Bone 46 (2010) 336–341

Contents lists available at ScienceDirect

Bone

journal homepage: www.elsevier.com/locate/bone

Peak bone mineral density, lean body mass and fractures

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ARTICLE INFO

Article history:
Received 23 April 2009
Revised 15 September 2009
Accepted 5 October 2009
Available online 13 October 2009

Edited by: R. Recker

Keywords:
Peak bone mass
Lean body mass
Fractures
Bone mineral density
Children

ABSTRACT

Background: During childhood and adolescence, bone mass and lean body mass (LBM) increase till a plateau is reached. In this longitudinal and cross-sectional study, the age of reaching the plateau was evaluated for lumbar spine and total body bone mass measurements and lean body mass. The association between fractures and bone mineral density (BMD) was studied.

Patients and methods: We included 501 healthy participants, 141 males and 360 females, aged 13–29 years. Of these 90 had participated in a previous longitudinal study of 444 participants, aged 4–20 years (for the first measurement) and 198 participants, aged 8–25 years (for a second measurement). BMD and body composition were measured with dual energy X-ray absorptiometry (DXA). Volumetric BMD (bone mineral apparent density, BMAD) was calculated. All the data were used to determine the age of reaching the plateau.

Results: The plateau for lumbar spine BMD, BMAD, total body BMD, bone mineral content and LBM was reached between 18 and 20 years of age in females and between 18 and 23 years in males. The prevalence of fractures was 37% in males and 28% in females. Total body BMD *Z*-score was significantly lower in all participants who had had a fracture ($p<0.05$), whereas lumbar spine BMD and BMAD was only significantly lower in females who had had fractures ($p=0.007$ and $p<0.001$, respectively). Mean lumbar spine BMAD Z-score at the previous measurement was significantly lower in the participants who had a first fracture between the last two measurements ($p=0.04$).

Conclusion: Peak BMD and peak LBM were attained between 18 and 20 years in females and between 18 and 23 years in males in this study using longitudinal and cross sectional data in the age range of 4 to 30 years. A significantly lower total body BMD was seen in participants who had had a fracture and a lower lumbar spine BMD and BMAD in females who had had a fracture. Lumbar spine BMAD *Z*-score seems to be a good predictor for future fractures.

Introduction

Osteoporosis is a major public health problem mainly involving postmenopausal women and older people. A low bone mass is an important risk factor for osteoporosis. Bone mass later in life is determined by the peak bone mass acquired during adolescence and the subsequent rate of bone loss. Because building up an adequate bone mass during childhood is essential for preventing osteoporosis, it is important to investigate peak bone mass.

During childhood and adolescence, bone mass increases till a plateau is reached, the peak bone mass. The age at which peak bone mass is attained may vary according to sex, type of measurement (dual energy X-ray absorptiometry (DXA) or computed tomography (CT)), and skeletal site [1–4]. CT measurements showed that vertebral bone mineral content (BMC) and bone mineral density (BMD) reached their peak around the time of sexual maturity and cessation of longitudinal growth in females [1]. Studies using DXA reported that peak lumbar spine volumetric BMD was attained in girls around 16 years and in boys around 18 years [3,5]. Areal BMD may increase till a later age because certain bones continue to increase in size [1,4,6]. About 85–90% of final adult bone mass is acquired by the age of 18 years in girls and 20 years in boys [4]. These were cross-sectional studies.

Bone strength is regulated by mechanical loads, especially muscle forces. In children and adolescents, lean body mass (LBM) and bone mass are highly related [7,8]. There are no data on the age of peak LBM.

We aimed to evaluate the age at which the plateau of BMD, volumetric BMD, BMC en LBM measured by DXA is attained.

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doi:10.1016/j.bone.2009.10.003

Previously, we reported the volumetric BMD, BMD and BMC of healthy children aged 4 to 20 years, with a second measurement made after 4 years, but we could not draw a conclusion about the age of peak bone mass [9–11]. We have measured 90 of these participants again, along with other young adults aged 20 and 30 years to evaluate the relation of bone mass with age. A new statistical model using longitudinal and cross sectional data was used to evaluate the peak bone mass and LBM. The association between prevalent and incident fractures and BMD was evaluated.

Subjects and methods

Subjects

In the first study 444 Caucasian children participated (188 boys and 256 girls), aged between 4 and 20 years ($t=1$) [9,10]. After a mean follow-up time of 4.3 years, 198 of them (84 boys and 114 girls) participated in the second study ($t=2$) [11]. Ninety of these (39 males, 51 females) participated in the third study ($t=3$); their mean age was 21.3 years (range 13.3 to 29.3).The mean time between $t2$ and $t3$ was 6.1 years (5.3–7.6). These ninety participants were supplemented with 411 new participants (141 male and 360 female) bringing the total number of participants to 501 for the third study. The mean age of the additional 411 patients was 24.2 years (range 18.3 to 31.0).

The new participants were recruited by advertisements in newspapers, the university and schools. The subjects of the previous studies had been recruited from schools of the city of Rotterdam in different socioeconomic areas [9]. Only Caucasians were included. Exclusion criteria were chronic diseases of kidney, liver or thyroid, diabetes mellitus, cystic fibrosis, metabolic bone disorders, and use of oral corticosteroids, immune suppression or anti-epileptic drugs.

The study was approved by the ethics committee of Erasmus MC Rotterdam and written informed consent was obtained from all participants.

Methods

Height was measured by a fixed stadiometer. Weight was measured without shoes on a standard clinical balance. BMD of the lumbar spine, total body and femoral neck was measured by dual energy X-ray absorptiometry (DXA, Lunar Prodigy). The coefficient of variation has been reported as 1.0% for lumbar spine BMD and 0.73% for total body BMD [12] and 1.5% for femoral neck [13]. Quality assurance was performed daily. Ancillary DXA-derived data were used to calculate lumbar spine volumetric BMD, bone mineral apparent density (BMAD), with the model $BMAD = BMD \times (4/(\pi \times width))$ [14], as reported before [9,11].

BMAD of the femoral neck was estimated assuming the femoral neck to be a cylinder, and calculated as $BMAD = ((BMD)^2 / BMC) \times 4k/\pi$), in which $k=1.5$ cm, the fixed length along the femoral neck [15]. Body composition was measured by the total body measurement of the same apparatus in bone mineral content (BMC), lean tissue mass (LBM in grams) and fat mass, and we determined percentage body fat (pfat). The coefficient of variation was reported for Lunar Prodigy as 1.29% for LBM, 2.59% for fat mass and 0.74% for BMC [16].

In our previous studies, BMD of the lumbar spine and of total body and body composition were measured by DXA (Lunar DPXL). For adolescents the mean difference between the Lunar Prodigy and DPXL machines was reported to be 1.6% or 0.016 g/cm^2 for lumbar spine BMD, which is 0.1 SD for boys and girls of 17 years old [12]. Non-significant differences between the machines were observed for total body BMD, LBM and body fat for the age range of 12 to 20 years [12]. Lunar Prodigy estimates of total body BMC were 3.1% or 66 g higher than the DPXL estimates.

A questionnaire was administered to all participants to determine previous fractures and number and site of fractures. Calcium intake was determined by a detailed food frequency questionnaire of dairy products [17].

Statistical analysis

An appropriate model to fit the measurements of BMD, BMAD, BMC and LBM over the complete age range is the logistic model [11,18]. However, by definition, with this model the maximum is only reached at the age of infinity. We therefore used the following approach.

First a logistic model was fitted to assess the age of the maximum increase. Next, the measurements done at ages higher than this age of maximum increase were selected. We fitted a non-linear model on this selection which was a combination of a parabola and, at the age where the top of the parabola is reached, a horizontal line. Using this model, the mean age at which the plateau is attained and the mean value of the plateau can be determined. Both models were fitted as non-linear mixed models, using a random effect per individual to account for the dependency between measurements on the same individual, since also longitudinal data were used.

A Z-score was calculated by using the reference values of our previous study for measurements at ages below the peak. For ages after the peak, the prediction was used as mean and SD of the variance of the measurements after the peak age. For femoral neck BMD and BMAD no significant association with age was observed and the Z-score was calculated using mean and SD, separately for males and females.

Two sample t-tests were applied to analyze differences between two groups in variables with a normal distribution and paired t-tests for analysis in time. Linear regression analysis was used to adjust for height Z-score. Pearson correlation coefficients were used to analyze the relation between two variables with a normal distribution. One sample t-test was used to test if the mean of a variable with a normal distribution was significantly different from zero.

Results

Clinical characteristics for the participants are shown in Table 1.

Table 1
Clinical characteristics of participants.

	$t=1$		$t=2$		$t=3$	
	$n=444$ (4–20 years)		$n=198$ (8–25 years)		$n=501$ (13–31 years)	
	Male	Female	Male	Female	Male	Female
Number	188	256	84	114	141	360
Age in yrs (SD)	12.1 (4.3)	13.1 (4.1)	14.5 (4.4)	16.0 (4.7)	23.5 (4.0)	23.8 (3.2)
Calcium intake, mg (SD)	1197 (470)	1158 (547)	1190 (618)	975 (496)	1081 (568)	795 (456)
Range	232–3442	93–4356	203–3640	126–3204	171–3835	20–4579
History of fracture	23.4%	18.4%	30.1%	21.6%	36.9%	27.8%

SD mean standard deviation; $t=$ time. Participants were measured at t = 1 and $t=2$. At $t=3$, 90/501 had participated at $t=1$ and $t=2$ and 411 were new.