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The value of fetal growth trajectory during pregnancy in predicting small for gestational age neonates at term

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Abstract

Background The predictive value of trajectory identified by group-based trajectory modeling (GBTM) has been discussed but its value in predicting small for gestational age (SGA) neonates is still unclear. This study aims to describe the trajectory of fetal growth of estimated fetal weight (EFW) during pregnancy and compare its performance to growth velocity of EFW and EFW z-scores at each scan in predicting SGA neonates at term.

Methods The growth trajectory for EFW obtained from ultrasound scan at around 23–24, 31–32, 37–39 weeks of gestation of 1699 women from Shenzhen Birth Cohort Study was identified using GBTM. The area under receiver operating characteristics curve (AUC), Brier scores and Decision curve analysis (DCA) was used to evaluate the discrimination, calibration performance and clinical usefulness of EFW growth trajectory, EFW growth velocity between each stage and EFW z-scores at each scan.

Results Four trajectory groups of EFW which described as "very low-stable", "low-stable", "average-stable", "rising-falling" were identified. The growth trajectory performed better in discrimination and calibration than growth velocity, with AUC of 0.76 (95%CI: 0.73–0.80) and Brier score of 0.067 in predicting SGA neonates at term. When compared to the EFW z-scores, growth trajectory performed better than EFW z-scores of 23–24 weeks (AUC = 0.72, 95%CI: 0.68–0.76, Brier score = 0.073), but not as well as EFW z-scores of 37–39 weeks of gestation (AUC = 0.88, 95%CI: 0.86–0.91, Brier score = 0.060).

Conclusions EFW z-scores of 37–39 weeks of gestation outperformed in predicting SGA neonates at term than growth trajectory and velocity. Growth trajectory has better potential for serial ultrasound examinations to describe the process of fetal growth and to predict SGA neonates at term than fetal growth velocity.

Keywords Small for gestational age neonates, Fetal growth trajectory, Group-based trajectory modeling, Prediction

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Introduction

Small for gestational age (SGA) neonates, which refer to the newborns with birth weight (BW) less than the 10 th percentile for gestational age, are in higher risks of a range of short-term or long-term adverse health effects, including neonatal mortality and morbidity, poor neurodevelopment in childhood and cardiovascular disease in adulthood [1, 2]. In China, the overall prevalence of SGA was 6.4%, with nearly 1.26 million newborns affected by SGA annually [3]. Therefore, prediction of SGA is crucial, as it facilitates early identification, timely monitoring, and intervention in high-risk pregnancies, thereby mitigating the forementioned adverse effects [4].

Estimated fetal weight (EFW), calculated using the combination of sonographic fetal biometry including head circumference (HC), biparietal diameter (BPD), abdominal circumference (AC), and femur length (FL) with different equations, was commonly used for the prenatally prediction of SGA neonates [5]. Even though the EFW of late pregnancy presented good discrimination for SGA neonates, with the area under receiver operating characteristics curve (AUC) ranging from 0.827 to 0.891, the performance of EFW of early or mid pregnancy was poor, which may be due to the dynamic growth process of fetus during pregnancy [6, 7]. In Vishal et al., the EFW of 18–24 week of gestational age (GA) was poor predictors of SGA with AUC of 0.69 [8]. Papastefanou et al. also found that EFW at 19–24 weeks only predicted 38% of SGA neonates delivered ≥ 37 weeks and only 43% for those delivered < 37 weeks of GA [9].

Recently, taking fetal growth as an evolving process, several studies discussed the predictive value of serial sonographic fetal biometry. Hiersch L et al. found an increased risk of neonatal morbidity in the subgroup of SGA with lowest velocity of AC, indicating the importance of serial ultrasound scans [10], but related studies showed that predicting value of velocity in SGA was inconsistent [7, 11, 12]. Therefore, new approaches to interpret information from serial ultrasound scans are warranted. In this regard, some studies explored to refine the interpretation of serial ultrasound scans, one of which was the fetal growth trajectory. Bommarito et al. identified four fetal EFW growth trajectories among large for gestational age with an application of group-based trajectory modeling (GBTM) [13]. It is also reported that intrauterine fetal growth trajectories identified by GBTM were associated with blood pressure, markers of adiposity and inflammation and insulin resistance in young adult [14–16]. Moreover, trajectory identified by GBTM has been applied for disease prediction or prognostication but its potential value in SGA prediction was still unknown [17–19].

Based on these findings, we made the hypothesis that growth trajectory could potentially predict SGA neonates at term. We aim to describe the process of fetal growth through identifying the trajectories of EFW z-score during pregnancy using GBTM and compare its performance to EFW z-score growth velocity and EFW z-scores at each scan in predicting SGA at term.

Materials and methods

Study population

This study was derived from the Shenzhen Birth Cohort Study (SZBCS, NCT03830879, Registration Date, Feb 5 th, 2019), a population-based prospective cohort study, which was designed to explore the environmental and genetic influence during pregnancy on fetal growth, birth outcome and childhood development in Nanshan Maternity and Child Healthcare Hospital in Shenzhen. According to the local standard protocol of antenatal healthcare, the pregnant women in this cohort study are suggested to receive ultrasound examination for at least 5 times at 11–13, 20–24, 31–32, 37–39 weeks of gestation respectively. The SZBCS was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Nanshan Maternity and Child Healthcare Hospital of Shenzhen (NSFYEC-KY- 2020031). Informed consent was obtained from all participants in this cohort study.

The study included 2,152 pregnant women from SZBCS who delivered between January 2018 and December 2021, with 1,750 of them meeting the inclusion criteria of receiving the ultrasound examinations for more than 3 times. As shown in Fig. 1, multiple gestation, aneuploidy and major fetal structural abnormalities were excluded in this study. Considering that 75% of the participants with preterm births were not maintained during the inclusion process, the growth trajectories determined based on this populations may not fully represent for fetal growth patterns in preterm births, therefore, participants with preterm births were also excluded from this study. The gestational age was determined by the scan of crown rump length (CRL) at 11–13 weeks of gestation. The ultrasound scans around 23–24, 31–32, 37–39 weeks of gestation were abstracted for analysis.

Baseline characteristics

Participants were required to complete a questionnaire about sociodemographic information and medical history at the first follow-up visit after recruitment and the questionnaire data were entered into database. The following variables were considered in this study, including maternal age in years, pre-pregnancy body mass index (BMI), marital status (married or unmarried), monthly income (< 5,000, 5,000–10,000, 10,000–15,000

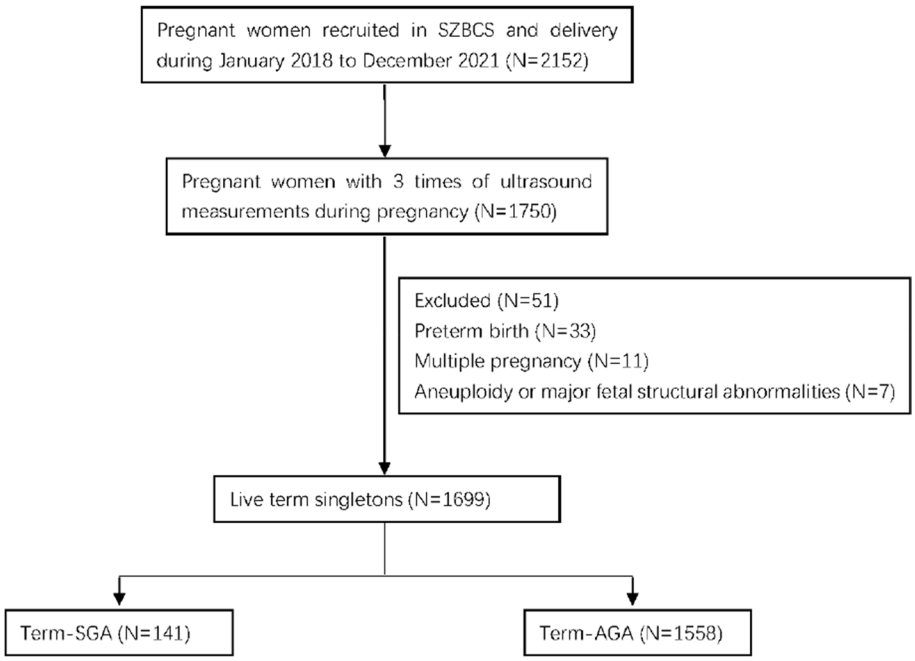

Fig. 1 Selection process of participants

or > 15,000 in Chinese yuan), education level (high school and lower, college or university, post-graduated and higher), employment status (employed or unemployed), smoking before pregnancy (yes or no), alcohol intake before pregnancy (yes or no), medical history (including chronic hypertension, renal disease, gestational hypertension, gestational and diabetes mellitus) and parity (nulliparous or parous).

Fetal growth scan

Ultrasound scan of fetal growth at around 23–24, 31–32, 37–39 weeks of gestation, including head circumference (HC), abdominal circumference (AC), femur length (FL) and biparietal diameter (BPD) was conducted with identical equipment by trained sonographers and data was abstracted from Hospital Information System (HIS). Estimated fetal weight (EFW) was calculated on the base of Hadlock Eq. 3: $\log10_{weight} = 1.326 - 0.00326 \times AC \times FL + 0.0107 \times HC + 0.0438 \times AC + 0.158 \times FL$ and then converted to z-scores using the generalized additive models for location, scale and shape (GAMLSS) [20–22].

Perinatal outcome

Birth outcomes including gestational age at the time of delivery in days, sex, and birthweight (BW) of the neonates were obtained from HIS. Neonates delivered after 36 weeks of gestation with BW < 10 th percentile according to the population-based gender-specific reference were recognized as SGA neonates at term in this study [23, 24].

Statistical analysis

We designed a three-step process for this study: (1) identifying the fetal growth trajectories and calculating growth velocity during pregnancy using EFW z-scores, (2) exploring the association between FGR and fetal growth trajectories or growth velocity, and (3) comparing the predictive performance of fetal growth trajectories, growth velocity and EFW z-scores at each scan.

In the first step, GBTM, which could identify groups of individuals with similar developmental trajectory and assign individuals into specific trajectory group according to posterior probability of group membership, was applied for identifying the fetal growth trajectories of EFW z-score during pregnancy [25, 26]. It is a finite mixture model that identifies groups of individuals following a similar trajectory of one or more repeated measures over time, in this study, EFW z-scores [27]. We explored models that ranged from 1–8 groups. The optimal group number and best order of each group's polynomial according to the balance of following criteria: the absolute Bayesian Information Criterion (BIC) closer to 0, an average posterior probability of group membership (PPGM) > 0.70, the smallest group had at least 5% of the sample, and the odds of correct classification (OCC) of each group > 5 [28, 29]. Among these criteria, the BIC was calculated by the formula: BIC

= log(L)—0.5 K log(N), proposed by Nagin et al. [28, 30]. According to the parameters of each group number solution shown in Table S1, the group number of four met the forementioned criteria with BIC of − 7280.39, an average PPGM of 0.84, smallest group's proportion of 5.35%, and the OCC of each group more than 5. Participants were assigned to trajectory group which PPGM was the highest. Trajectory group with average growth (EFW z-score close to zero) would be used as reference group in further analysis. Regarding the growth velocity, it was defined as the EFW z-scores between two ultrasound scans divided by the time interval in week in this study [31]. Accordingly, growth velocity between 23–24 to 31–32, 31–32 to 37–39, and 23–24 to 37–39 weeks of gestation was calculated and named as growth velocity$_1$, growth velocity$_2$, and growth velocity$_3$ respectively.

In the second step, univariable and multivariable logistic regression analyses were used to determine whether growth trajectories, growth velocity between each stage and EFW z-scores at each scan were significant contributors to the prediction of SGA delivered at term. According to relevant studies, covariates including maternal age, pre-pregnancy BMI, maternal marital status, monthly income, education level, employment status, smoking and alcohol intake before pregnancy and maternal medical history were adjusted in the multivariable logistic regression [32, 33].

In the third step, growth trajectories, growth velocity between each stage and EFW z-scores at each scan were treated as single predictor and their performance were compared. The area under receiver operating characteristics curve (AUC) was used to evaluate the discrimination performance and compared with the Delong test. The calibration performance was assessed with Brier scores, which was defined as the average squared difference between predicted probability and observed outcome. It ranges from 0 to 1, while 0 represents the best possible calibration [33]. Decision curve analysis (DCA) was performed to assess the clinical usefulness through quantifying the net benefit at a range of threshold [34]. Considering the relatively small sample size of this study, bootstrap validation 1000 times were performed as an internal validation [35].

To describe data, values were presented as means ± standard deviation or median and interquartile range depending on whether normally distributed or not for continuous variables and number (%) for categorical variables. Continuous variables were compared using Student's t-test or Kruskal–Wallis test based on their distribution, while and categorical variables were compared using Chi-squared test. The fitting of GBTM was performed with traj package of Stata (Release 17, StataCorp, Texas, USA) and other statistical analyses were performed using R (version 4.2.2, R Foundation for Statistical Computing, Vienna, Austria). P value < 0.05 (two-sided) was considered to be statistically significant.

Results

Baseline characteristics

A total of 1,699 participants were included in this study. The characteristics of study participants are shown in Table 1. The maternal age, body mass index (BMI), estimated fetal weight (EFW) z-scores at each scan and birthweight (BW) of participants in small for gestational age (SGA) group were significantly lower when compared with the non-SGA group. More women were nulliparous in SGA group when comparing to non-SGA group.

Trajectory of EFW z-scores

Based on the result of the group-based trajectory model results (Supplementary material: Table S1, Table S2), four trajectory groups were identified in this study and are shown in Fig. 2. The trajectory groups are described as "very low-stable" (Group- 1, n = 147 [8.7%]), with lowest EFW z-scores throughout the pregnancy, "low-stable" (Group- 2, n = 635 [37.4%]), where neonates had EFW z-scores slightly lower than the zero during the pregnancy, "average-stable" (Group- 3, reference group, n = 829 [48.8%]), in which neonates had EFW z-scores higher than the zero across the gestation, and "rising-falling" (Group- 4, n = 88 [5.2%]), in which neonates had highest EFW z-scores throughout the pregnancy and whose relative size was highest at 30–32 weeks of gestation. Participants assigned to "very low-stable" trajectory group were lower in age, pre-pregnancy BMI. The EFW z-scores of each scan and the birthweight were lowest in "very low-stable" trajectory group (Supplementary material: Table S2).

Association between growth trajectory and small for gestational age (SGA) delivered at term

As shown in Table 2, in multivariable logistic regression analyses, when comparing to reference group that fetal growth was average and EFW z-scores were close to zero, participants assigned to Group- 1 and Group- 2 had higher risks of SGA with aOR of 34.38 (95%CI = 17.67 ~ 72.59) and 5.67 (95%CI = 3.12 ~ 11.38), demonstrating significant contribution of growth trajectory in predicting SGA delivered at term. Additionally, growth velocity between 23–24 to 31–32 weeks, 31–32 to 37–39, weeks and 23–24 to 27–39 weeks of gestation also presented significant predictive contribution for SGA delivered at term, with aOR of 0.13 (95%CI = 0.04 ~ 0.41), 0.15 (95%CI = 0.05 ~ 0.45), and1.37e- 6 (95%CI = 4.95e- 80 ~ 1.25e- 29).

Table 1 Characteristics and birth outcome of study population stratified by small for gestational age (SGA) delivered at term

Characteristics	Non-SGA *n* = 1,558	SGA *n* = 141	*P*-value
Maternal characteristics			
Maternal age (years)	30.58 (4.3)	29.67 (4.6)	0.016
Pre-pregnancy BMI (kg/m^2)	21.15 (2.9)	20.53 (3.1)	0.017
Marital status (% married)	1,481 (95.1)	134 (95.0)	0.999
Education level, %			0.748
High school and lower	233 (15.0)	23 (16.3)	
College or University	1,140 (73.2)	104 (73.8)	
Post-graduated and higher	185 (11.9)	14 (9.9)	
Employment (% employed)	1,384 (88.8)	127 (90.1)	0.757
Monthly income in yuan, %			0.075
< 5,000	265 (17.0)	21 (14.9)	
5,001–10,000	638 (40.9)	73 (51.8)	
10,001–15,000	363 (23.3)	29 (20.6)	
> 15,000	292 (18.7)	18 (12.8)	
Hypertension, %	4 (0.3)	0 (0.0)	1.000
Renal disease, %	9 (0.6)	1 (0.7)	1.000
Gestational hypertension, %	203 (13.0)	13 (9.2)	0.243
Gestational diabetes mellitus, %	12 (0.8)	2 (1.4)	0.742
Parity (% parous)	773 (49.6)	44 (31.2)	< 0.001
Pre-pregnancy cigarette intake, %	77 (4.9)	3 (2.1)	0.192
Pre-pregnancy alcohol intake, %	207 (13.3)	13 (9.2)	0.213
EFW z-scores			
EFW z-scores of 23–24 weeks	0.08 (1.01)	− 0.67> (0.90)	< 0.001
EFW z-scores of 31–32 weeks	0.34 (1.17)	− 0.78 (1.11)	< 0.001
EFW z-scores of 37–39 weeks	0.08 (0.98)	− 1.35 (0.79)	< 0.001
Growth velocity			
Growth velocity$_1$	0.03 (0.14)	− 0.02 (0.14)	< 0.001
Growth velocity$_2$	− 0.04 (0.16)	− 0.09 (0.13)	< 0.001
Growth velocity$_3$	0.00 (0.07)	− 0.05 (0.06)	< 0.001
Birth outcome			
Gestational age at delivery (days)	276.79 (6.50)	276.71 (7.04)	0.883
Birthweight (g)	3,359.05 (348.9)	2,689.26 (222.9)	< 0.001
Sex (% male)	835 (53.6)	74 (52.5)	0.869

Data are presented as mean (standard deviation) or n (%)

Growth velocity$_1$, growth velocity between 23–24 to 31–32 weeks of gestation

Growth velocity$_2$, growth velocity between 31–32 to 37–39 weeks of gestation

Growth velocity$_3$, growth velocity between 23–24 to 37–39 weeks of gestation

BMI body mass index, *EFW* estimated fetal weight

Performance of growth trajectory, velocity and EFW z-scores in predicting SGA delivered at term

The discrimination and calibration performance of growth trajectories, growth velocity between each stage and EFW z-scores at each scan in predicting SGA delivered at term were presented in Table 3. As shown in Table 3 and Fig. 3A, the area under receiver operating characteristics curve (AUC) of the growth velocity between 23–24 to 31–32, 31–32 to 37–39, and 23–24 to 37–39 weeks of gestation was 0.60 (95%CI = 0.55 ~ 0.65), 0.61 (95%CI = 0.57 ~ 0.66), and 0.69 (95%CI = 0.65 ~ 0.73) respectively. Delong tests showed that the AUC of the growth trajectory (AUC = 0.76, 95%CI = 0.73 ~ 0.80) was significantly higher than that of the growth velocity ($p < 0.001$). The brier score of the growth trajectory (Brier score = 0.067) was closer to 0 than that of the growth velocity. The internal validation

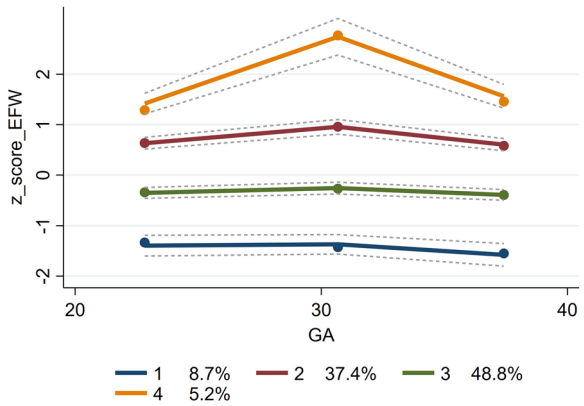

Fig. 2 Fetal growth trajectories for estimated fetal weight obtained from ultrasound scan at 23–24, 31–32, 37–39 weeks of gestational age (GA) using group-based trajectory modelling (GBTM) from study population. Percentages represent group membership for each group. Dotted lines represent 95% confidence intervals

results of growth trajectories, and growth velocity in Table S3 were in line with the present results.

In Table 3 and Fig. 3B, the discrimination performance of EFW z-scores at 23–24, 31–32 and 37–39 weeks were similar, with AUC of 0.72 (95%CI =0.68 ~ 0.76), 0.78 (95%CI =0.74 ~ 0.82) and 0.88 (95%CI =0.86 ~0.91). Delong test showed that the growth trajectory had AUC higher than EFW z-scores of 23–24 weeks ($p < 0.05$) and lower than EFW z-scores of 37–39 weeks significantly ($p < 0.001$). These results were also similar to the internal validation method of bootstrapping in Table S3. The growth trajectory also had a Brier score closer to 0 than EFW z-scores of 23–24 weeks, but not when compared to EFW z-scores of 37–39 weeks.

Decision curve analysis (DCA) was performed and presented in Fig. 4. In accordance with its discrimination and calibration performance, growth trajectory displayed better clinical usefulness and overall net benefit than growth velocity in prediction of SGA delivered at term (Fig. 4A). Additionally, it also shows poorer clinical usefulness than that of EFW z-scores at 37–39 weeks of gestation, but better than that of EFW z-scores at 23–24 weeks of gestation (Fig. 4B).

Discussion

This study described the process of fetal growth through identifying trajectories of EFW z-score during pregnancy. Four EFW trajectory groups which were described as "very low-stable", "low-stable", "average-stable", "rising-falling" were identified. Additionally, when predicting SGA neonates delivered at term, EFW z-scores of 37–39 weeks of gestation outperformed in predicting SGA neonates at term than growth trajectory and velocity. The EFW z-score trajectory groups performed better than

Table 2 Logistic regression analyses in prediction of small for gestational age (SGA) delivered at term by estimated fetal weight (EFW) trajectory, EFW velocity, and EFW z-scores at each scan

Variables	Univariable		Multivariable	
	Crude OR (95% CI)	*P*-value	Adjusted OR[a] (95% CI)	*P*-value
Growth trajectory group				
Average-stable	Reference	-	Reference	-
Very low-stable	36.16 (18.69, 76.04)	< 0.001	34.38 (17.67,72.59)	< 0.001
Low-stable	5.83 (3.22, 11.68)	< 0.001	5.67 (3.12,11.38)	< 0.001
Rising-falling	1.32e- 6 (3.82e- 80, 1.25e- 16)	0.975	1.37e- 6 (4.95e- 80,1.25e- 29)	0.974
Growth velocity				
Growth velocity$_1$	0.11 (0.04,0.36)	< 0.001	0.13 (0.04,0.41)	< 0.001
Growth velocity$_2$	0.14 (0.05,0.41)	< 0.001	0.15 (0.05,0.45)	< 0.001
Growth velocity$_3$	1.47e- 4(1.25e- 5,1.63e- 3)	< 0.001	2.17e- 4(1.76e- 5,2.54e- 3)	< 0.001
EFW z-scores				
EFW z-scores of 23–24 weeks	0.47 (0.39,0.56)	< 0.001	0.46 (0.38,0.56)	< 0.001
EFW z-scores of 31–32 weeks	0.38 (0.31,0.46)	< 0.001	0.39 (0.32,0.47)	< 0.001
EFW z-scores of 37–39 weeks	0.16 (0.12,0.21)	< 0.001	0.16 (0.12,0.21)	< 0.001

Growth velocity$_1$, growth velocity between 23–24 to 31–32 weeks of gestation

Growth velocity$_2$, growth velocity between 31–32 to 37–39 weeks of gestation

Growth velocity$_3$, growth velocity between 23–34 to 37–39 weeks of gestation

CI Confidence Interval

[a] Models were adjusted for maternal age, pre-pregnancy BMI, maternal marriage status, monthly income, education level, employment status, smoking and alcohol intake before pregnancy and maternal medical history

Table 3 Performance of estimated fetal weight (EFW) z-scores trajectory, EFW z-scores velocity between each stage, and EFW z-scores at each scan for predicting small for gestational age (SGA) delivered at term

Predictors	AUC (95% CI)	*P* value[a]	Brier scores
Growth trajectory	0.76 (0.73,0.80)	NA	0.067
Growth velocity			
Growth velocity$_1$	0.60 (0.55,0.65)	< 0.001	0.076
Growth velocity$_2$	0.61 (0.57,0.66)	< 0.001	0.076
Growth velocity$_3$	0.69 (0.65,0.73)	0.009	0.074
EFW z-scores			
EFW z-scores of 23–24 weeks	0.72 (0.68,0.76)	0.019	0.073
EFW z-scores of 31–32 weeks	0.78 (0.74,0.82)	0.185	0.069
EFW z-scores of 37–39 weeks	0.88 (0.86,0.91)	< 0.001	0.060

Growth velocity1, growth velocity between 23–24 to 31–32 weeks of gestation

Growth velocity2, growth velocity between 31–32 to 37–39 weeks of gestation

Growth velocity3, growth velocity between 23–24 to 37–39 weeks of gestation

AUC area under receiver operating characteristics curve

[a] The AUC was compared with the Delong test

EFW z-score growth velocity during the pregnancy, but the performance lies between EFW z-scores at 37–39 and 23–24 weeks of gestation in the aspect of discrimination, calibration, and clinical usefulness.

The predictive value of trajectories identified by GBTM has been explored in various studies. For instance, electroencephalographic trajectories can enhance the predictions for the cardiac arrest outcome, while trajectories of epileptiform abnormalities and the middle cerebral artery can predict delayed cerebral ischemia after subarachnoid hemorrhage [17, 18]. However, research on growth trajectories and their link to adverse health outcome is limited. Some studies have found connections between fetal growth trajectories identified by GBTM and adverse birth or health outcomes. For example, the Generation R cohort study identified three fetal growth trajectories among SGA neonates, linking smaller mid-pregnancy size to poorer children neurodevelopment [36]. Additionally, Ashish et al. found that head and abdominal

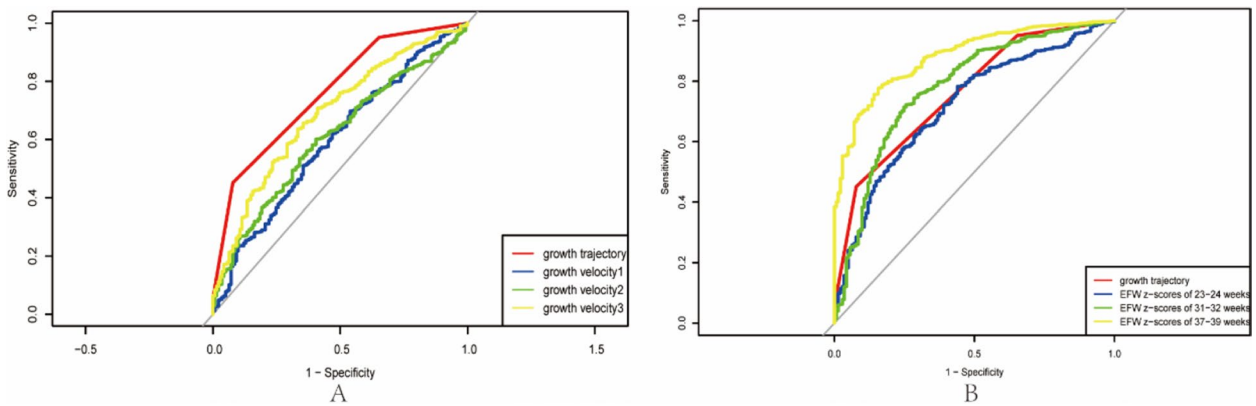

Fig. 3 Receiver–operating characteristics curves (ROC) of estimated fetal weight (EFW) growth trajectory, EFW growth velocity (**A**) and EFW z-scores (**B**) in the prediction of small for gestational age (SGA) delivered at term

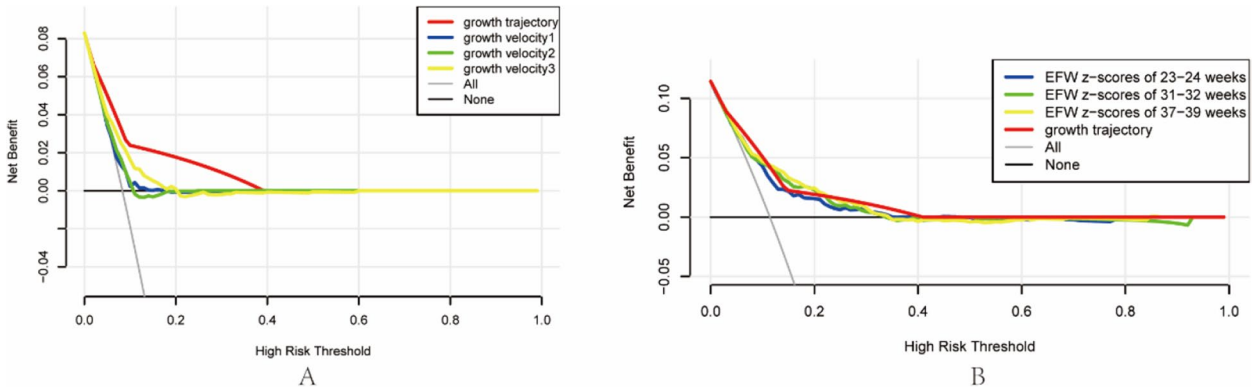

Fig. 4 Decision curve of estimated fetal weight (EFW) growth trajectory, EFW velocity (**A**), and EFW z-scores (**B**) in the prediction of small for gestational age (SGA) delivered at term

circumference trajectories during pregnancy were related to higher insulin resistance and systolic blood pressure in adulthood [14, 16]. This study identified four EFW trajectories during pregnancy. Analysis revealed that fetuses in the "very low-stable" and "low-stable" groups had a higher risk of SGA neonates at term, indicating its potential predictive value.

Predicting SGA neonates is challenging due to the inconsistent performance of EFW at different pregnancy stages, as the fetus grows. Researchers suggested that serial ultrasound scans, which track fetal growth over time, may be more effective than measuring fetal size at a single point [10]. Improved maternity insurance has made these serial scans feasible in local antenatal care. This study evaluates the predictive value of EFW trajectories compared to growth velocity and EFW z-scores at each scan, focusing on discrimination, calibration and clinical usefulness. Several studies have examined the use of serial ultrasound scans to assess fetal growth velocity and its ability to predict SGA neonates. Ciobanu et al. found that measuring the growth velocity of EFW between 32–36 weeks and 20–36 weeks did not enhance predictive performance. The AUC for velocity between 32–36 weeks was 0.61 and between 20–36 weeks was 0.74, both lower than EFW z-scores for predicting SGA neonates [7, 32]. This study also analyzed growth velocity for predicting SGA at term, with AUC of 0.54, 0.50, and 0.54, for different gestational periods, differing from previous findings. The predictive performance of growth velocity can be influenced by factors like outcome definition, ultrasound timing, women's characteristics (race, ethnicity, occupation), and study design. Delong test results indicated that growth velocity has significantly lower discrimination performance compared to growth trajectory, suggesting that growth trajectory is a better method for using serial ultrasound to predict term SGA neonates.

This study also analyzed the predictive accuracy of EFW z-scores at different gestational ages, with AUC of 0.72 at 23–24 weeks, 0.78 at 31–32 weeks and 0.88 at 37–39 weeks. These results align with previous studies showing AUC of 0.69 and 0.83 at 18–24 weeks and 32–36 weeks for predicting SGA neonates [6, 8]. The Delong test results indicated that the growth trajectory was more effective than EFW z-scores at 23–24 weeks ($p < 0.05$), similar to those at 31–32 weeks ($p > 0.05$), but less effective than EFW z-scores at 37–39 weeks ($p < 0.001$) in predicting SGA neonates delivered at term. Despite the superior performance of EFW z-scores at 37–39 weeks, monitoring and intervention for SGA fetuses predicted at this timepoint were not optimally effective. Based on the results of this study, while growth trajectory had lower discrimination than the EFW z-scores of 37–39 weeks, it is recommended as a better predictor of SGA neonates at term than fetal growth velocity. It also offers a promising approach for interpreting serial ultrasounds to describe fetal growth, though further research is needed to assess its clinical value.

This prospective cohort study used GBTM to outline fetal growth via EFW z-scores trajectories and compared its ability to predict SGA at term against EFW z-scores growth velocity and individual EFW z-scores. Nonetheless, this study has several limitations. Firstly, this study's use of growth velocity assumes linear fetal growth over time, which may be less accurate and could underestimate the predictive value of growth velocity. Secondly, the information about characteristics of pregnant women in this study was collected by questionnaire, which reporting bias may exist. Thirdly, the small sample size may have missed other potential fetal growth trajectories. Future studies should use larger population to thoroughly explore fetal growth trajectories during pregnancy. Fourthly, this study did not analyze other SGA risk factors like maternal serum levels of PPAP-A, placental growth factor and sFlt- 1 due to the hospital's qualification limitations. Filthy, considering that only term SGA were included in this study, the interpretation of determined growth trajectory and the prediction performance might be restricted. Moreover, while maternity insurance allows for serial ultrasound exam during pregnancy, implementing this in daily clinical practice remains impractical and challenging for women in low-resource settings. Lastly, since all participants were recruited from a single hospital in Shenzhen, China, selection bias may restrict the generalizability of our findings. Multicenter studies are needed to validate these results further.

Conclusions

In conclusion, the results of this study indicated that EFW z-scores of 37–39 weeks of gestation demonstrated better performance for SGA neonates at term than growth trajectory and velocity. Growth trajectory has better potential for serial ultrasound examinations to describe the process of fetal growth and to predict SGA neonates at term than fetal growth velocity.

Supplementary Information

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Supplementary Material 1

Authors' contributions

Conceptualization, CWQ; methodology, CWQ; software, ZHM; validation, ZHM, LXX and LXM; formal analysis, ZHM; investigation, WM, LXX, LXM, LJ, FXM; resources, WZ, LJ, FXM; data curation, WM, LXX, LXM; writing—original draft preparation, ZHM; writing—review and editing, CWQ; visualization, ZHM; supervision, CWQ; project administration, CWQ, WZ, WM; funding acquisition, CWQ. All authors reviewed the manuscript.

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Data availability
The data supporting the findings of this study are available on request from the corresponding author. The data is not publicly available due to privacy or ethical restrictions.

Declarations

Ethics approval and consent to participate
This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Nanshan Maternity and Child Healthcare Hospital of Shenzhen and (NSFYEC-KY- 2020031). Inform consent was obtained from all participants in this cohort study.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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