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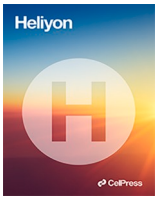

Research article

Body composition trajectories during childhood predict skeletal maturation at puberty: A longitudinal study

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ABSTRACT

Nutritional status significantly impacts linear bone growth. We aimed to determine the relationship between the trajectories of four body composition indicators and pubertal advanced bone age. Trajectories of body mass index z-score (BMI z-score), visceral fat area z-score (VFA z-score), fat mass index z-score (FMI z-score), and fat-free mass index z-score (FFMI z-score) were identified based on three body composition measurements conducted from October 2018 to April 2023 within a pediatric cohort (the PROC study). We assessed pubertal bone age using the Tanner-Whitehouse 3-Chinese Radius-Ulna-Short (TW3-C RUS) method among 1402 primary school children. Children with a trajectory of higher BMI z-score, VFA z-score, FMI z-score, and FFMI z-score since childhood were more likely to have advanced bone age. The risk of advanced bone age was higher in children who were consistently in the high VFA z-score group (odds ratio [OR] = 6.73) or consistently in the high BMI z-score group (OR = 5.57), as compared to those in the low VFA z-score and low BMI z-score groups. Regular monitoring and maintenance of normal VFA during childhood may reduce the risk of advanced bone age at puberty. Furthermore, BMI monitoring is optional, especially in cases where specialized body composition equipment is not available.

1. Introduction

Bone age (BA) serves a crucial indicator of maturity from childhood to adolescence and plays a key role in predicting eventual growth potential, specifically the attainment of final height [1,2]. When BA exceeds chronological age by one year or more, it suggests accelerated skeletal maturation [3]. Accelerated skeletal maturation may lead to a shortened pubertal growth spurt, early epiphyseal closure, and premature cessation of growth, resulting in a reduced final height [4]. The evolving long-term trend in the physical growth of Chinese children has gained significance along with the economy develops and living standards improve [5]. Consequently, the final height and related advanced BA during puberty garnered high attention among parents and pediatricians.

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Previous research indicates that childhood obesity is a primary contributor to the onset of advanced BA [6,7]. This association is attributed to optimal nutritional status on the growth plate chondrocytes [8] and endochondral ossification [9]. As a result, children with obesity exhibit great height than their peers in early childhood, but later experience earlier puberty and faster growth plate fusion, leading to potential long-term effects on final height [10]. However, findings from a cross-sectional study conducted in Louisville, USA contradicted this association, reporting no significant link between overweight or obesity and advanced skeletal maturation in adolescents [11]. These inconsistent findings may be due to differences in economic development resulting in long-term BA secular trends between countries [12–14]. The majority of these studies were limited by their cross-sectional design and by enrolling participants from hospitalized children, which might introduce confounding factors into the relationship between obesity and advanced BA. In addition, most studies rely on body mass index (BMI) as an indicator of overweight or obesity. Since BMI cannot differentiate adiposity or lean body mass, as well as fat distribution [15], there is a gap in understanding the impact of childhood fat mass on the occurrence of pubertal advanced BA.

To address these limitations, we propose utilizing longitudinal data from a child cohort (the PROC study) in Beijing, China. We aim to investigate the associations between BMI, visceral fat area (VFA), fat mass index (FMI), and fat-free mass index (FFMI) trajectories during childhood to adolescence and pubertal advanced BA. We hypothesize that there exists a longitudinal association between body composition and advanced BA. We suggest a healthy weight and optimal body fat level may help prevent the occurrence of advanced BA and benefit the long-term physical growth of Chinese children.

2. Materials and methods

2.1. Study design and participants

The PROC study enrolled 1914 children aged 6–8 years from six non-boarding primary schools in Beijing in 2018 (details of recruitment have been published previously [16,17], https://www.chictr.org.cn/index.html, unique identifier: ChiCTR2100044027, official website: https://www.procstudy.com). All participants accepted three waves of repeated anthropometry, body composition measurements, and sociodemographic questionnaires between October 2018 and April 2023. In the third wave, participants had pubertal examination, BA radiography, and relevant questionnaires (Fig. 1). The study involved human participants, was conducted in accordance with the Declaration of Helsinki, and was approved by the Ethics Committee of Capital Medical University (No. 2018SY82).

2.2. Anthropometrics and body composition measurements

We conducted anthropometrics and body composition measurements three waves. (1) height: A mechanical height meter was employed to ascertain the height of participants while standing barefoot and wearing light clothing. The two height measurements

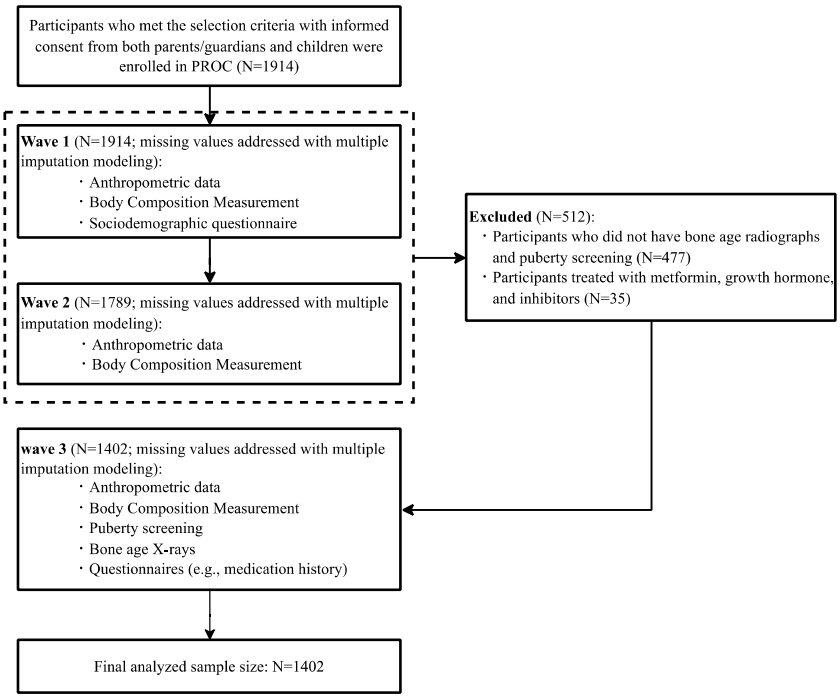

Fig. 1. Flowchart of the procedure for the study.

were subsequently averaged and recorded in the body composition machine to obtain body composition measurements. (2) weight and body composition measurements: We measured bioelectrical impedance with an H-Key350 body composition analyzer (Beijing Seehigher Technology Co., Ltd., Beijing, China) to assess participants' body composition (visceral fat area, body fat mass and fat-free mass) and weight at baseline (wave 1). The InBody 770 body composition analyzer (InBody Co., Ltd, Seoul, KOREA) was employed to assess body composition and weight during the first and second follow-up visits (wave 2 and wave 3) per the instrument protocol. (3) BMI, FMI and FFMI: BMI is calculated as weight/height^2. The BMI and BMI z-score were calculated according to Chinese children and adolescent growth charts [18]. Fat mass index (FMI) = body fat mass/height^2, the unit is kg/m^2. Fat-free mass index (FFMI) = fat-free mass/height^2, the unit is kg/m^2. The FMI and FFMI assess the nutritional status of participants [19].

2.3. Skeletal maturation

X-rays of the left hand and wrist were taken with a portable digital X-ray machine (Hangzhou Canglan Medical Technology Co., Ltd., Zhejiang, China). The researcher helped the children position their left palm facing down on the film. The axis of the middle finger was aligned directly with that of the forearm, and the fingers were naturally separated to remain contact-free. Of note, the device has a built-in shielding system to protect the child, effectively reducing the radiation dose. Skeletal maturation was assessed by comparing the radiographs obtained with the Tanner-Whitehouse 3-Chinese Radius-Ulna-Short (TW3-C RUS) standard [20]. A skilled pediatrician carefully examined the bone morphology of the radius, ulna, and metacarpals (I, III, V), as well as the proximal phalanges (I, III, V), middle phalanges (III, V), and distal phalanges (I, III, V) using the TW3-C RUS standard, and then determined the BA of each participant. The difference between BA and CA within the range of −1 and 1 was defined as normal BA, while a difference exceeding 1 was defined as advanced BA [21].

2.4. Data collection of covariates

(1) Sociodemographic surveys: Participants' parents completed a survey with sociodemographic information conducted by Wenjuanxing® (Changsha RanXing Information Technology Co., Ltd., Changsha, China) software. We obtained parental heights and calculated the children's genetic height in centimeter. Boys' genetic height= (father's height + [mother's height+13])/2. Girls' genetic height= ([father's height–13]+mother's height)/2 [22]. (2) Assessment of pubertal development: pubertal stages were assessed through physical examination using the 5-stage scale defined by Marshall and Tanner [23,24]. Two pediatric specialists, one male and one female, evaluated the Tanner stages, which included genitalia stage (G1-G5) and testicular volume (TV1-TV5) for boys and breast stage (B1–B5) for girls, and pubic hairs stage (PH1-PH5) for both sexes. Genitalia stage and breast stage were determined through visual inspection and palpation. Testicular volume was estimated using a Prader orchidometer, and the larger measurement was recorded if the testicular volumes of the two testes were unequal. Similarly, the same protocol was applied to breast measurement. Pubic hair stage was assessed by visual inspection. Age at menarche for girls and age at voice change for boys were accurately obtained through the physical examination. Tanner stages were defined as Tanner I (pre-puberty), Tanner II (onset), Tanner III (on-going), Tanner IV (nearly complete) or Tanner V (complete and adult-like). Testicular volume was categorized as TV1: <4 ml, TV 2: 4–8 ml, TV 3: 10–12 ml, TV 4:15–20 ml and TV 5:≥20 ml. Tanner's five stages of puberty were simplified into three phases of pre-puberty (Tanner I), in puberty (Tanner II and Tanner III), and completing puberty (Tanner IV and Tanner V) [25]. (3) Medication history survey: parents were surveyed to determine if their child had a history of medication use, such as metformin, growth hormone, and inhibitors. Meanwhile, during the puberty examination, the doctor asked about a history of medications such as metformin, growth hormone, and depressants that had been used or were being used to valid the survey results. A history of medications that affect bone growth or pubertal development is determined based on either the response to the survey or the results of the child's medication history reporting during the pubertal assessment. It is judged as yes if either or both indicate a history of relevant medications. Children with a history of medication use were excluded.

2.5. Statistical analysis

Descriptive statistics were presented by sex and survey waves. Tanner stage of genitals, Tanner stage of breasts in girls, Tanner stage of PH, Tanner stage, and TW3-C RUS groups are presented as counts and percentages. Height, weight, BMI z-score, parental height, genetic height, TV, BA, VFA, FMI, and FFMI are described as mean ± standard deviation. Student t-test was used to examine sex differences in height, weight, BMI z-score, parental height, genetic height, VFA, FMI, and FFMI. Standardized VFA, FMI, and FFMI were calculated by sex and each year group using SAS PROC STDIZE procedure. We generated generalized linear regression models (GLM) to determine the associations between BMI z-score, VFA z-score, FMI z-score, FFMI z-score, and BA with estimated coefficients and 95 % confidence intervals (CI).

The SAS PROC TRAJ procedure was used for latent category modeling to separate the participants by categorizing the trajectories of the BMI z-score, the VFA z-score, the FMI z-score, and the FFMI z-score separately using three waves of data from the PROC study to estimate a discrete mixture model for clustering of longitudinal data series. Groups may represent distinct subpopulations or alternatively, components of a discrete approximation for a potentially complex data distribution [26]. The optimal model was determined based on the process described by Andruff et al. to select the number of categorical activity trajectories and their respective shape (e.g., linear, quadratic, or cubic) [27]. Two categories were identified based on the best modeling of BMI z-score, VFA z-score, FMI z-score, and FFMI z-score. These categories were labeled as the 'low group' and the 'high group'. For BMI z-score, the 'low group' followed a linear trajectory, while the 'high group' followed a cubic trajectory. For VFA z-score, both the 'low group' and the 'high group' were

modeled with cubic trajectories. For FMI z-score, the 'low group' exhibited a linear shape, while the "high group" followed a quadratic shape. Similarly for FFMI z-score, both groups were modeled with quadratic quadratic trajectories. The probability of group trajectory membership for each individual's BMI z-score, VFA z-score, FMI z-score, and FFMI z-score was determined based on their average z-score across all available time points. Sex was adjusted for in the all four trajectory models.

GLM was used to analyze the relationship between different trajectory groups of BMI z-score, VFA z-score, FMI z-score, and FFMI z-score and BA. Logistic regression models were used to determine the associations between different trajectory groups of BMI z-score, VFA z-score, FMI z-score, and FFMI z-score and advanced BA with crude and adjusted ratios (cOR and aOR) and 95 % CI. Multivariate models were adjusted for sex, age at wave 3, genetic height, and pubertal stage. The number of multiply imputed datasets was selected based on the maximum fraction of incomplete observations [28]. This fraction ranged from 3.6 % to 20 %, suggesting that we needed imputed datasets≥20, so we chose M = 20 as the number of multiply imputed datasets required. Each of the imputed datasets was analyzed separately and then the resulting point estimates and standard errors from each imputed dataset were combined (pooled) using Rubin's rules implemented in PROC MIANALY [29]. Statistical significance was determined using a two-tailed p value of 0.05. All analyses were performed using Statistical Analysis System V.9.4 M3 (SAS Institute Inc., Cary, NC, USA). Fig. 2 was produced using the GraphPad Prism software version 9.0.

3. Results

3.1. Sociodemographic characteristics

We observed significant sex differences in height z-score, weight z-score, BMI z-score, genetic height, VFA, FMI, and FFMI at baseline among 1914 children enrolled from the PROC study. Similarly, there were significant sex differences in BMI z-score, genetic height, VFA, FMI, and FFMI at the first follow-up (wave 2), and in weight z-score, BMI z-score, genetic height, VFA, FMI, and FFMI at the second follow-up (wave 3). BMI z-score, VFA, FMI, and FFMI increased from 0.7 ± 1.4, 26.0 ± 21.5 cm^2, 3.9 ± 2.3 kg/m^2, and 12.8 ± 1.0 kg/m^2 at wave 1, to 0.9 ± 1.5, 46.2 ± 33.2 cm^2, 5.2 ± 2.9 kg/m^2, and 13.1 ± 1.2 kg/m^2 at wave 2, respectively. At wave 3, BMI

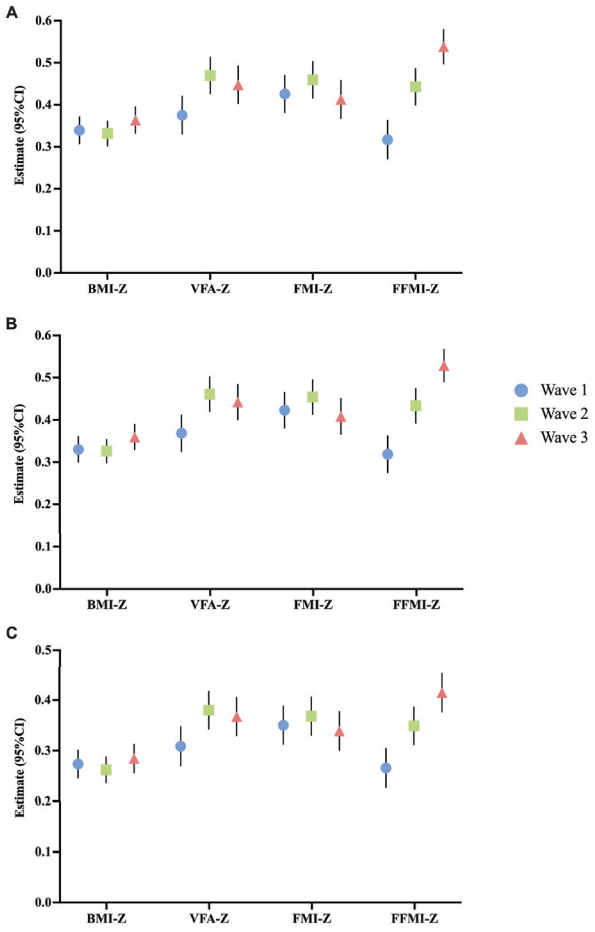

Fig. 2. Association between BMI-z score, VFA-z score, FMI-z score, and FFMI-z score at three waves, and BA at wave 3. (A) Model 1: unadjusted; (B) Model 2: adjusted sex and age of wave 3; (C) Model 3: adjusted sex, age of wave 3, genetic height and Tanner stage.

z-score, VFA, FMI, and FFMI were 1.1 ± 1.3, 71.9 ± 44.7 cm^2, 6.5 ± 3.3 kg/m^2 and 14.5 ± 1.6 kg/m^2, respectively, and the same pattern of increase was also demonstrated in boys and girls (Table 1). We performed the pubertal examination and BA radiographs at wave 3. Among 1402 participants, there were 400 (55.8 %) boys in G2 stage, 589 (82.1 %) in PH1 stage, 54 had changed voice, and the average TV size was 5.7 ± 4.1 ml. There were 248 (36.2 %) girls in B4 stage and 239 (34.9 %) in PH2 stage, and 260 already had their menarche. Only 6 (0.8 %) boys and 11 (1.6 %) girls not entered puberty. In boys and girls, the average BA was 12.0 ± 0.9 years and 11.6 ± 0.9 years, respectively, and the rate of advanced BA was 40.9 % and 21.2 %, respectively (Table 2).

3.2. Relationship between BMI z-score, VFA z-score, FMI z-score, FFMI z-score at three waves and pubertal BA

BMI z-score, VFA z-score, FMI z-score, and FFMI z-score were significantly associated with pubertal BA. After adjusting for sex and age at each wave, the FMI z-score had the largest effect on BA at wave 1, i.e., for each increase in FMI z-score by 1 SD, BA increased by 0.42 years ($\beta = 0.42$; 95 % *CI*: 0.38, 0.46). This was followed by the VFA z-score, which increased BA by 0.37 years per 1 SD increase ($\beta = 0.37$; 95 % *CI*: 0.33, 0.41). At wave 2, the VFA z-score had the largest effect on BA, which was 0.46 years per 1 SD increase ($\beta = 0.46$; 95 % *CI*: 0.42, 0.50), then followed by FMI z-score with 0.45 years per 1 SD increase ($\beta = 0.45$; 95 % *CI*: 0.41, 0.50). At wave 3, the FFMI z-score had the largest effect on BA, which was 0.53 years per 1 SD increase ($\beta = 0.53$; 95 % *CI*: 0.49, 0.57), then followed by the VFA z-score with 0.44 years per 1 SD increase ($\beta = 0.44$; 95 % *CI*: 0.40, 0.48). Further adjusting for genetic height and Tanner stage, the results remained consistent with model 2. FMI z-score, VFA z-score, and FFMI z-score were found to be the most influential indicators of pubertal BA at wave 1, wave 2, and wave 3, respectively. For each 1 SD increase in these three indicators, pubertal BA increased by 0.35 ($\beta = 0.35$; 95 % *CI*: 0.31, 0.39), 0.38 ($\beta = 0.38$; 95 % *CI*: 0.34, 0.42), and 0.41 ($\beta = 0.41$; 95 % *CI*: 0.38,0.45) years, respectively (Fig. 2A–C).

3.3. Linear associations of BMI z-score, VFA z-score, FMI z-score, and FFMI z-score trajectories and pubertal BA

Trajectory fitting model was performed for each of the four anthropometric indicators, after adjusting for sex, children were categorized into two trajectory groups. The proportions of children in the low BMI-z score, low VFA-z score, low FMI-z score, and low

Table 1
Sociodemographic characteristics of the children from PROC in Beijing, China.

Characteristics	All	Boys	Girls	*p*
Wave 1 (in 2018)				
N (%)	1914 (100)	956 (49.9)	958 (50.1)	
Age (year)	6.7 ± 0.3	6.7 ± 0.3	6.6 ± 0.3	0.145
Height z-score	0.3 ± 1.0	0.4 ± 1.0	0.3 ± 1.0	0.019
Weight z-score	0.7 ± 1.4	0.8 ± 1.4	0.6 ± 1.3	0.002
BMI z-score	0.7 ± 1.4	0.7 ± 1.4	0.6 ± 1.3	0.015
Father height (cm)	174.8 ± 5.1	174.8 ± 5.0	174.8 ± 5.2	0.952
Mother height (cm)	161.9 ± 4.9	161.9 ± 5.2	161.9 ± 4.6	0.868
Genetic height (cm)	168.3 ± 7.6	174.8 ± 3.9	161.8 ± 3.9	<0.001
Visceral fat area (cm^2)	26.0 ± 21.5	27.5 ± 24.4	24.4 ± 17.9	0.001
Body fat mass index (kg/m^2)	3.9 ± 2.3	4.0 ± 2.5	3.8 ± 2.0	0.009
Fat-free mass index (kg/m^2)	12.8 ± 1.0	13.2 ± 1.0	12.5 ± 0.8	<0.001
Wave 2 (in 2020)				
N (%)	1789 (100)	890 (49.7)	899 (50.3)	
Age (year)	8.5 ± 0.3	8.6 ± 0.3	8.5 ± 0.3	0.226
Height z-score	0.5 ± 1.0	0.5 ± 1.0	0.5 ± 1.0	0.535
Weight z-score	0.9 ± 1.4	0.9 ± 1.3	0.8 ± 1.4	0.178
BMI z-score	0.9 ± 1.5	1.0 ± 1.5	0.8 ± 1.4	0.003
Father height (cm)	174.7 ± 5.1	174.7 ± 5.0	174.8 ± 5.2	0.665
Mother height (cm)	161.9 ± 4.9	161.9 ± 5.3	161.9 ± 4.5	0.952
Genetic height (cm)	168.3 ± 7.5	174.8 ± 3.9	161.8 ± 3.8	<0.001
Visceral fat area (cm^2)	46.2 ± 33.2	51.1 ± 37.0	41.3 ± 28.1	<0.001
Body fat mass index (kg/m^2)	5.2 ± 2.9	5.7 ± 3.2	4.7 ± 2.5	<0.001
Fat-free mass index (kg/m^2)	13.1 ± 1.2	13.6 ± 1.2	12.7 ± 1.1	<0.001
Wave 3 (in 2023)				
N (%)	1402 (100)	717 (51.1)	685 (48.9)	
Age (year)	11.1 ± 0.3	11.1 ± 0.3	11.1 ± 0.3	0.604
Height z-score	0.9 ± 1.0	0.9 ± 1.0	0.8 ± 1.0	0.086
Weight z-score	1.1 ± 1.2	1.2 ± 1.3	1.0 ± 1.2	0.001
BMI z-score	1.1 ± 1.3	1.2 ± 1.3	0.9 ± 1.3	0.001
Father height (cm)	174.9 ± 5.0	174.8 ± 5.0	175.1 ± 5.0	0.392
Mother height (cm)	162.0 ± 4.8	162.0 ± 5.1	162.0 ± 4.6	0.865
Genetic height (cm)	168.6 ± 7.5	174.9 ± 3.9	162.0 ± 3.7	<0.001
Visceral fat area (cm^2)	71.9 ± 44.7	79.9 ± 49.3	63.5 ± 37.4	<0.001
Body fat mass index (kg/m^2)	6.5 ± 3.3	7.1 ± 3.6	5.8 ± 2.8	<0.001
Fat-free mass index (kg/m^2)	14.5 ± 1.6	14.9 ± 1.6	14.1 ± 1.6	<0.001

Note: Wave 1: at baseline; wave 2: follow-up 1; wave 3: follow-up 2.

Table 2
Distribution of the Tanner staging and BA outcomes among 11-13-year-old children in Beijing, China (N = 1402).

Index	Boys	Girls
Secondary sexual characteristic*		
G1/B1	6 (0.8)	11 (1.6)
G2/B2	400 (55.8)	108 (15.8)
G3/B3	248 (34.6)	228 (33.3)
G4/B4	60 (8.4)	248 (36.2)
G5/B5	3 (0.4)	90 (13.1)
PH1	589 (82.1)	161 (23.5)
PH2	63 (8.8)	239 (34.9)
PH3	48 (6.7)	164 (23.9)
PH4	15 (2.1)	101 (14.7)
PH5	2 (0.3)	20 (2.9)
TV (ml)	5.7 ± 4.1	–
Menarche or voice change*		
Yes	54 (7.5)	260 (38.0)
No	663 (92.5)	425 (62.0)
Tanner stage*		
Pre-puberty	6 (0.8)	11 (1.6)
In puberty	623 (86.9)	334 (48.8)
Completing puberty	88 (12.3)	340 (49.6)
TW3-C RUS (year)	12.0 ± 0.9	11.6 ± 0.9
TW3-C RUS group*		
Normal BA	424 (59.1)	540 (78.8)
Advanced BA	293 (40.9)	145 (21.2)

Note: G: genitalia; G#: stage of genitalia. G1: testes, scrotum, and penis are of about the same size and proportion as in early childhood.; G2: testes and scrotum have enlarged and there is a change in the texture of the scrotal skin; G3: growth of the penis has occurred and there has been further growth of testes and scrotum; G4: penis further enlarged in length and breadth with development of glans. Testes and scrotum further enlarged. There is also further darkening of the scrotal skin; G5: genitalia adult in size and shape. B: breast; B#: stage of breast. B1: elevation of papilla only; B2: elevation of breast and papilla as a small mound, enlargement of areola diameter; B3: further enlargement of breast and areola, with no separation of their contours; B4: projection of areola and papilla to form a secondary mound above the level of the breast; B5: mature stage; projection of papilla only, due to recession of the areola to the general contour of the breast. PH: pubic hair; PH#: stage of pubic hair. PH1: no pubic hair; PH2: sparse growth of long, slightly pigmented, downy hair, straight or only slightly curled, appearing chiefly along the labia; PH3: considerably darker, coarser, and more curled. The hair spreads sparsely over the junction of the pubes; PH4: hair is now adult in type, but the area covered by it is still considerably smaller than in most adults; PH5: adult like in quantity and type, distributed as an inverse triangle of the classically feminine pattern; TV: testicular volume [30]; BA: bone age; * counts and percentages.

FFMI-z score groups were 56.4 %, 80.2 %, 71.9 %, and 64.9 %, respectively. The proportions of children in the high BMI-z, high VFA-z, high FMI-z, and high FFMI-z groups were 43.6 %, 19.8 %, 28.1 %, and 35.1 %, respectively. (Figs. S1A–D). Generalized linear models determined that associations existed between different trajectory groups of BMI z-score, VFA z-score, FMI z-score, FFMI z-score, and pubertal BA. Unadjusted model 1, adjusted model 2 (adjusted for sex and age of wave 3), and adjusted model 3 (adjusted for sex, age of

Table 3
Associations of BMI z-score, VFA z-score, FMI z-score, and FFMI z-score trajectories and BA using generalized linear models among 6–13-year-old children in Beijing, China (N = 1402).

Independent variables	Model 1		Model 2		Model 3	
	β (95%CI)	p	*β* (95%CI)	p	*β* (95%CI)	p
BMI z-score						
Low group	Ref.		Ref.		Ref.	
High group	0.73 (0.64, 0.81)	<0.001	0.71 (0.63, 0.79)	<0.001	0.58 (0.51, 0.66)	<0.001
VFA z-score						
Low group	Ref.		Ref.		Ref.	
High group	0.84 (0.73, 0.95)	<0.001	0.83 (0.73, 0.93)	<0.001	0.71 (0.62, 0.80)	<0.001
FMI z-score						
Low group	Ref.		Ref.		Ref.	
High group	0.76 (0.66, 0.85)	<0.001	0.74 (0.65, 0.83)	<0.001	0.61 (0.53, 0.69)	<0.001
FFMI z-score						
Low group	Ref.		Ref.		Ref.	
High group	0.71 (0.62, 0.80)	<0.001	0.69 (0.61, 0.78)	<0.001	0.53 (0.46, 0.61)	<0.001

Model 1: crude model; Model 2: adjusted sex and age at wave 3; Model 3: adjusted sex, age at wave 3, genetic height, and Tanner stage.

wave 3, genetic height, and Tanner stages) showed a greater pubertal BA in the high trajectory group compared with the low trajectory group for BMI z-score, VFA z-score, FMI z-score, and FFMI z-score. Among the high trajectory groups for all four indicators, the VFA z-score exhibited the most robust association with elevated BA (adjusted model 3: $\beta = 0.71$; 95 % *CI*: 0.62, 0.80, $p < 0.001$). Following this, the next most notable association was observed with the FMI z-score (adjusted model 3: $\beta = 0.61$; 95 % *CI*: 0.53, 0.69, $p < 0.001$) (refer to Table 3).

3.4. Association of BMI z-score, VFA z-score, FMI z-score, and FFMI z-score trajectories with advanced BA

Further logistic regression showed that each a high trajectory group of BMI z-score, VFA z-score, FMI z-score, and FFMI z-score was associated with an increased risk of pubertal advanced BA. In unadjusted model 1, adjusted model 2 (adjusted for sex and age of wave 3), and adjusted model 3 (adjusted for sex, age of wave 3, genetic height, and Tanner stage) showed that high VFA z-score (adjusted model 3: aOR = 6.73; 95 % *CI*: 4.87, 9.31, $p < 0.001$) was the most significant risk factor for advanced BA in the high trajectory group, followed by high BMI (adjusted model 3: aOR = 5.57; 95 % *CI*: 4.20, 7.39, $p < 0.001$) (Table 4).

4. Discussion

This study used relatively large longitudinal data from a general Chinese pediatric population to examine the association between BMI and body composition trajectories (VFA, FMI and FFMI) in childhood and skeletal maturation at puberty. We found that children with consistently high BMI z-score, VFA z-score, FMI z-score and FFMI z-score trajectories from childhood were more likely to develop advanced BA. After adjustment for sex, age, genetic height and Tanner stage, the risk of advanced BA was 6.73 and 5.57 times higher in children with a consistently high VFA z-score or consistently high BMI z-score, respectively, than in those with a low VFA z-score or low BMI z-score. This finding highlights the need to maintain normal visceral fat mass and body weight from childhood to reduce the increased risk of advanced BA during puberty.

First, our research found that the BMI z-score, VFA, FMI and FFMI of the study participants increased over time and were higher in boys than in girls. This finding was consistent with a US study on body composition in Asian children and adolescents aged 5–18 years [31]. However, the FMI of boys showed an increase in childhood and a decrease in adolescence in another American study [32]. Inconsistent results from studies of changes in body composition in different children and adolescents may be due to differences in study design (cross-sectional v.s cohort studies), variations in ethnicity, and the methods used to measure body composition. There are few studies of VFA changes among children and adolescents in body composition studies so far. A Japanese study that measured VFA in children and adolescents aged 6–17 years showed that boys had greater VFA than girls and that boys were more likely to accumulate VFA [33], which is consistent with the results of our study. The prevalence of advanced BA in present study was 40.9 % in boys and 21.2 % in girls, which was higher than the prevalence of advanced BA in an Australian study of boys and girls aged 10–13 years, where the number of people with delayed BA was higher, especially in boys [34]. This is probably because the rate of advanced BA is not uniform across countries due to differences in health conditions, nutrition status, and socio-economic and political environments, which are intricately linked to the long-term trend patterns in skeletal maturity [35].

Second, we performed linear correlation analyses between pubertal BA and three times BMI z-score, VFA z-score, FMI z-score, and FFMI z-score. The unadjusted models and after adjusting for covariates (sex, age, genetic height, and Tanner stage) both showed consistent positive correlations between pubertal BA and three times BMI z-score, VFA z-score, FMI z-score, and FFMI z-score. Nutrition status has always been known to be important for bone health and development [36]. Previous studies have found that weight gain or increased fat during childhood is associated with accelerated bone growth [4,37,38], but fewer studies have examined the relationship between change of fat mass and BA, the mechanism by which fat mass affects BA is not clear and more complex [39]. Recent study has suggested that fat mass influences bone maturation may be through hormones [40,41]. Higher fat mass was

Table 4
Associations of BA with BMI z-score, VFA z-score, FMI z-score, and FFMI z-score trajectories subgroups using Logistic regression models among 6–13-year-old children in Beijing, China (N = 1402).

Independent Variables	Model 1		Model 2		Model 3	
	cOR (95%CI)	*p*	aOR (95%CI)	*p*	aOR (95%CI)	*p*
BMI z-score						
Low group	Ref.		Ref.		Ref.	
High group	5.31 (4.15, 6.08)	<0.001	5.25 (4.07, 6.75)	<0.001	5.57 (4.20, 7.39)	<0.001
VFA z-score						
Low group	Ref.		Ref.		Ref.	
High group	6.24 (4.69, 8.30)	<0.001	6.55 (4.86, 8.81)	<0.001	6.73 (4.87, 9.31)	<0.001
FMI z-score						
Low group	Ref.		Ref.		Ref.	
High group	5.02 (3.91, 6.46)	<0.001	5.21 (4.02, 6.76)	<0.001	5.18 (3.91, 6.88)	<0.001
FFMI z-score						
Low group	Ref.		Ref.		Ref.	
High group	4.47 (3.51, 5.70)	<0.001	4.91 (3.80, 6.33)	<0.001	4.34 (3.30, 5.73)	<0.001

Model 1: crude model; Model 2: adjusted sex and age at wave 3; Model 3: adjusted sex, age at wave 3, genetic height, and Tanner stage.

associated with higher serum leptin concentrations, which affects pubertal onset by permissive activation of the GnRH pulse generator via signaling of adequate energy stores, leading to higher sex hormone levels, earlier pubertal onset and accelerated bone growth [42,43]. Similarly, another study on the relationship between hormones and growth in preschool children found that adipose tissue in overweight/obese children may lead to an increase in growth hormone and IGF-1, potentially affecting skeletal maturation [44].

Finally, we classified the trajectory model results into low and high trajectory groups based on BMI z-score, VFA z-score, FMI z-score and FFMI z-score. After adjusting for sex, age, genetic height, and Tanner stage, the risk of advanced BA was greater in the high trajectory group of the four metrics compared to the low trajectory group, with the high trajectory group of the VFA z-score as the most accurate predictor of the risk of advanced BA among the four metrics. It showed the accuracy of some studies that overweight and obesity is one of the major causes of advanced BA [10,44], and more importantly, VFA was one of the significant indicators of abdominal obesity [16], which also showed that abdominal obesity in childhood has an independent effect on advanced BA in puberty. Notably, although the high trajectory group of VFA z-score overwhelms BMI z-score in predicting advanced BA, suggesting that BMI failed to discriminate between the amount of fat in children and adolescents given unclear fat distribution [15]. However, we recommend that in primary care or home health care where body composition equipment is not available, continuous monitoring of changes in BMI from childhood and maintaining BMI within the normal range may still reduce the risk of advanced BA in puberty.

The strengths of this study include its cohort design and the use of repeated measures for anthropometric and body composition data. The repeated measures enhances the study's robustness, allowing for a comprehensive examination of changes spanning from childhood to puberty. We used a portable BA device to facilitate BA photography, reduced radiation exposure and obtained BA radiographs quickly. Our study also has limitations. First, bioelectrical impedance analysis (BIA) has been reported to underestimate fat mass compared with the accepted four-compartment model of body fat percentage. In addition, compared with quantitative computed tomography (QCT), which can precisely distinguish between subcutaneous and visceral fat [45], BIA uses a specific algorithm to estimate visceral fat that is not as accurate as QCT [46]. However, the four-compartment model and QCT face challenges when applied in large-scale epidemiologic studies because of their high cost, technical complexity, and the presence of radiation in QCT [15]. Despite these limitations, BIA is commonly used in large-scale epidemiologic studies due to its cost-effectiveness, radiation-free, quick and easy execution, and widespread acceptance among children and adolescents [47]. It has been successfully used to assess childhood overweight/obesity in many countries, including China [48], Mexico [49], and Thailand [50] and demonstrating high consistency with QCT. Second, we used different models of body composition instruments at baseline and follow-up, potentially introducing bias. Although we conducted controlled experiments with both models of devices using the same cohort of children, and the test results showed a high degree of agreement between the two models, confounding factors may still be present. Third, BA and pubertal measurements were taken only once in our study. Fourth, our study was conducted on a single-center Chinese urban pediatric cohort, thus the results may need external validation.

5. Conclusions

We examined the association between body composition trajectories from childhood and pubertal skeletal maturity in Chinese children. Our findings indicate that children with consistently high VFA z-score from childhood exhibited a greater likelihood of advanced BA during puberty, which overwhelms the traditional BMI z-score to predict the risk of advanced BA. These findings underscore early monitoring and maintaining normal VFA levels in children. Furthermore, it is crucial to monitor BMI from an early stage and ensure it remains within normal ranges in primary care or home monitoring, even in the absence of specialized body composition equipment, due to the strong association between VFA and BMI.

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Ethics declarations

The study involved human participants and was conducted per the Declaration of Helsinki and was approved by the Ethics Committee of Capital Medical University (No. 2018SY82). All participants provided informed consent to participate in the study.

Data availability statement

The data that support the findings of this study are not publicly available but are available from the corresponding author (Y.H.) upon reasonable request.

CRediT authorship contribution statement

Wen Shu: Writing – original draft, Software, Methodology, Formal analysis, Data curation. **Menglong Li:** Validation, Methodology, Data curation. **Sten H. Vermund:** Writing – review & editing. **Hui Li:** Writing – review & editing, Conceptualization. **Yifei Hu:**

Writing – review & editing, Resources, Project administration, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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