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ORIGINAL ARTICLE

Title:

Familial correlation of bone mineral density, birth data and lifestyle factors among adolescent daughters, mothers and grandmothers

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Key words: bone mineral density, lifestyle, familial correlation, estrogen deficiency

Abstract

This study aimed to clarify the relationship between skeletal or lifestyle factors among Japanese daughter-mother, mother-grandmother and daughter-grandmother pairs.

We performed a cross-sectional study in a cohort of Japanese adolescent daughters (12-18 years of age), their mothers (339 pairs) and grandmothers on their mothers' side (34 pairs). Gestational age, birth weight, age at menarche and presence of menarche or menopause were surveyed in the participants. Height, body weight and lumbar 2–4 bone mineral density (BMD) were measured. Dietary intake and current physical activity were assessed by using questionnaires.

Gestational age and age at menarche were significantly correlated between daughters, mothers and grandmothers ($P < 0.001$). BMD was significantly correlated between daughters and mothers ($P < 0.001$), while it was not significantly correlated between daughters and grandmothers or between mothers and grandmothers. Dietary intake of calcium and vitamin D, and the frequency, duration and intensity of current physical activity were significantly correlated between daughters and mothers ($P < 0.05$), although no significant correlation was found between daughters and grandmothers, or between mothers and grandmothers.

The parameters for exercise indicated a positive correlation for BMD in the daughters and the mothers, but not in the grandmothers. The results suggested that estrogen deficiency decreases familial correlation for BMD after menopause. Achieving high BMD through exercise may be important for prevention of postmenopausal osteoporosis in premenopausal low-height mothers.

Introduction

According to the National Institutes of Health (NIH) report [1], osteoporosis is characterized by deteriorated bone strength. It is a considerable national healthcare burden in our aging society because of its high susceptibility to bone fractures, which could result in the impaired quality of life of affected patients [2-5]. Therefore, prevention of osteoporosis is compellingly important. There are two strategies currently available for increasing bone strength: first, by increasing bone mineral density (BMD) and, second, by improving bone quality. Of these two contributing factors, BMD accounts for seventy percent of bone strength [1]. Therefore, acquisition of higher BMD in younger years is important for prevention of osteoporosis in later years [6, 7].

Heritability is reported to determine up to 60% to 80% of an individual's BMD in twins studies [8, 9], while correlation between heredity and BMD is reported to decrease at a rate of 7–19% in a postmenopausal twins study [10]. On the other hand, a strong intergeneration and familial correlation was reported for lumbar BMD between daughters and their mothers [11], and Lutz et al. reported a stronger correlation between daughters and their postmenopausal mothers than between daughters and their pre-menopausal mothers, with a significant correlation shown between dietary intake of calcium and the BMD values for the daughters, but not for the mothers [12]. McKay et al. reported a significant correlation for femoral BMD between mothers and grandmothers, with differences found in correlation for BMD by site of bone [13]. It follows, then, that BMD values in a daughter can be predicted from those in her mother, but that BMD values in her mother cannot be predicted from those in her grandmother. We previously reported that skeletal parameters within the BMD category and lifestyle parameters are strongly correlated between daughters and their mothers [14]. To the best of our knowledge, there is no report available on correlation between skeletal and lifestyle parameters between daughters and their grandmothers or between mothers and their grandmothers in a Japanese population.

The purpose of this cross-sectional study was to examine skeletal and lifestyle factors for correlation among Japanese daughter-mother, mother-grandmother, and daughter-grandmother pairs.

Subjects and Methods

Study subjects

This study was carried out from July to September 2006 in Tokyo, Japan [14]. The participants were schoolgirls aged twelve to eighteen years old attending girls' junior and senior high schools, their mothers (339 pairs), and their grandmothers (34 pairs). Participants were excluded if they had not reached menarche or if they had systemic or metabolic disorders or were receiving medications with known effects on bone metabolism. All grandmothers showed signs of normal aging and no pathological abnormalities. The study protocol was approved by the Ethics Committee of Tokyo Women's Medical University and informed consent was obtained from all candidate subjects who agreed to participate.

Assessment of skeletal indices

Lumbar 2–4 BMD was measured in the participants by QDR-4500 (Hologic, Waltham, MA). The inter-assay variance of BMD measurement was 0.5 ± 0.5% (mean ± SD). Height and body weight were also measured, and blood samples were collected from the participants to measure their serum calcium and phosphorus levels.

Assessment of birth- and menarche-related status

Gestational age, birth weight, presence of menarche, and ages at menarche and menopause were assessed through interviews with the participants.

Assessment of lifestyle factors

As for dietary habits, nutrient intake was assessed by using the self-administered Diet History Questionnaire (DHQ) developed by Sasaki S, et al [15, 16]. The daily intake of calories and all nutrients and the number of breakfasts skipped per week were calculated based on the DHQ results.

The DHQ is a 16-page structured questionnaire that consists of the following 7 sections: general dietary behavior, major cooking methods, frequency of consumption of 6 alcoholic beverages as well as their portion sizes, semi-quantitative frequency of intake of 121 selected foods and nonalcoholic beverage items, dietary supplements, frequency of consumption of 19 staple foods (rice, bread, noodles, and other wheat foods) and *miso* (fermented soybean paste) soup as well as their amounts, and open-ended food items consumed regularly (≥ 1 times/week) not listed in the DHQ. The food and beverage items and portion sizes in the DHQ were derived primarily from data in the National Nutrition Survey of Japan and several recipe books on Japanese dishes [16]. Dietary intake of 147 food and beverage items, energy, fat, total carbohydrate, alcohol, and dietary fiber were calculated by using an ad hoc computer algorithm developed for the DHQ, which was based on the Standard Tables of Food Composition in Japan [17]. A convenient, interview-based method validated in the previous study [14] was used to assess current physical activity ("Yes" or "No"), kinds of exercises undertaken, their frequency and duration per month, and level of intensity (1, light; 2, moderate; and 3, vigorous). For participants with multiple exercises, the highest level of intensity was assigned.

Statistical analysis

In the descriptive analysis of the participant characteristics, numerical data were expressed as mean ± SD. Given that BMD, height and body weight might be influenced by duration of exposure to female hormones, their measured values were converted to standard deviation (SD) by using the values obtained for the participants at each age. The BMD-SD in the mothers and grandmothers was calculated by using standard values in Japanese [18]. BMD-SD, height-SD, body weight-SD, birth-related data, age at menarche and lifestyle factors were examined for correlation between daughters, mothers and grandmothers by using Spearman's rank correlation coefficient. A value of $P < 0.05$ was regarded as statistically significant. Variables found to be significantly correlated with each BMD-SD were selected with the exclusion criterion being a P-value less than 0.05. ANOVA test was used to clarify the effect of any determinant factors on the BMD-SD in the grandmothers. All statistical analyses were performed with the JMP version 5.1.2 (SAS Inst, Inc., Cary, NC, USA).

Results

Correlation between daughters, mothers and grandmothers

The participant characteristics are shown in Table 1. The sample size for the grandmothers was small. There were no significant differences between daughters, mothers and grandmothers in birth weight, number of breakfasts skipped, total energy intake and calcium intake ($P > 0.05$). There were significant differences among the three-generation participants in exercise-related parameters ($P < 0.05$). The mean age at menarche in the daughters was significantly shorter and earlier than that in the mothers and grandmothers ($P < 0.001$). None of the mothers had reached menopause and all the grandmothers had reached menopause. No abnormal serum calcium or phosphorus levels were noted in the participants.

All the parameters examined for correlation between the daughters, mothers and grandmothers are shown in Table 2. BMD-SD showed a significant correlation between daughters and mothers but no correlation between mothers and grandmothers or between daughters and grandmothers. Height-SD and weight-SD in the mothers were both significantly correlated with those in the grandmothers ($P < 0.05$), while none of the factors examined were significantly correlated between daughters and grandmothers ($P > 0.05$).

Correlation between the BMD-SD and lifestyle parameters

Correlation between BMD-SD and lifestyle parameters in each generation is shown in Table 3. The exercise-related parameters indicate a positive correlation for BMD-SD in the daughters and the mothers, but not in the grandmothers.

Correlation between the BMD-SD in the grandmothers and all parameters in the mothers

Single linear regression analyses were performed to examine correlation between the BMD-SD in the grandmothers and all parameters in the mothers. Only height-SD in the mothers was significantly correlated with BMD-SD in the grandmothers (P = 0.004). Analysis of all parameters in the grandmothers showed that weight-SD was significantly correlated with BMD-SD (r = 0.636, P < 0.001).

Interaction between BMD-SD in the grandmothers and height-SD in the mothers

The mean BMD-SD values in the grandmothers were plotted against the four height categories in the mothers in quartile analysis (Fig. 1). The mean height ± SD in the mothers were 152.0 ± 2.3 cm in the first quartile, 156.6 ± 0.9 cm in the second quartile, 159.6 ± 0.9 cm in the third quartile, and 163.8 ± 2.3 cm in the fourth quartile, respectively. There was a positive interaction between the mean BMD-SD in the grandmothers and height in the mothers in the second, third, and fourth quartiles.

Discussion

Osteoporosis is widely recognized as an important public health problem in an aging society, and BMD is one of the major predictors of osteoporotic fracture [19]. BMD is influenced by both genetic and lifestyle factors [20]. In our previous study, we found a significant correlation between lumbar BMD, physical activity and dietary habits between daughters and their mothers [14]. However, there is no report on intergeneration correlation for BMD according to menopausal status in Japan. In this study, we investigated intergenerational correlation between skeletal parameters, including BMD values in grandmothers, and lifestyle factors in the same study cohort [14].

In this study, skeletal parameters including BMD and a number of lifestyle indices were shown to be significantly correlated between daughters and mothers, and study findings suggest that BMD measurement in mothers may be useful for predicting future BMD values in their daughters. Furthermore, it was suggested that improvement of exercise and dietary habits at home may be useful for preventing osteoporosis. In regard to the lifestyle factors, previous studies reported familial correlation for physical activity and intake of milk [11, 21, 22]. However, we found no significant correlation for BMD between mothers and grandmothers or between daughters and grandmothers.

The small sample size for the grandmothers might account for the fact that there was no correlation found between the grandmother and the others, but the trend shown in this study is consistent with that in a previous report [11]. Since postmenopausal estrogen deficiency is reported to be the main determinant for decreasing BMD [23], it was suggested that the effect of estrogen deficiency on BMD might have dominated over familial similarity.

In addition, we examined lifestyle factors for correlation with BMD in each generation and found that frequency, duration and intensity of physical activity were significantly correlated with BMD in the daughters and mothers, while none of the factors involved in physical activity were correlated with BMD in the grandmothers. Previous studies reported that estrogen was increased, and 50-60% of peak bone mass is formed by estrogen in cooperation with other hormones, during puberty [23, 24]. During the period, physical activity, especially weight-bearing exercise, is also reported to be effective in ensuring high peak bone mass [25, 26]. On the other hand, after menopause, estrogen replacement therapy (ET) and intake of calcium are reported to be independent determinants for BMD [27], with the additive effect of ET and weight-bearing exercise on BMD also reported [28, 29]. Moreover, a recent study suggested that ER-alpha polymorphism modulates the association between exercise and bone mass [30]. Given the experimental data suggesting that the effects of mechanical strain and estrogen on osteoblast function concur through a common afferent pathway [23], these data may provide a plausible explanation as to why BMD is little increased by mechanical stress loading, such as exercise after menopause, due to lack of estrogen.

For these reasons, it may be desirable that intervention for BMD through modification of lifestyle factors is implemented before menopause when women still have a sufficient natural supply of estrogen. Since height in the mothers significantly correlated with the BMD values in the grandmothers, height in the mothers may serve as a predictor of BMD values in the grandmothers. Given the significantly negative interaction between the mean BMD-SD values in the grandmothers and height in the mothers in the first quartile, it may be practically important that low-height mothers be encouraged to exercise before menopause in order to achieve higher BMD.

However, there are some limitations in this study. First, the number of the participating grandmothers was small, although this study population of daughters, mothers and grandmothers living together or in the neighborhood accounted for a small regional bias in our assessment of lifestyle-related factors including hours of exposure to sunlight. Thus, a larger sample-sized study is necessary to confirm our study findings. Second, all variables related to current physical activity, kinds of exercises undertaken, their frequency, duration per month, and level of intensity are not continuous but categorical variables. However, we found a reasonably significant correlation between the daughters and their mothers by using these physical activity-related parameters. The convenient interview-based method used in this study was considered to be useful.

In conclusion, we found a significant familial correlation for BMD, physique and lifestyles between daughters and mothers, and these results suggested the possibility that physical activity could be useful in ensuring high BMD values. On the other hand, there was no correlation for BMD and lifestyles between daughters and grandmothers or between mothers and grandmothers, suggesting that the familial correlation for BMD disappeared due to the menopause-associated estrogen deficiency in place. As the BMD values in the grandmothers were correlated with height in the mothers, intervention through exercise may be important for the prevention of postmenopausal osteoporosis in premenopausal low-height mothers.

Acknowledgment

This work was partly supported by a Grant-in-aid from the Japan Osteoporosis Foundation.

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Figure legends

Fig. 1 Quartiles for height in the mothers and mean lumbar bone mineral density-SD in the grandmothers. Mean lumbar bone mineral density was significantly lower in the first quartile than the other quartiles (ANOVA, *P* = 0.017).

Table 1 Characteristics of daughters, mothers and grandmothers

	Daughters (n = 339)	Mothers (n = 339)	Grandmothers (n = 34)	ANOVA P
Age (years)	14.8 ± 1.7	46.4 ± 4.0	71.9 ± 4.5	< 0.001
Height (cm) [a]	157.1 ± 5.4	158.0 ± 4.7	151.2 ± 5.9	< 0.001
Body weight (kg) [a]	49.0 ± 6.9	53.0 ± 7.6	52.3 ± 7.9	< 0.001
BMI (kg/m^2) [a]	19.8 ± 2.4	21.1 ± 3.0	22.9 ± 3.4	< 0.001
Birth weight (g) [b]	3054.3 ± 431.9	3047.0 ± 432.9	2810.6 ± 361.6	0.290
Gestational age (weeks) [c]	39.1 ± 1.9	39.8 ± 1.5	37.2 ± 3.6	< 0.001
Age at menarche (years) [d]	11.9 ± 1.2	12.5 ± 1.2	13.5 ± 1.1	< 0.001
BMD (g/cm^2)	0.94 ± 0.12	1.02 ± 0.13	0.82 ± 0.16	< 0.001
Frequency of exercise (/month)	8.5 ± 9.9	6.7 ± 9.3	9.2 ± 10.9	0.041
Total duration of exercise (hour/month)	12.4 ± 18.0	7.1 ± 12.3	7.7 ± 12.3	< 0.001
Maximum intensity of exercise [e]	1.3 ± 1.3	1.0 ± 1.1	0.9 ± 0.8	< 0.001
No. of breakfasts skipped (/week)	0.5 ± 1.3	0.6 ± 1.5	0.5 ± 1.7	0.712
Energy intake (kcal/day)	2024.6 ± 569.4	1949.4 ± 482.2	1903.0 ± 569.9	0.122
Calcium intake (mg/day)	596.9 ± 268.4	581.5 ± 215.7	672.7.0 ± 215.7	0.111
Vitamin D intake (μg/day)	7.1 ± 4.4	7.5 ± 3.9	12.5 ± 7.0	< 0.001

Data are expressed as mean value ± SD

[a] mothers, n = 338; grandmothers, n = 33

[b] daughters, n=299; mothers, n = 274; grandmothers, n = 8

[c] daughters, n=278; mothers, n = 250; grandmothers, n = 5

[d] mothers, n = 335; grandmothers, n = 33

[e] intensity level of exercise: 1 = light; 2 = moderate; and 3 = vigorous

Table 2 Correlation coefficients for all variables examined within daughter-mother, mother-grandmother, and daughter-grandmother pairs in Spearman's rank test

Variable	Daughters -Mothers (n = 339)		Mothers -Grandmothers (n = 34)		Daughters -Grandmothers (n = 34)	
	r	*P*	*r*	*P*	*r*	*P*
Height-SD[a]	0.498	<0.001	0.602	<0.001	0.178	0.321
Body weight-SD[a]	0.240	<0.001	0.362	0.039	0.296	0.095
BMD-SD[a]	0.302	<0.001	0.243	0.166	0.029	0.870
Birth weight[b]	0.278	<0.001	-0.360	0.428	-0.405	0.368
Gestational age[c]	0.105	0.132	0.500	0.391	0.866	0.333
Age at menarche[d]	0.299	<0.001	0.326	0.064	-0.039	0.828
Frequency of exercise	0.147	0.007	-0.232	0.186	-0.094	0.598
Total duration of exercise	0.163	0.003	-0.280	0.109	-0.187	0.289
Maximum intensity level of exercise[e]	0.135	0.013	-0.316	0.069	-0.181	0.307
No. of breakfasts skipped	0.118	0.030	0.135	0.445	0.096	0.588
Calcium intake	0.387	<0.001	0.102	0.565	0.138	0.436
Vitamin D intake	0.459	<0.001	0.332	0.055	0.045	0.799

[a] mothers, n = 338; grandmothers, n = 33

[b] daughters, n=299, mothers, n = 274; grandmothers, n = 8

[c] daughters, n=278, mothers, n = 250; grandmothers, n = 5

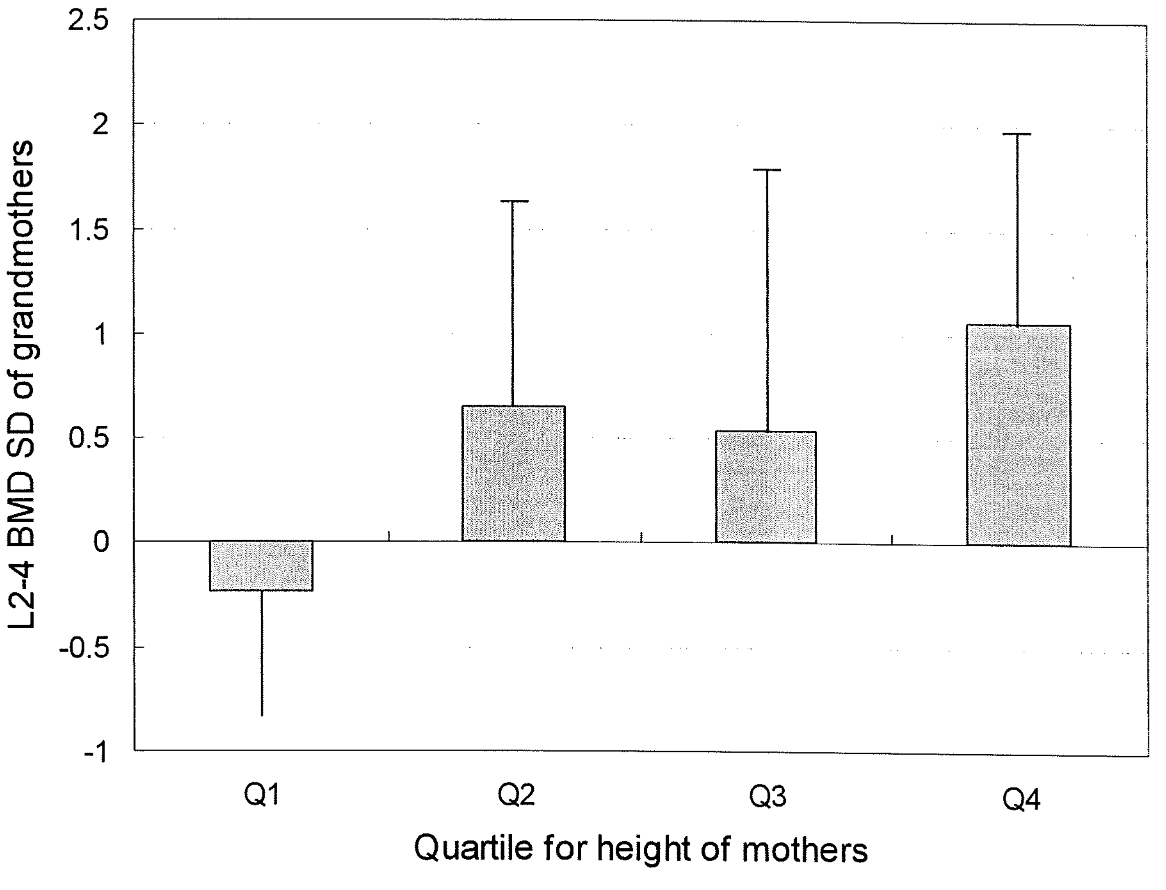
[d] mothers, n = 335; grandmothers, n = 33

[e] intensity level of exercise: 1 = light; 2 = moderate; and 3 = vigorous

Table 3 Correlation coefficients for bone mineral density and lifestyle variables in three generations in Spearman's rank test

Variable	Daughters		Mothers		Grandmothers	
	r	*P*	*r*	*P*	*r*	*P*
Frequency of exercise	0.133	0.014	0.102	0.059	-0.036	0.841
Total duration of exercise	0.146	0.007	0.121	0.026	-0.112	0.527
Maximum intensity level of exercise	0.193	<0.001	0.164	0.002	-0.179	0.310
No. of breakfasts skipped	-0.011	0.846	-0.041	0.456	-0.150	0.398
Calcium intake	0.058	0.285	-0.026	0.632	0.060	0.735
Vitamin D intake	-0.010	0.849	-0.033	0.547	0.219	0.214

Figure 1



2.5
2
1.5
1
0.5
0
-0.5
-1
L2-4 BMD SD of grandmothers
Q1
Q2
Q3
Q4
Quartile for height of mothers

J Bone Miner Metab (2009) 27:89–94
DOI 10.1007/s00774-008-0014-x

ORIGINAL ARTICLE

Association between lumber bone mineral density and vascular stiffness as assessed by pulse wave velocity in postmenopausal women

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Received: 18 January 2008 / Accepted: 25 April 2008 / Published online: 5 December 2008

Abstract Recent studies have showed a significant correlation between vascular calcification and bone mineral density (BMD). Therefore, an investigation was carried out on the association between arterial stiffness, lumbar BMD and bone metabolic markers in Japanese postmenopausal women. Brachial-ankle PWV (baPWV) and BMD of the lumbar spine and serum bone-specific alkaline phosphatase (BAP) levels in 143 postmenopausal women were measured, where there was a significant negative correlation between baPWV and BMD ($r = -0.21$; $P = 0.0135$). An additional analysis included the remaining 75 subjects, but excluded subjects with hypertension and obesity. Here, a more negative correlation between baPWV and BMD ($r = -0.315$; $P = 0.006$), and a positive correlation between baPWV and BAP ($r = 0.248$; $P = 0.032$) were also significant. A group analysis, where the women were age matched and stratified into three groups of different bone density, i.e., normal BMD, osteopenic and osteoporotic, were further made. This showed lower PWV values in the normal BMD group than in the other two groups. A study also showed that the tertile with the highest BAP was associated with significantly higher PWV values than the other tertiles. However, when the multiple linear regression analysis was carried out, there was no correlation between PWV and BAP values. Low BMD and arterial stiffness show some correlation, suggesting that BAP may reflect the degree of arterial stiffness present.

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Keywords Bone mineral density · Brachial-ankle PWV · Bone-specific alkaline phosphatase · Arteriosclerosis · Osteoporosis

Introduction

Arteriosclerosis progresses with age, and the risk of arteriosclerosis in women increases significantly after menopause [1, 2]. On the other hand, bone mass decreases with age regardless of sex. However, women are at higher risk especially after menopause, when bone mass decreases rapidly due to a decrease in estrogen [3, 4]. It was recently shown that the degree of vascular calcification is significantly correlated with changes in bone density, suggesting that vascular sclerosis and decreased bone mass are closely linked pathological conditions [5–8].

Pulse wave velocity (PWV) can be used to measure the elasticity of arteries, thus providing an easy measure of progression of arteriosclerosis. Indeed, despite the fact that PWV values do not directly describe calcification of blood vessels, PWV is used as an effective measure of arteriosclerosis. Carotid-femoral PWV (cfPWV) has been a traditional method used to measure PWV. However, this method requires some technical skills. On the other hand, brachial-ankle PWV (baPWV), now available as a more convenient method, only requires placing blood pressure cuffs on the extremities. It has been reported that baPWV and cfPWV values are extremely well correlated within the same patient, suggesting that baPWV is as equally reliable as cfPWV as an index for the severity of arteriosclerosis as well as a prognostic indicator in the care of patients with hypertension [9, 10].

The most important objective of osteoporosis treatment lies in the prevention of bone fractures, which occur as