 0.913 (95% CI 0.706–0.977), 0.924 (95% CI 0.739–0.980), and 0.963 (95% CI 0.866–0.990), respectively. The Bland–Altman plot of the logarithm of the average of the measured values between Auto FS measured using the 2DT method and the FS calculated using the M-mode is shown in Fig. 4. Subtraction errors were noted in the traditional FS measurements compared with Auto FS measurements.

Table 1 Clinical characteristics and pregnancy outcomes of patients

	Value
Maternal age (years)	33.5* (16–44)
Parity	0* (0–4)
Gestational age at measurement (weeks)	27.9* (16.0–41.0)
Gestational age at delivery (weeks)	39.5* (35.5–41.8)
Birth weight (g)	3032* (1891–4026)

*Data are provided as median

Table 2 Mean and SD equation for each Auto FS measurement

R-Auto FS
$\text{Mean} = 0.0478GA^2 - 3.3679GA + 82.754$
$R^2 = 0.36729$
$\text{SD} = 0.0094GA^2 - 0.6881GA + 15.568$
L-Auto FS
$\text{Mean} = 0.0433GA^2 - 3.1003GA + 87.065$
$R^2 = 0.21137$
$\text{SD} = 0.0239GA^2 - 1.6398GA + 31.767$
Combined-Auto FS
$\text{Mean} = 0.0311GA^2 - 2.3343GA + 62.954$
$R^2 = 0.46108$
$\text{SD} = 0.0092GA2 - 0.6147GA + 12.378$

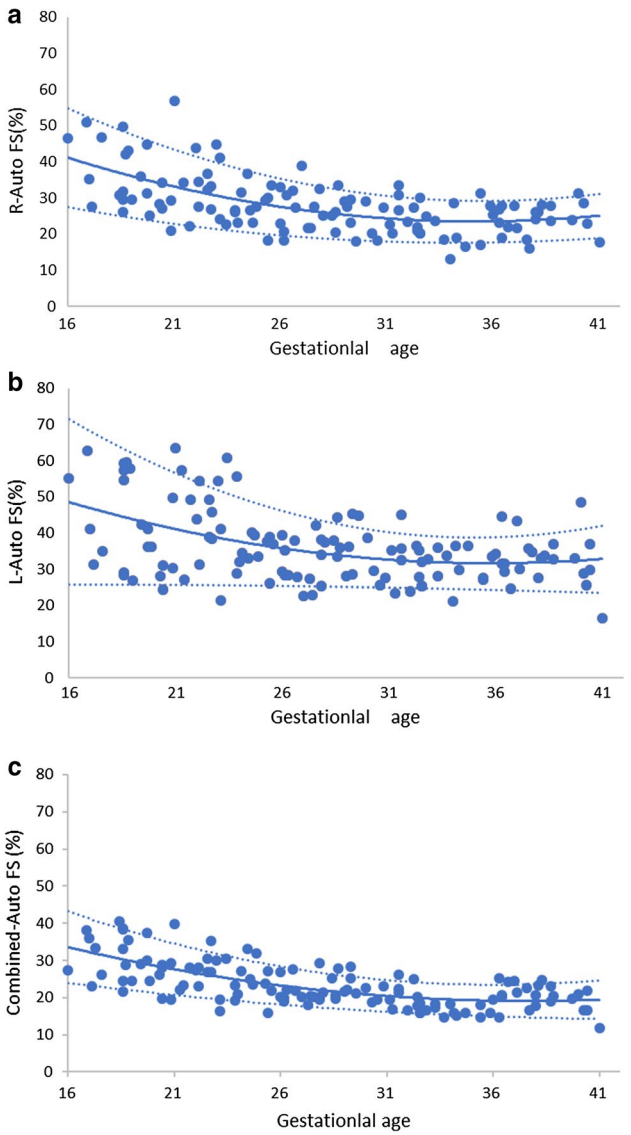

Fig. 3 Scatterplots of Auto FS in 131 normal fetuses, showing the correlation between gestational age: R-Auto FS (**a**), L-Auto FS (**b**), and Combined-Auto FS (**c**), with regression curves and the SD (+1.96 SD, −1.96 SD) indicated

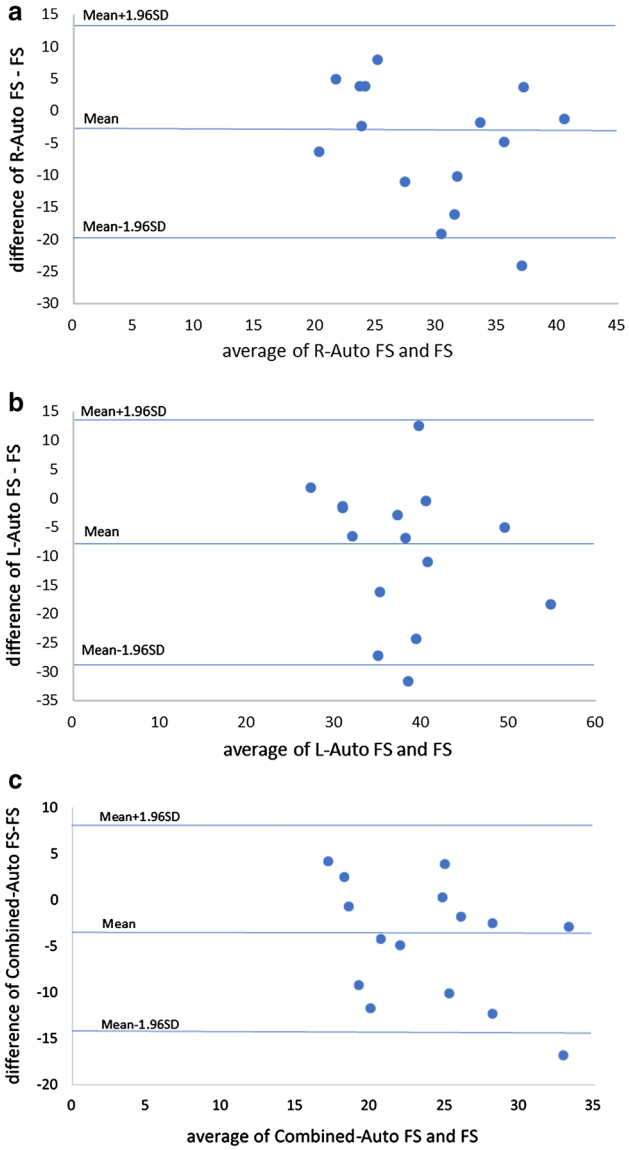

Fig. 4 Bland–Altman plot for the comparison between Auto FS and FS calculated using the M-mode: right (**a**), left (**b**), and combined (**c**), with mean ± 1.96 SD indicated

Discussion

To our knowledge, this is the first report on automated fetal FS (Auto FS) measurement using the 2DT method. The ventricle contracts not only along the short axis, but also along the long axis [12–14]. Therefore, FS using the M-mode measures temporal changes along the same straight line, but cannot measure the fetal cardiac contraction rate at the same site during both the systolic and the diastolic phases. The 2DT method can track the heart muscles, which contract along the long axis direction, by setting the ROI on the heart muscles using the four-chamber view. Therefore, Auto FS measures the contract rate,

taking into consideration the myocardial movement along the long axis direction.

Second, although FS previously measured using the M-mode was inaccurate because the ICC errors were large, the Auto FS method used in this study improved in this regard. Template matching processing and destination automatic correction processing loaded on the Arietta 70 enable measurement regardless of the displacement of the fetal heart and artificial error. Therefore, both intra-observer ICCs and inter-observer ICCs for all Auto FS measurements were high.

We succeeded in defining an Auto FS reference value for normal singleton pregnancies. Each Auto FS measurement had a negative correlation with the gestational age. FS reported to date was calculated using the M-mode, and it was generally considered that more than 28% of the measured values were normal regardless of the number of gestational weeks [5]. In contrast, in a study that used cardio-STIC-M, FS had a negative correlation with the gestational age, similar to that observed in this study [15]. The negative correlation with gestational age could be explained by the influence of the increased intracardiac pressure in correlation with the gestational age [16], and by the increase in the afterload due to the increased circulatory blood flow of the fetus. However, clinical significance has not been established. The relatively high negative correlation of the right ventricle and the Auto FS of both ventricles with the gestational age may be because fetal circulation is a right ventricle-dominant parallel circulation [17], and the right cardiac output is higher than the left ventricular output [18–20].

We measured Combined-Auto FS because the fetal circulation is a parallel circulation by the bilateral ventricles. We found that the Combined-Auto FS value was lower than that for each ventricle. Combined-Auto FS is calculated from the dimensional change between the right and left free wall, which does not include the interventricular septum. In contrast, R-Auto FS and L-Auto FS are calculated from the motion of both the free wall and interventricular septum. Subsequently, Combined-Auto FS ignores ventricular septum thickening during the systolic phase. In addition, fractional shortenings by the M-mode method in a previous study actually indicated a lowest value using both ventricles [2].

A limitation of this study is that the pathophysiological significance of Auto FS measurement is still not known, and measurement cannot be performed on a fetus that cannot be visualized on the four-chamber view.

Conclusion

This study investigated Auto FS measurement by the 2DT method in normal fetuses. Auto FS tended to decrease with an increase in the number of gestational weeks. This technique can assess fetal heart contractility more easily, and we propose that the Auto FS method can be a new way to evaluate fetal heart function more easily and accurately by considering even a pathological fetus.

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Author contributions Sumito Nagasaki designed the study and wrote the initial manuscript draft. Masahiko Nakata contributed to the analysis and interpretation of data and assisted in the preparation of the manuscript. All other authors contributed to data collection and interpretation, and critically reviewed the manuscript. All authors approved the final version of the manuscript and agreed to be 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.

Compliance with ethical standards

Conflict of interest All declare that they there is conflict of interest.

Ethical approval This manuscript has not been published or presented elsewhere in part or in entirety and is not under consideration by another journal. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional) and with the Helsinki Declaration of 1964 and later versions. All study participants provided informed consent, and the study design was approved by the appropriate ethics review board.

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