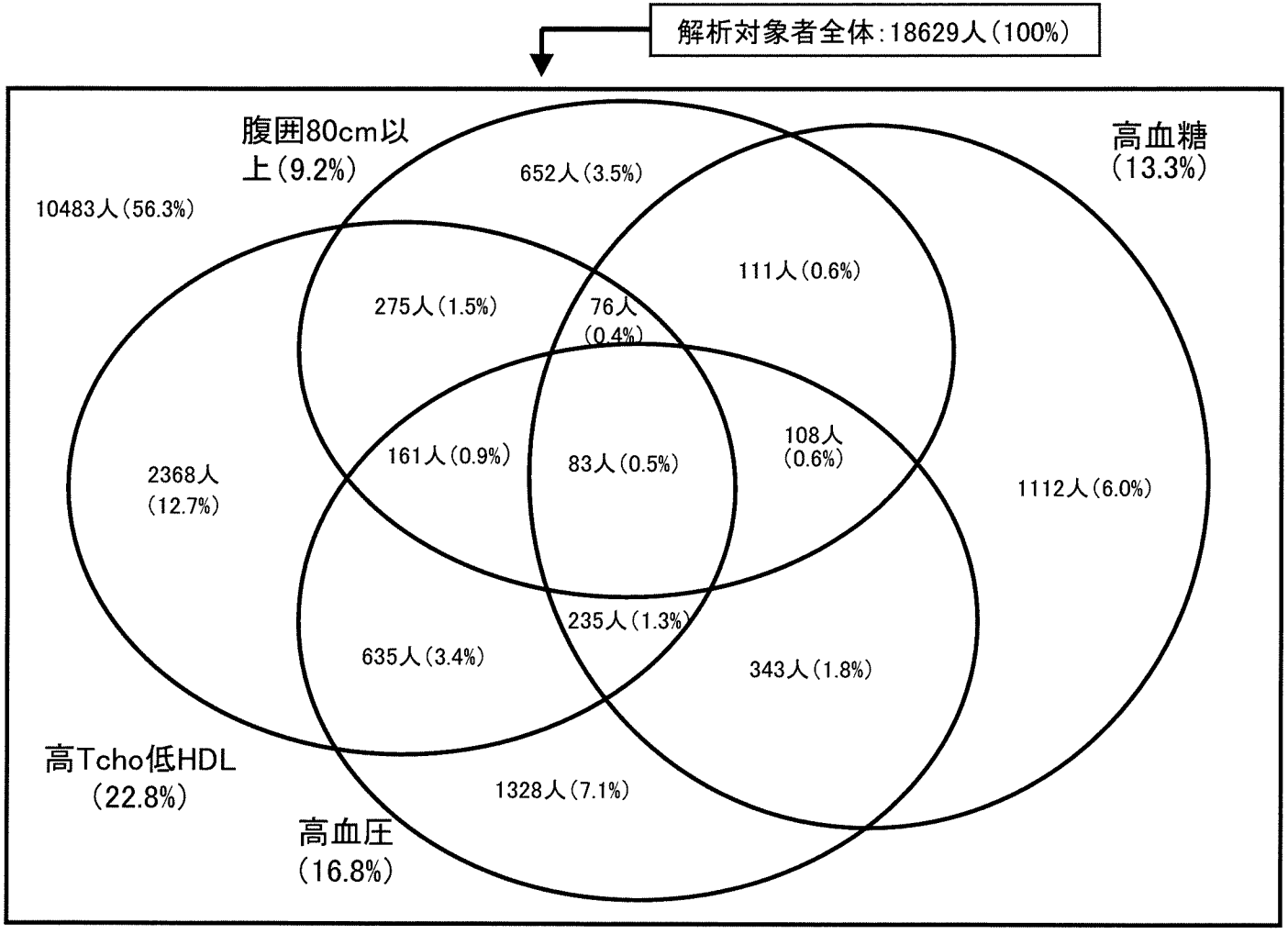

図4　メタボリックシンドロームの各診断項目の分布

表1　メタボリックシンドローム構成項目の有病状況

		40歳未満（6623名）	40歳代（7912名）	50歳以上（4394名）	計（18629名）
腹囲90cm以上者割合（%）		1.2	1.8	3.3	2.0
腹囲85cm以上者割合（%）		2.3	3.9	6.9	4.1
腹囲80cm以上者割合（%）		5.4	9.2	14.5	9.2
腹囲75cm以上者割合（%）		11.5	18.2	24.7	17.4
BMI値25以上者割合（%）		8.7	14.8	18.0	13.5
高血圧者割合（%）[1)]		6.2	15.5	34.5	16.8
高血糖者割合（%）[2)]		7.5	13.2	22.0	13.3
高コレステロール・低HDL者割合（%）[3)]		11.5	20.6	43.0	22.8
メタボリックシンドローム者割合（%）	腹囲基準：90cm	0.3	0.4	1.5	0.6
	腹囲基準：85cm	0.4	0.9	2.6	1.1
	腹囲基準：80cm	0.8	1.8	5.5	2.3
	腹囲基準：75cm	1.1	3.1	8.7	3.7

1）高血圧者：SBP≧130mmHg and /or DBP≧85mmHg
2）高血糖者：空腹時血糖値≧100mg/dL
3）高コレステロール・低HDL者：血清総コレステロール値≧220mg/dL and /or HDLコレステロール値≦40mg/dL

表2　年齢階級別にみたメタボリックシンドローム有病状況

	メタボリックシンドローム		計	χ^2	p
	無し	有り			
	n=18201	n=428	n=18629		
	(%)	(%)	(%)		
年齢階級					
40歳未満(6323人)	99.2	0.8	100.0		
40歳代(7912人)	98.2	1.8	100.0	272.514	<0.0001
50歳以上(4394人)	94.5	5.5	100.0		

表3　メタボリックシンドローム有病状況と飲酒頻度との関係

年齢階級	摂取頻度	メタボリックシンドローム		χ^2	p
		無し n=18201 (%)	有り n=428 (%)		
40歳未満	飲まない	98.9	1.1	5.779	0.2162
	月に1～2日程度	99.2	0.8		
	1回／週	99.7	0.3		
	2回／週	99.3	0.7		
	3回以上／週	99.6	0.4		
40歳代	飲まない	97.5	2.5	10.908	0.0276
	月に1～2日程度	98.5	1.5		
	1回／週	98.1	1.9		
	2回／週	98.8	1.2		
	3回以上／週	98.7	1.3		
50歳以上	飲まない	94.2	5.8	10.697	0.0302
	月に1～2日程度	93.2	6.8		
	1回／週	93.8	6.2		
	2回／週	94.8	5.2		
	3回以上／週	96.4	3.6		
計	飲まない	97.0	3.0	22.104	0.0002
	月に1～2日程度	97.7	2.3		
	1回／週	97.9	2.1		
	2回／週	98.0	2.0		
	3回以上／週	98.4	1.6		

表4　メタボリックシンドローム有病状況と牛肉摂取頻度との関係

年齢階級	摂取頻度	メタボリックシンドローム		χ^2	p
		無し n=18201 (%)	有り n=428 (%)		
40歳未満	まったくとらない	99.3	0.7	1.212	0.7502
	週に1日程度	99.2	0.8		
	週に2～3日	99.2	0.8		
	週に4日以上	100.0	0.0		
40歳代	まったくとらない	98.7	1.3	2.310	0.5107
	週に1日程度	98.1	1.9		
	週に2～3日	98.1	1.9		
	週に4日以上	98.2	1.8		
50歳以上	まったくとらない	94.8	5.2	2.296	0.5134
	週に1日程度	94.3	5.7		
	週に2～3日	95.5	4.5		
	週に4日以上	92.8	7.2		
計	まったくとらない	97.8	2.2	2.233	0.5254
	週に1日程度	97.6	2.4		
	週に2～3日	98.0	2.0		
	週に4日以上	97.6	2.4		

表5　メタボリックシンドローム有病状況と豚肉摂取頻度との関係

年齢階級	摂取頻度	メタボリックシンドローム		χ^2	p
		無し n=18201 (%)	有り n=428 (%)		
40歳未満	まったくとらない	99.4	0.6	0.302	0.9596
	週に1日程度	99.2	0.8		
	週に2～3日	99.2	0.8		
	週に4日以上	99.1	0.9		
40歳代	まったくとらない	98.4	1.6	1.246	0.7419
	週に1日程度	98.1	1.9		
	週に2～3日	98.4	1.6		
	週に4日以上	98.4	1.6		
50歳以上	まったくとらない	96.3	3.7	5.202	0.1576
	週に1日程度	94.0	6.0		
	週に2～3日	94.7	5.3		
	週に4日以上	96.1	3.9		
計	まったくとらない	98.0	2.0	9.814	0.0202
	週に1日程度	97.3	2.7		
	週に2～3日	98.0	2.0		
	週に4日以上	98.1	1.9		

表6　メタボリックシンドローム有病状況と鶏肉摂取頻度との関係

年齢階級	摂取頻度	メタボリックシンドローム		χ^2	p
		無し n=18201	有り n=428		
		(%)	(%)		
40歳未満	まったくとらない	99.4	0.6	0.747	0.8621
	週に1日程度	99.3	0.7		
	週に2～3日	99.2	0.8		
	週に4日以上	98.8	1.2		
40歳代	まったくとらない	98.1	1.9	0.809	0.8472
	週に1日程度	98.3	1.7		
	週に2～3日	98.3	1.7		
	週に4日以上	97.7	2.3		
50歳以上	まったくとらない	95.6	4.4	2.959	0.3979
	週に1日程度	94.5	5.5		
	週に2～3日	93.9	6.1		
	週に4日以上	95.9	4.1		
計	まったくとらない	97.6	2.4	0.708	0.8713
	週に1日程度	97.7	2.3		
	週に2～3日	97.8	2.2		
	週に4日以上	97.6	2.4		

表7　メタボリックシンドローム有病状況と魚摂取頻度との関係

年齢階級	摂取頻度	メタボリックシンドローム		χ^2	p
		無し n=18201 (%)	有り n=428 (%)		
40歳未満	まったくとらない	99.5	0.5	1.330	0.7220
	週に1日程度	99.1	0.9		
	週に2～3日	99.3	0.7		
	週に4日以上	99.4	0.6		
40歳代	まったくとらない	98.9	1.1	1.814	0.6119
	週に1日程度	98.4	1.6		
	週に2～3日	98.3	1.7		
	週に4日以上	97.9	2.1		
50歳以上	まったくとらない	96.4	3.6	1.627	0.6530
	週に1日程度	95.3	4.7		
	週に2～3日	94.4	5.6		
	週に4日以上	94.4	5.6		
計	まったくとらない	98.7	1.3	21.261	<0.0001
	週に1日程度	98.2	1.8		
	週に2～3日	97.8	2.2		
	週に4日以上	96.9	3.1		

表8　メタボリックシンドローム有病状況と牛乳・乳製品摂取頻度との関係

年齢階級	摂取頻度	メタボリックシンドローム		χ^2	p
		無し n=18201	有り n=428		
		(%)	(%)		
40歳未満	まったくとらない	98.6	1.4	7.975	0.0925
	週に1日程度	98.7	1.3		
	週に2～3日	99.4	0.6		
	週に4日～5日以上	99.7	0.3		
	ほぼ毎日	99.3	0.7		
40歳代	まったくとらない	99.3	0.7	9.061	0.0596
	週に1日程度	97.7	2.3		
	週に2～3日	98.8	1.2		
	週に4日～5日以上	98.0	2.0		
	ほぼ毎日	98.1	1.9		
50歳以上	まったくとらない	96.5	3.5	2.427	0.6578
	週に1日程度	94.6	5.4		
	週に2～3日	94.0	6.0		
	週に4日～5日以上	94.6	5.4		
	ほぼ毎日	94.6	5.4		
計	まったくとらない	98.3	1.7	5.803	0.2144
	週に1日程度	97.3	2.7		
	週に2～3日	98.0	2.0		
	週に4日～5日以上	97.8	2.2		
	ほぼ毎日	97.6	2.4		

表9　メタボリックシンドローム有病状況と豆腐摂取頻度との関係

年齢階級	摂取頻度	メタボリックシンドローム		χ^2	p
		無し n=18201 (%)	有り n=428 (%)		
40歳未満	まったくとらない	99.4	0.6	5.913	0.2057
	週に1日程度	98.9	1.1		
	週に2～3日	99.5	0.5		
	週に4日～5日以上	99.3	0.7		
	ほぼ毎日	99.3	0.7		
40歳代	まったくとらない	98.4	1.6	0.521	0.9715
	週に1日程度	98.1	1.9		
	週に2～3日	98.3	1.7		
	週に4日～5日以上	98.2	1.8		
	ほぼ毎日	98.3	1.7		
50歳以上	まったくとらない	96.9	3.1	11.517	0.0213
	週に1日程度	94.3	5.7		
	週に2～3日	93.3	6.7		
	週に4日～5日以上	95.7	4.3		
	ほぼ毎日	95.9	4.1		
計	まったくとらない	98.6	1.4	3.322	0.5054
	週に1日程度	97.7	2.3		
	週に2～3日	97.6	2.4		
	週に4日～5日以上	97.9	2.1		
	ほぼ毎日	97.8	2.3		

表10　メタボリックシンドローム有病状況と納豆摂取頻度との関係

年齢階級	摂取頻度	メタボリックシンドローム		χ^2	p
		無し n=18201 (%)	有り n=428 (%)		
40歳未満	まったくとらない	99.0	1.0	4.176	0.3827
	週に1日程度	99.2	0.8		
	週に2～3日	99.4	0.6		
	週に4日～5日以上	99.8	0.2		
	ほぼ毎日	99.4	0.6		
40歳代	まったくとらない	98.3	1.7	3.795	0.4345
	週に1日程度	98.5	1.5		
	週に2～3日	97.8	2.2		
	週に4日～5日以上	98.4	1.6		
	ほぼ毎日	98.0	2.0		
50歳以上	まったくとらない	93.6	6.4	3.267	0.5142
	週に1日程度	95.1	4.9		
	週に2～3日	94.4	5.6		
	週に4日～5日以上	95.5	4.5		
	ほぼ毎日	94.4	5.6		
計	まったくとらない	97.6	2.4	8.650	0.0705
	週に1日程度	98.1	1.9		
	週に2～3日	97.5	2.5		
	週に4日～5日以上	97.9	2.1		
	ほぼ毎日	97.0	3.0		

表11　メタボリックシンドローム有病状況とみそ汁摂取頻度との関係

年齢階級	摂取頻度	メタボリックシンドローム		χ^2	p
		無し n=18201 (%)	有り n=428 (%)		
40歳未満	週に1日以下	98.9	1.1	4.208	0.2399
	週に2～3日	99.2	0.8		
	週に4日～5日以上	99.6	0.4		
	ほぼ毎日	99.3	0.7		
40歳代	週に1日以下	98.1	1.9	0.871	0.8326
	週に2～3日	98.5	1.5		
	週に4日～5日以上	98.3	1.7		
	ほぼ毎日	98.2	1.8		
50歳以上	週に1日以下	94.1	5.9	11.728	0.0084
	週に2～3日	94.1	5.9		
	週に4日～5日以上	92.6	7.4		
	ほぼ毎日	95.8	4.2		
計	週に1日以下	97.6	2.4	2.344	0.5042
	週に2～3日	97.9	2.1		
	週に4日～5日以上	97.4	2.6		
	ほぼ毎日	97.8	2.2		

表12　メタボリックシンドローム有病状況と朝食摂取頻度との関係

年齢階級	摂取頻度	メタボリックシンドローム		χ^2	p
		無し n=18201	有り n=428		
		(%)	(%)		
40歳未満	週に1日以下	99.3	0.7	1.252	0.5349
	週に2～5日	98.9	1.1		
	ほぼ毎日	99.3	0.7		
40歳代	週に1日以下	98.6	1.4	2.429	0.2969
	週に2～5日	98.7	1.3		
	ほぼ毎日	98.1	1.9		
50歳以上	週に1日以下	94.9	5.1	6.462	0.0395
	週に2～3日	91.7	8.3		
	ほぼ毎日	94.7	5.3		
計	週に1日以下	98.3	1.7	3.274	0.1945
	週に2～5日	97.5	2.5		
	ほぼ毎日	97.6	2.4		

表13　メタボリックシンドローム有病状況と朝食の主食との関係

年齢階級	摂取頻度	メタボリックシンドローム		p
		無し n=18201	有り n=428	
		(%)	(%)	
40歳未満	パン食が中心	99.4	0.6	0.2898
	米食が中心	99.1	0.9	
40歳代	パン食が中心	98.7	1.3	0.0068
	米食が中心	97.9	2.1	
50歳以上	パン食が中心	95.3	4.7	0.1019
	米食が中心	94.0	6.0	
計	パン食が中心	98.2	1.8	0.00002
	米食が中心	97.3	2.8	

表14　多重ロジスティック回帰分析結果

項　　目	オッズ比	オッズ比の95%信頼区間
年齢(3階級)	2.909	2.472-3.425
飲酒頻度(5階級)	0.881	0.820-0.945
みそ汁摂取頻度(4階級)	0.879	0.791-0.977
朝食の主食(2階級)	1.650	1.294-2.104

Ⅲ　研究成果の刊行に関する一覧表

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
折戸征也, 太田博明　他	Age–related Distribution of Bone and Skeletal Parameters in 1,322 Japanese Young Women.	J Bone Miner Metab	27(6)	698-704	2009
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ORIGINAL ARTICLE

Age-related distribution of bone and skeletal parameters in 1,322 Japanese young women

Seiya Orito · Tatsuhiko Kuroda · Yoshiko Onoe · Yasuto Sato · Hiroaki Ohta

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Abstract We explored factors that could serve as indices for therapeutic intervention aimed at prevention of osteoporosis. In this cross-sectional study, we investigated the timing of peak bone mass (PBM) in 1,322 Japanese women aged 12–30 years old. We measured height, body weight, bone mineral density (BMD), bone mineral content (BMC), and bone area at the lumbar spine and total hip, as well as the blood markers calcium, phosphorus, and the bone metabolic markers bone alkaline phosphatase (BAP) and type I collagen cross-linked N-telopeptide (NTX). All measurements were standardized with the mean at age 18 defined as 100% to identify age-related differences. In the total hip, BMD peaked at age 18, while, in the lumbar spine, BMD peaked at age 29, of which 99.8% was attained at age 18, suggesting that peak BMD was attained at age 18 at both the total hip and lumbar spine. No age difference was observed in serum calcium, while there was a 15.1% decrease between ages 12 and 18 in serum phosphorus. There were 273.8% and 208.5% decreases in serum BAP and NTX, respectively, between ages 12 and 18, while these levels remained constant thereafter, suggesting that bone and calcium metabolism are constant between ages 19 and 30. Factors that had stronger correlations with BMD, BMC, and bone area from 12 years to 18 years were height and body weight. PBM was reached at age 18. Control of body weight by using total hip BMD as an index for intervention should be reasonable.

Keywords Adolescence · Young adulthood · Bone mineral density · Peak bone mass · Bone metabolic markers

S. Orito · T. Kuroda · Y. Onoe · H. Ohta (✉)
Department of Obstetrics and Gynecology,
Tokyo Women's Medical University, 8-1 Kawada-cho,
Shinjuku-ku, Tokyo 162-8666, Japan
e-mail: ohtah@obgy.twmu.ac.jp

Y. Sato
Department of Hygiene and Public Health II,
Tokyo Women's Medical University, Tokyo, Japan

Introduction

Osteoporosis is widely recognized as an important public health problem because of the significant morbidity and even mortality associated with its complications, including fractures [1, 2]. While osteoporosis is primarily a disease affecting postmenopausal women, it is also a disease that reflects the bone status from early childhood to adolescence [3, 4]. Peak bone mass (PBM) is defined as a maximum amount of bone accrual in early life. Osteoporosis develops as a result of bone loss after the perimenopausal period [5], which is accounted for by two major causes: lower PBM and greater bone loss associated with aging [3, 4, 6]. Thus, in order to prevent onset of osteoporosis, it is considered important to keep bone mass from decreasing after the perimenopausal period and to obtain as high a PBM as possible in early life. Elucidating the timing of PBM is of critical importance as it allows an effective timing for intervention to be determined.

There are various reports in the literature on the timing of PBM. Some studies reported that peak bone mass is reached by late adolescence [7–11], whereas others reported bone mass gains, albeit small, during the third decade of life [12–16]. However, most studies reported that bone mass peaks at most sites by late adolescence [12, 15].

Thus, we aimed in this study to identify the optimal timing for intervention for osteoporosis and associated

indices for such intervention by determining the timing of PBM in 1,322 Japanese young healthy volunteers aged 12–30 years. In addition, we aimed to elucidate the age-related distribution of bone mineral density (BMD) at the lumbar spine and total hip as well as serum bone metabolic markers in these subjects.

Materials and methods

Subjects

In this cross-sectional cohort study, we recruited 1,322 Japanese women aged 12–30 years. The subjects were healthy volunteers composed of junior and senior high school students, nursing students at the School of Nursing and the Nursing Vocational School, both of which belong to Tokyo Women's Medical University, and nurses working at hospitals affiliated with the university. The subjects were excluded if they had systemic or metabolic disorders or were receiving medications that could affect bone metabolism. The study protocol was approved by the Ethics Committee of Tokyo Women's Medical University School of Medicine. Written consent was obtained from each subject. If a subject was under 20, written consent was obtained also from her guardian.

Measurements

Each subject completed a questionnaire on her background including age at the time of study entry, age at menarche, birth weight, gestational age at birth, and current menstrual status. We measured height and body weight. The bone parameters BMD, bone mineral content (BMC), and bone area were assessed at the lumbar spine (L2–L4) and the total hip or the femoral neck by using dual-X ray absorptiometry (DXA) (QDR-4500 absorptiometer; Hologic Inc., Bedford, MA). Fasting blood samples were taken simultaneously and routine blood chemistry tests were performed by SRL, Inc. to measure serum calcium, phosphorus, albumin, and the bone metabolic markers, bone alkaline phosphatase (BAP) and type I collagen cross-linked N-telopeptide (NTX).

Statistical analysis

Continuous parameters were expressed as mean ± SD to describe the subjects. Height, body weight, BMD, BMC, bone area, serum calcium, phosphorus, BAP, and NTX values were standardized by the mean at age 18 defined as 100% to evaluate age-related differences. We evaluated relevant parameters with the Spearman rank-order correlation to see if they might serve as potential indices for intervention in BMD, BMC, and bone area.

Results

Age-related distribution of the measured values

The characteristics of the 1,322 subjects are shown in Table 1. The number of subjects who had not yet experienced menarche were 42 at age 12 (35.6% of those their age), 24 at age 13 (24.5%), 11 at age 14 (9.9%), and 3 at age 15 (2.8%).

The age-related distribution of skeletal parameters (height and body weight) is shown in Fig. 1. Maximum mean height was 159.8 cm at age 18, with subjects' height remaining almost constant thereafter. Maximum mean weight was 55.3 kg at age 21, with subjects' weight continuing to increase even after their height stopped increasing.

Maximum mean BMD in the total hip was 0.934 g/cm^2 at age 18, while that in the lumbar spine was 1.027 g/cm^2 at age 29, of which 99.8%, 1.025 g/cm^2, was attained at age 18 (Fig. 2a). Maximum BMC in the total hip was 29.1 g at age 18, while that in the lumbar spine was 48.4 g at age 29, of which 95.2%, 44.2 g, was attained at age 18 (Fig. 2b). Maximum mean bone area in the total hip was 32.6 cm^2, of which 95.8%, 31.2 cm^2, was attained at age 18, while that in the lumbar spine was 45.4 cm^2 at age 23, of which 94.7%, 43.0 cm^2, was attained at age 18 (Fig. 2c).

Table 1 Characteristics of all subjects

Variables	*n*	Mean	SD
Age (years)	1,322	19.5	5.6
Height (cm)	1,322	157.5	5.5
Weight (kg)	1,322	50.2	7.6
BMI (kg/m^2)	1,322	20.2	2.6
Age at menarche (years)	1,229	12.0	1.2
Birth weight (g)	1,222	3,101	431
Gestational age at birth (weeks)	981	39.2	1.8
Lumbar spine			
BMD (g/cm^2)	1,322	0.961	0.119
BMC (g)	1,322	41.2	8.1
Bone area (cm^2)	1,322	42.6	4.5
Total hip			
BMD (g/cm^2)	1,322	0.879	0.106
BMC (g)	1,322	26.9	4.5
Bone area (cm^2)	1,322	30.5	3.3
Serum markers			
Calcium (mg/dL)	1,322	9.6	0.4
Phosphorus (mg/dL)	1,322	4.0	0.5
Albumin (g/dL)	1,322	4.8	0.2
BAP (U/L)	1,322	41.2	37.9
NTX (nmol BCE/L)	1,322	8.2	12.4

BMD bone mineral density, *BMC* bone mineral content, *BAP* bone alkaline phosphatase, *NTX* type I collagen cross-linked N-telopeptide

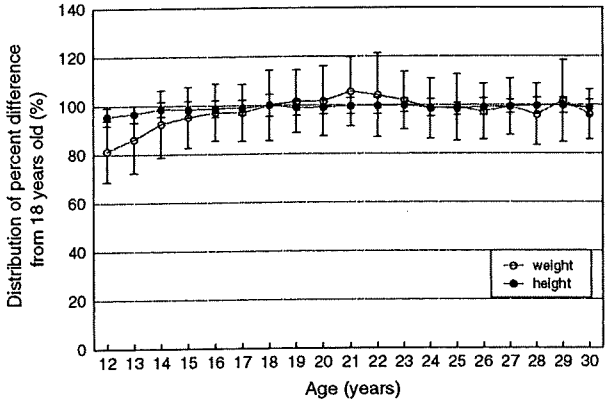

Fig. 1 Age-related distribution of skeletal parameters: height and weight. Maximum mean height was 159.8 cm at age 18. Height remained almost constant thereafter. Maximum mean weight was 55.3 kg at age 21. Weight continued to increase even after height stopped increasing. Means at each age were divided by the mean at age 18

The age-related distribution of blood markers is shown in Fig. 3. Serum calcium was constant at 9.6 ± 0.4 mg/dL between ages 12 and 30. Serum phosphorus gradually decreased from age 12 to 18, with a difference of 15.1%, which, however, remained constant thereafter. In regard to the serum bone metabolic markers BAP and NTX, there were differences of 273.8 and 208.5%, respectively, from 12 to 18 years old, with these values remaining almost constant thereafter.

Correlation between BMD, BMC, bone area and other parameters

In the age group ranging from 12 to 18 years old, where an age-related difference was observed, we analyzed the parameters examined for correlation. Results of the statistical analyses of these parameters performed every 2 years are shown in Tables 2 and 3. At age 12, age at menarche, height, body weight, serum phosphorus, BAP, and NTX were significantly correlated with lumbar spine BMD. As the subjects grew older, there was less correlation between these parameters. The same was true with the total hip BMD. On the other hand, these parameters were significantly correlated with both lumbar spine BMC and total hip BMC from ages 12 to 18. Height and weight were significantly correlated with lumbar spine bone area, while height alone was significantly correlated with total hip bone area during the same period.

Discussion

It is reported that there are two growth spurts in BMD: 1–4 and 12–17 years [17, 18], suggesting their association with

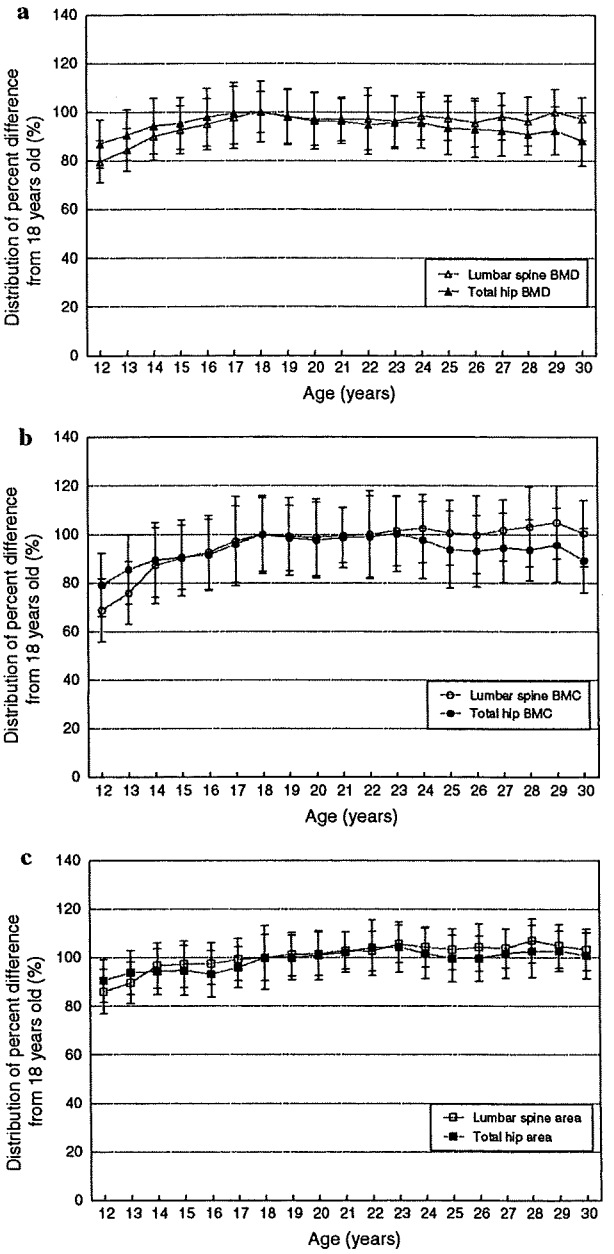

Fig. 2 Age-related distribution of BMD at the lumbar spine and total hip (**a**), BMC at the lumbar spine and total hip (**b**), bone area at the lumbar spine and total hip (**c**). Means at each age were divided by the mean at age 18. **a** Age-related distribution of BMD at the lumbar spine and total hip. Maximum mean total hip BMD was 0.934 g/cm^2 at age 18. Maximum lumbar spine BMD was 1.027 g/cm^2 at age 29, of which 99.8%, 1.025 g/cm^2, was attained at age 18. **b** Age-related distribution of BMC at the lumbar spine and total hip. Maximum total hip BMC was 29.1 g at age 18. Maximum lumbar spine BMC was 48.4 g at age 29, of which 95.2%, 44.2 g, was attained at age 18. **c** Age-related distribution of bone area at the lumbar spine and total hip. Maximum mean total hip bone area was 32.6 cm^2, of which 95.8%, 31.2 cm^2, was attained at age 18. Maximum mean lumbar spine bone area was 45.4 cm^2 at age 23, of which 94.7%, 43.0 cm^2, was attained at age 18

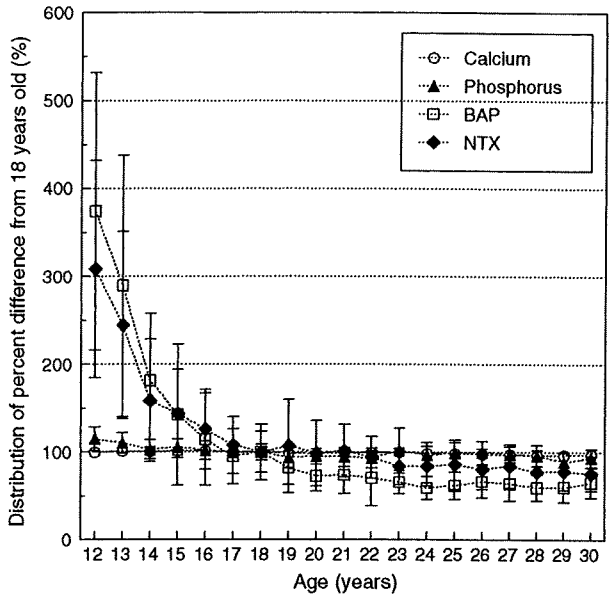

Fig 3 Age-related distribution of blood markers: serum calcium, phosphorus, BAP, and NTX. *BAP* bone alkaline phosphatase, *NTX* type I collagen cross-linked N-telopeptide. Serum calcium was constant at 9.6 ± 0.4 mg/dL between the ages of 12 and 30. Serum phosphorus gradually decreased, from age 12 to 18, with a difference of 15.1%. Thereafter, it was constant. With regard to the serum bone metabolic markers BAP and NTX, there were 273.8% and 208.5% differences, respectively, from 12 to 18 years, while these levels remained almost constant thereafter. Means at each age were divided by the mean at age 18

bone formation, given that these spurts occur during the period of growth in height, body weight and development in Tanner stage [19]. There have been several hypotheses put forward about when bone mass reaches its peak. Some studies report bone mass plateauing by late adolescence [7–11], whereas others report gains, albeit small, during the third decade of life [12–16]. Many studies report bone mass reaches its peak at most sites by late adolescence [12, 15]. We selected subjects aged 12–30 years old for this study to clarify the effect of duration of exposure to estrogen after menarche in the subjects in whom the mean age at menarche was shown to be 12. While there are reports that suggest gains after the 20s, we defined the upper limit as age 30, so that the study results would not have to be adjusted for age-related differences which would make our analysis complex. We included birth weight and gestational age at birth for analysis of their potential association with genetic factors. We also included height and body weight, assuming that increases in height and body weight might affect BMC and bone area. We also postulated that there existed a relationship between calcium and bone metabolic markers.

Our study showed that BMD peaked at age 18 at both the lumber spine and total hip, which was consistent with

Table 2 Age-related correlation between lumbar spine BMD, BMC, bone area and other parameters

	Age group			
	12 years old	14 years old	16 years old	18 years old
BMD				
Birth weight	−0.053	0.022	0.121	−0.103
Gest. age at birth	0.163	0.071	0.154	−0.101
Age at menarche	−0.315**	−0.308**	−0.156	0.044
Height	0.363***	0.312**	0.292**	0.057
Weight	0.555***	0.504***	0.430***	0.479
Calcium	0.118	0.145	−0.080	0.334
Phosphorus	−0.416***	−0.051	−0.016	−0.069
BAP	−0.454***	−0.293**	−0.031	−0.475
NTX	−0.455***	−0.274**	−0.203*	−0.043
BMC				
Birth weight	−0.013	0.027	0.142	−0.147
Gest. age at birth	0.201*	0.055	−0.028	−0.620*
Age at menarche	−0.219	−0.310**	−0.062	0.155
Height	0.594***	0.526***	0.543***	0.589*
Weight	0.614***	0.606***	0.493***	0.736**
Calcium	0.161	0.202*	−0.138	0.024
Phosphorus	−0.384***	−0.133	−0.051	0.155
BAP	−0.489***	−0.339***	0.028	−0.168
NTX	−0.494***	−0.295**	−0.053	−0.002
Bone area				
Birth weight	0.061	0.004	0.111	0.187
Gest. age at birth	0.193*	0.005	−0.159	−0.701**
Age at menarche	−0.140	−0.184	0.055	0.195
Height	0.681***	0.593***	0.677***	0.811***
Weight	0.538***	0.495***	0.414***	0.657**
Calcium	0.147	0.158	−0.199	−0.223
Phosphorus	−0.296***	−0.194*	−0.075	0.094
BAP	−0.427***	−0.247***	0.096	0.096
NTX	−0.403***	−0.236*	0.130	0.013

Spearman's rank-order correlation coefficient

BMD bone mineral density, *BMC* bone mineral content, *BAP* bone alkaline phosphatase, *NTX* type I collagen cross-linked N-telopeptide, *Gest.* age at birth, gestational age at birth

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$

the reports of Matkovic et al. [12] and Nguyen et al. [15]. More recently, Nordstorm et al. [20] conducted an eight-year longitudinal study of BMD as assessed by DXA in young adult men, 17–25 years of age, and found that, after bone mass peaked at age 19 in the subjects, there was a progressive decrease in BMD of up to 1.5% per year in the hip, while the peak BMD was maintained as measured at the lumbar spine and the total body. Our study revealed similar results showing that BMD began to decrease at age 18, consistent with a published report that BMD peaks at

Table 3 Age-related correlation between total hip BMD, BMC, bone area and other parameters

	Age group			
	12 years old	14 years old	16 years old	18 years old
BMD				
Birth weight	0.044	0.030	0.180	0.011
Gest. age at birth	0.002	0.009	0.299**	−0.130
Age at menarche	−0.050	−0.170	−0.086	−0.251
Height	0.301**	0.286**	0.177	0.000
Weight	0.559***	0.442***	0.353**	0.496
Calcium	0.224*	0.219*	−0.247*	0.044
Phosphorus	−0.276**	−0.057	0.145	0.096
BAP	−0.327***	−0.297**	−0.029	−0.521*
NTX	−0.329***	−0.173	−0.048	−0.316
BMC				
Birth weight	0.113	0.126	0.104	0.108
Gest. age at birth	0.083	−0.010	0.075	−0.488
Age at menarche	0.105	−0.023	0.010	0.361
Height	0.603***	0.518***	0.444***	0.589*
Weight	0.676***	0.594***	0.328**	0.696**
Calcium	0.063	0.172	−0.099	0.162
Phosphorus	−0.188*	−0.074	0.029	0.115
BAP	−0.236*	−0.128	0.091	−0.254
NTX	−0.260**	−0.119	0.151	−0.125
Bone area				
Birth weight	0.165	0.170	0.038	0.125
Gest. age at birth	0.209*	−0.054	−0.180	−0.620*
Age at menarche	0.154	0.131	0.181	0.576*
Height	0.616***	0.511***	0.508***	0.829***
Weight	0.442***	0.459***	0.124	0.507
Calcium	−0.097	0.034	0.137	0.049
Phosphorus	0.018	−0.066	−0.098	0.197
BAP	0.005	0.103	0.222*	0.239
NTX	−0.022	−0.054	0.235*	0.131

Spearman's rank-order correlation coefficient

BMD bone mineral density, *BMC* bone mineral content, *BAP* bone alkaline phosphatase, *NTX* type I collagen cross-linked N-telopeptide, *Gest.* age at birth, gestational age at birth

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$

the hip before age 20, followed by the whole body in 6–10 years [21] and another demonstrating that BMD peaks at the femoral neck before the lumbar spine [22]. While there are studies reporting that the timing of peak BMD is not clear [23, 24], we believe our study showed that BMD peaks before age 18, at least in the total hip, given that the mean at age 18, 0.934 g/cm^2, was shown to be the maximum. As for the reference value in Japan, a report published in 2000 defined the young adult mean BMD at the total hip as 0.863 ± 0.110 g/cm^2, which represents the mean total hip BMD in subjects aged 19–39 years old [25], using the same QDR machine for measurements as we used in our study. However, the PBM value was shown to be higher at 0.934 g/cm^2 in our study than the Japanese reference value for the young adult mean. Although this may reflect differences in the cohorts as well as in the concept of PBM and the young adult mean, it is worth noting that the mean was shown to be higher in our study than in the previous study.

On the other hand, as for the lumbar spine, the peak BMD was shown to be 1.027 g/cm^2 at age 29. As Heaney et al. [21] and Neville et al. [22] reported, bone mass peaks later at the lumbar spine than at the total hip. Although not representing the peak value, the young adult mean in the lumbar spine, the mean in individuals aged 20–40 years, was reported to be 1.011 ± 0.119 g/cm^2 in 1998 [26]. As compared with our peak BMD value, 1.027 g/cm^2, the previously determined young adult mean was low as was the mean at the total hip, suggesting that the BMD in the Japanese population is increasing, given that there are reports showing that more than 95% of BMD at all sites of the body is attained by age 20. In our study, at age 18, the BMD value accounted for 99.8% of the peak value to be attained at age 29. Thus, we consider it reasonable to conclude that peak BMD is attained at age 18, consistent with the previous reports demonstrating that at least 90% of the peak BMD is attained, regardless of body sites, by the end of adolescence [13, 27]. Of note, there is a report [12] showing that BMC continues to increase in adults after BMD attains its peak with the increase after age 18 being greater in BMC than BMD and that total hip BMC peaks at age 18 with no increase occurring after that. In our study, 95.2% of the peak BMC was attained in the lumbar spine at age 18, while 99.8% of the peak BMC was attained in the total hip at age 18. There have been no reports regarding the peak time in bone area. In our study, bone area peaked at age 23 at both the lumbar spine and total hip.

In this study, we analyzed relevant parameters for association with BMD, BMC, and bone area. During the period of change in BMD, height and body weight were significantly correlated with BMD, BMC, and bone area at both the lumbar spine and total hip. While it is hardly possible to intervene for height, it appears possible to intervene for body weight through lifestyle modifications. However, there is a report [28] showing that weight gain in late adolescence might inhibit periosteal expansion, thus presenting an obstacle to enhancing bone strength. Thus, hip structure analysis may be necessary. There is no report on the age-related distribution of bone metabolic markers from adolescence to age 30. In this regard, our results are consistent with those of the report by Yilmaz et al. [29] on Thai women 11–15 years, showing that bone metabolic markers decrease as the Tanner stage progresses.