〈Original Article〉

A three-year prospective study of the risk factors influencing bone mineral density and bone resorption among postmenopausal women

Tadayuki Iida[1)], Chiho Chikamura[2)], Hiroaki Ishikawa[3)], Tadashi Koyama[4)], Satomi Aoi[4)], Hiromi Ikeda[4)], Kazuhiro Katada[5)], Yuichiro Ono[1)] and Fumiko Ishizaki[6)]

Summary Purpose: The risk factors for postmenopausal osteoporosis were studied prospectively in healthy women for three years from 2000 to 2003. Methods: We examined physical features (height, weight, and body mass index (BMI)), bone mineral density (BMD) of the lumbar spine and femoral neck, and bone resorption markers (urinary N-telopeptide of type Ⅰ collagen: u-NTx, urinary deoxypyridinoline: u-D-Pyr) in 128 women with a mean (SD) age of 56.5 (7.6). Results: In a Cox proportional hazards model, a 1% rise in BMD of the lumbar spine and femoral neck exerted a preventive action against low BMD of the lumbar spine in 2003 with relative risks (RR) of 0.93 (95%CI:0.90-0.95) and 0.96 (0.93-0.99) respectively, and against low femoral neck BMD in 2003 with RRs of 0.96 (0.93-0.98) and 0.92 (0.89-0.95), respectively. Higher u-NTx levels increased the risk of BMD reduction of the lumbar spine, while higher BMI decreased the risk. A 1% rise in BMI exerted preventive action against BMD reduction over the three-year study period (RR: 0.93(0.84-0.99)), a 1% rise in BMD of the lumbar spine also showed such preventive action (RR: 0.98(0.96-1.00)). Higher BMI, however, was related to the risks of higher u-NTx and u-D-Pyr levels three years later (u-NTx RR: 1.10 (1.00-1.23), u-D-Pyr RR: 1.11 (1.02-1.20)). Conclusions: We discussed the reasons why a high BMI reduces the risk of osteopenia but increases the levels of bone absorption markers.

Key words: Bone mineral density, Urinary N-telopeptide of type Ⅰ collagen, Urinary deoxypyridinoline, Lumbar spine, Femoral neck

[1)]Department of Public Health, Fujita Health University, Toyoake, Aichi 470-1192, Japan
[2)]Attached Clinic, Prefectural University of Hiroshima, 1-1 Gakuen-cho, Mihara, Hiroshima 723-0053, Japan
[3)]Department of Medical Technology, Fujita Health University, Toyoake, Aichi 470-1192, Japan
[4)]Department of Nursing, Prefectural University of Hiroshima, 1-1 Gakuen-cho, Mihara, Hiroshima 723-0053, Japan
[5)]Department of Radiology, Fujita Health University, Toyoake, Aichi 470-1192, Japan
[6)]Department of Communication Sciences and Disorders, Prefectural University of Hiroshima, 1-1 Gakuen-cho, Mihara, Hiroshima 723-0053, Japan

Received for Publication June 24, 2009
Accepted for Publication July 3, 2009

Ⅰ. Introduction

Early diagnosis of osteopenia in menopausal and postmenopausal women is regarded as important for preventing osteoporosis[1]. This is partly supported by a report showing that most menopausal women are diagnosed with osteopenia, a prodromal disorder of osteoporosis[2]. Epidemiological studies among healthy women found that the bone mineral density (BMD) of the lumbar spine was significantly reduced with age but increased with body weight and body mass index (BMI)[3-6]. Osteoporosis, which involves a reduction of BMD, is associated with femoral neck fractures[3]. However, there have been few epidemiological studies on the BMD of the femoral neck among postmenopausal Japanese women. Most women commonly have bone loss resulting from an increase of bone absorption due to a reduction of endogenous hormones[1, 2, 4]. However, longitudinal epidemiological studies on bone metabolism have not examined bone resorption markers in postmenopausal Japanese women in any detail.

Thus, a 3 year follow-up study was conducted among healthy postmenopausal women aimed at elucidating the prognostic factors for an increase of bone resorption and BMD reduction in the lumbar spine and femoral neck.

Ⅱ. Materials and Methods

1. Subjects

The subjects of the study were recruited from among the inhabitants using an advertisement in a local public relations magazine of M city. Healthy women aged 40-69 living in M city, Hiroshima Prefecture were studied. Those with a past history of hospitalization or of being ambulatory patients were excluded. Health examinations were carried out twice: from February to March in 2000 and from February to March in 2003. Two-hundred-eighty-two women participated in 2000, 241 of whom were within 20 years of menopause in 2000, while 196 women participated again in 2003. Thirty-two women with a past history of hysterectomy, oophorectomy, disorders related to bone metabolism (hyperthyroidism, thyrotoxicosis, etc.) and 36 women lacking some of their examination data were excluded. Finally, we analyzed the data of the remaining 128 who had a mean age of 56.5±7.6 years in 2000. The participants had the content and method of the study explained to them in advance and gave their written informed consent. The study was conducted in accordance with the Declaration of Helsinki and was approved by the ethical committee of the Hiroshima Prefectural College of Health Sciences.

2. Methods

We studied the subjects' physical features, BMD, and markers of bone resorption. BMI (kg/m^2) was calculated from height and weight. Dual x-ray absorptiometry (DXA) (Hologic Company QDR-4500, USA) was used for measurements of BMD. BMDs of the lumbar spine (L2-L4) and the left femoral neck were measured.

To measure urinary deoxypyridinoline (u-D-Pyr), the subjects were asked to provide a urine sample from their second urination of the day. These samples were obtained early in the morning and centrifuged at 500×g for 5 minutes. The supernatant fluids were then frozen at -20℃. These samples were analyzed by means of HPLC with fluorescence detection according to the method described by Yamamoto et al.[7]. The u-D-pyr levels were adjusted with urinary creatinine[7]. To measure urinary N-telopeptide of type I collagen (u-NTx), samples of the urine specimens were collected and stored at -20℃. These samples were analyzed by an enzyme-linked immunosorbent assay (ELISA) technique, using Osteomark, a reagent for the detection of NTx (Sumitomo Pharmaceutical Co., Ltd.)[8]. Urinary NTx levels were also adjusted with urinary creatinine. The standard range was set at 14.0-99.5 nmol BCE/mmol/Cr for u-NTx and 2.8-7.6 pmol/μmol/Cr for u-D-Pyr according to Hirota et al.[8].

The Young Adult Mean percentage (YAM%) of the BMD of the lumbar spine and femoral neck were calculated by the following formula (1).

$$\text{YAM\% (\%)} = \frac{\text{BMD (g/cm}^2\text{) of subject}}{\text{Mean BMD (g/cm}^2\text{) at age 20-44}} \times 100 \cdot\cdot\cdot (1)$$

Mean BMD at age 20-44 was based on a report of the Japanese Society for Bone and Mineral Research[9].

A YAM% of 80% or more was regarded as normal. In 2003, the YAM% of the lumbar spine and femoral neck were below normal levels in 51 and 53 women, respectively. The decrease in BMD was calculated by subtracting the BMD level in 2003 from that in 2000. A decrease of less than 2.6% for the lumbar spine and of less than 2.4% for the femoral neck was regarded as normal[9, 10]. Thus, 57 women fell within the normal range for the lumbar spine as did 93 women for the femoral neck. A level of u-NTx less than 55 nmolBCE/mmol/Cr was defined as normal[11], with 98 women so classified in 2003[7]. A level of u-D-pyr less than 5.9 pmol/μ mol/Cr was regarded as normal, yielding 76 women classified as normal in 2003[7].

3. Statistical analyses

The paired *t*-test was used for comparing continuous data from 2000 with those from 2003. The outcome variables dichotomized according to the normal levels were used as dependent variables in Cox proportional hazards models. Before applying explanatory variables to the models, associations were examined among age, height, weight, BMI, YAM% for the lumbar spine and femoral neck in 2000, and reductions in weight and BMI over 3 years. Strong correlations were found between weight and BMI in 2000, between BMD (YAM%) of the lumbar spine and femoral neck, and between weight and BMI reduction (0.7 or more and $p<0.001$). Thus, age, BMI, u-NTx, BMD (YAM%) of the lumbar spine, and reductions in height and BMI over 3 years were used as explanatory variables in Model 1. Although the BMD (YAM%) of the femoral neck was used as an explanatory variable instead of that of the lumbar spine in Model 2, the other explanatory variables were the same as those in Model 1. Statistical analyses were conducted with SPSS12.0J (SPSS Japan Inc., Tokyo) software. For all analyses, the level of significance was set at $p < 0.05$.

Ⅲ. Results

We observed significant decreases in height and BMD (YAM%) of the lumbar spine and femoral neck, and increases in weight and BMI during the three-year study period (Table 1). The exclusions differing from those of subjects in 2003 were as follows: age (yrs) [mean (SD): 56.5(7.6) vs. 56.7(5.6), p=0.750]; height (cm) [153.7(5.1) vs. 153.1(4.9), p=0.442]; weight (kg) [55.2(7.8) vs. 55.9(6.4), p=0.535]; BMI [23.4(3.3) vs. 23.7(3.9), p=0.492]; BMD in the lumbar spine (g/cm^2) [0.87(0.15) vs. 0.91(0.16), p=0.070]; BMD (YAM%) in the lumbar spine (%) [86.8(14.9) vs. 91.2(15.6), p=0.070]; BMD in the femoral neck (g/cm^2) [0.71(0.11) vs. 0.73(0.12), p=0.267]; BMD (YAM%) in femoral neck (%) [90.1(14.5) vs. 92.7(14.9), p=0.267]. No significant differences existed between any other variables.

Table 2 shows associations of risk factors with low BMD of the lumbar spine and femoral neck in 2003. The low BMD (YAM%) in 2003 as a dependent variable was determined by a dichotomous classification into normal (>=80%) and low (<80%) in the models. In Cox proportional hazards models (Model 1) in which YAM% of the lumbar spine and that of the femoral neck were used as dependent variables, a 1% rise in BMD (YAM%) of the lumbar spine in 2000 proved preventive against low BMDs of the lumbar spine (RR: 0.93) and femoral neck (RR: 0.96) in 2003 (Table 2A). In Model 2, a 1% rise in BMD (YAM%) of the femoral neck in 2000 was also preventive against low BMDs of the lumbar spine (RR: 0.96) and femoral neck (RR: 0.92) in 2003 (Table 2B).

Table 3 shows the associations of risk factors with decrease in BMDs of the lumbar spine and femoral neck for three years from 2000 to 2003. The decrease in BMD (YAM%) for those three years as a dependent variable was determined by a dichotomous classification into normal (<2.6%) and decrease (>=2.6%) for the lumbar spine, and into normal (<2.4%) and decrease (>=2.4%) for the femoral neck in the models. In Model 1, a 1pmol/μ mol/Cr rise in the u-NTx level in 2000 increased the risk of BMD reduction of the lumbar spine (RR: 1.02), while a 1 point increase in BMI in 2000 decreased it (RR: 0.93) (Table 3A). In Model 2, a 1pmol/μ mol/Cr increase in the u-NTx level also increased the risk of BMD reduction of the lumbar spine (RR: 1.02), but a 1 point increase in BMI in 2000 decreased it (RR: 0.93) (Table 3B). In Model 1, a 1% rise in BMD (YAM%)

Table 1　Comparison of the physical features, BMD, and levels of bone metabolic markers in 2000 and 2003

Year	2000		2003		Difference (2003-2000)		p	Exclusion of subjects		p※
n	128		128					68		
Age (year)	56.5	(7.6)	59.5	(7.6)				56.7	(5.6)	0.750
height (cm)	153.7	(5.1)	153.4	(5.3)	-0.2878125	(1.1)	0.003	153.1	(4.9)	0.442
weight (kg)	55.2	(7.8)	55.7	(8.1)	0.450390625	(2.9)	0.090	55.9	(6.4)	0.535
BMI (kg/m^2)	23.4	(3.3)	23.7	(3.5)	0.285637631	(1.3)	0.011	23.7	(3.9)	0.492
BMD in lumbar spine (g/cm^2)	0.87	(0.15)	0.85	(0.15)	-0.020733646	(0.04)	<0.001	0.91	(0.16)	0.070
BMD (YAM%) in lumbar spine (%)	86.8	(14.9)	84.8	(14.8)	-2.065104167	(1.2)	<0.001	91.2	(15.6)	0.070
BMD in femoral neck (g/cm^2)	0.71	(0.11)	0.67	(0.11)	-0.041932344	(0.03)	<0.001	0.73	(0.12)	0.267
u-D-Pyr (pmol/μ mol/Cr)	ND		5.6	(1.76)	ND			ND		
u-NTx (nmolBCE/mmol/Cr)	45.9	(19.7)	42.1	(19.2)	-3.8	(26.1)	0.102	ND		

Mean value (standard deviation),　ND: not detected,　※ V.S. Inclusion of subjects in 2000

Table 2　Associations of risk factors with low BMD of lumbar spine and femoral neck in 2003

〔A〕〔Model 1〕

	low BMD of lumbur spine in 2003			low BMD femoral neck in 2003		
	relative risk	95%CI	p	relative risk	95%CI	p
Age in 2000 (year)	1.00	0.94 - 1.06	0.902	1.02	0.96 - 1.08	0.529
Height in 2000 (cm)	1.02	0.95 - 1.09	0.608	0.98	0.92 - 1.04	0.456
BMI in 2000 (kg/m^2)	0.94	0.85 - 1.03	0.202	0.94	0.85 - 1.03	0.186
u-NTx in 2000 (nmolBCE/mmol/Cr)	1.00	0.98 - 1.01	0.760	0.99	0.98 - 1.01	0.368
BMD(YAM%) of lumbur spine in 2000 (%)	0.93	0.90 - 0.95	<0.001	0.96	0.93 - 0.98	0.001
Height reduction for 3 years (cm/year)	1.15	0.55 - 2.39	0.708	0.99	0.46 - 2.17	0.989
BMI reduction for 3 years (kg/m^2/year)	0.81	0.37 - 1.81	0.612	0.77	0.36 - 1.64	0.499

〔B〕〔Model 2〕

	low BMD of lumbur spine in 2003			low BMD femoral neck in 2003		
	relative risk	95%CI	p	relative risk	95%CI	p
Age in 2000 (year)	1.04	0.98 - 1.10	0.227	0.99	0.93 - 1.05	0.696
Height in 2000 (cm)	1.01	0.95 - 1.08	0.778	1.00	0.93 - 1.06	0.909
BMI in 2000 (kg/m^2)	0.93	0.84 - 1.03	0.168	1.00	0.91 - 1.11	0.933
u-NTx in 2000 (nmolBCE/mmol/Cr)	1.00	0.99 - 1.02	0.568	0.99	0.98 - 1.01	0.288
BMD(YAM%) of femoral neck in 2000 (%)	0.96	0.93 - 0.99	0.005	0.92	0.89 - 0.95	<0.001
Height reduction for 3 years (cm/year)	0.97	0.45 - 2.06	0.929	0.82	0.39 - 1.73	0.600
BMI reduction for 3 years (kg/m^2/year)	1.05	0.46 - 2.40	0.906	0.69	0.30 - 1.57	0.377

Footnote: The low BMD (YAM%) in 2003, as adependent variable, was determined by a dichotomous classification into normal (>=80%) and low (<80%) in the models of the lumbar spine in 2000 was preventive against a BMD reduction of the femoral neck (RR: 0.98) (Table 3A), while in Model 2 it was not (Table 3B).

Table 4 shows the associations of risk factors with high levels of bone resorption in the lumbar spine and femoral neck in 2003. High levels of bone resorption as dependent variables were determined by a dichotomous classification into normal (<55 nmoleBCE/mmol) and high (>=55) for u-NTx, and into normal (<5.9 pmol/μ mol/cr) and high (>=5.9) for u-Dpyr in the model. In Model 1, a 1-point rise in BMI in 2000 increased the risk of high u-NTx levels in 2003 (RR: 1.10), whereas a 1% rise in BMD (YAM%) of the lumbar spine in 2000 decreased it (RR: 0.96) (Table 4A). In Model 2, a 1-point increase in BMI in 2000 increased the risk of high u-NTx levels in 2003 (RR: 1.12), while a 1% increase in BMD (YAM%) of the femoral neck in 2000 was preventive against high u-NTx levels (Table 4B). In Model 1, a 1-point rise in BMI in 2000 increased the risk of high u-D-pyr levels in 2003 (RR: 1.11), whereas a 1% rise in BMD (YAM%) of the lumbar spine in 2000 decreased it (RR: 0.97) (Table 4A). In Model 2, a 1-point increase in BMI in 2000 also increased the risk of high u-D-pyr levels in 2003 (RR: 1.11) (Table 4B).

Ⅳ. Discussion

In this three-year-follow-up study on postmenopausal women, we found that higher BMD (YAM%) levels proved to be preventive against low BMDs of the lumbar spine and femoral neck, and a BMD reduction of the femoral neck. We also found that BMD levels of the lumbar spine in 2000 were associated with those of the femoral neck in 2003, and vice versa, suggesting to us it was possible to prevent decreases in bone density. The amount of bone in postmenopausal women was reported to be related to the sreatest amount of bone achieved in a growth period. In this study, we concluded that if the bone density of a growth period was high, this would prevent decreases in bone density[12), 13)].

The fact that osteoporosis is regarded as a lesion of the entire physiological system[14), 15)] suggested that the relationship between BMD levels of the lumbar spine and femoral neck in our study displayed a biological coherence.

High u-NTx levels were found to have a relationship with BMD reductions of the lumbar spine three years later. It is recognized that bone resorption markers are not an absolute index but rather a useful substitute in measuring fracture risk[16)]. This can be regarded as biologically coherent because an increase in u-NTx levels reflects an augmentation of bone resorption[17), 18)]. Accordingly, u-NTx levels can be utilized not only for diagnostic and therapeutic indices, but also for the actual prevention of osteoporosis. It was also found that higher levels of BMI were preventive against BMD reductions of the lumbar spine over a three-year period. Decreases in BMD induced by quadriplegia, postoperative immobility, or the microgravity of spaceflight have been reported[19)]. Therefore it could be explained that higher levels of BMI produce a larger load on the spine, consequently preventing bone loss[20)-23)].

Higher BMI levels were found to increase u-NTx and u-D-Pyr levels over a three-year period while preventing BMD reductions of the lumbar spine. This may be interpreted to suggest that the increase in the spinal load due to a higher BMI intensifies the formation and absorption of the bone and consequently inhibiting bone loss[18)]. This requires further confirmation by an examination of the levels of bone formation markers.

In this study, higher BMD levels of the lumbar spine lowered the risk of incurring abnormally high u-D-Pyr levels three years later. As the bone metabolism in women with high BMD levels is still unclear, it is necessary to study changes in bone metabolism markers longitudinally among them[22), 23)]. Since our subjects showed almost the same anthropometric (height, weight, and BMI) averages as women of a similar aged in Japan[2)], it is suggested that the results of our study can be applied to average healthy women around 50 to 60 years of age.

Acknowledgements

We wish to express our deep gratitude to the teaching staff and students for their valuable cooperation with us at the University of Health Welfare, Hiroshima Prefecture.

Table 3　Associations of risk factors with decrease in BMD of lumbar spine and femoral for three years from 2000 to 2003

〔A〕〔Model 1〕

	Decrease of BMD of lumbur spine for three years			Decrease of BMD of femural neck for three years		
	relative risk	95%CI	p	relative risk	95%CI	p
Age in 2000 (year)	1.00	0.95 - 1.04	0.835	1.01	0.97 - 1.05	0.645
Height in 2000 (cm)	1.01	0.95 - 1.07	0.679	1.01	0.95 - 1.08	0.649
BMI in 2000 (kg/m^2)	0.93	0.84 - 0.99	0.048 *	0.99	0.97 - 1.00	0.080
u-NTx in 2000 (nmolBCE/mmol/Cr)	1.02	1.00 - 1.03	0.049 *	1.07	0.98 - 1.17	0.127
BMD(YAM%) of lumbur spine in 2000 (%)	1.01	0.99 - 1.03	0.507	0.98	0.96 - 1.00	0.029 *
Height reduction for 3 years (cm/year)	1.14	0.55 - 2.34	0.725	1.60	0.55 - 4.68	0.389
BMI reduction for 3 years (kg/m^2/year)	0.82	0.40 - 1.72	0.605	1.29	0.71 - 2.38	0.405

〔B〕〔Model 2〕

	Decrrease of BMD of lumbur spine for three years			Decrease of bone density of femural neck for three years		
	relative risk	95%CI	p	relative risk	95%CI	p
Age in 2000 (year)	0.99	0.95 - 1.04	0.714	1.01	0.98 - 1.05	0.507
Height in 2000 (cm)	1.01	0.95 - 1.07	0.716	0.99	0.94 - 1.04	0.666
BMI in 2000 (kg/m^2)	0.93	0.85 - 0.99	0.048 *	1.00	0.99 - 1.01	0.843
u-NTx in 2000 (nmolBCE/mmol/Cr)	1.02	1.01 - 1.04	0.049 *	1.00	0.93 - 1.07	0.923
BMD(YAM%) of femoral neck in 2000 (%)	1.01	0.98 - 1.03	0.648	1.01	0.99 - 1.03	0.358
Height reduction for 3 years (cm/year)	1.16	0.56 - 2.40	0.687	0.80	0.40 - 1.61	0.537
BMI reduction for 3 years (kg/m^2/year)	0.82	0.40 - 1.69	0.583	0.77	0.47 - 1.25	0.286

Footnote: The decrease in BMD (YAM%) for three years, as a dependent variable, was determined by dichotomous classification into normal (<2.6%) and decrease (>=2.6%) for lumbar spine, and into normal (<2.4%) and decrease (>=2.4%) for femoral neck in the models.

Table 4　Associations of risk factors with high levels of bone resorption in lumbar spine and femoral neck in 2003

〔A〕〔Model 1〕

	high u-NTx in 2003			high u-DPyr in 2003		
	relative risk	95%CI	p	relative risk	95%CI	p
Age in 2000 (year)	0.98	0.92 - 1.05	0.611	0.98	0.93 - 1.03	0.379
Height in 2000 (cm)	1.03	0.95 - 1.11	0.472	1.01	0.95 - 1.07	0.793
BMI in 2000 (kg/m^2)	1.10	1.00 - 1.23	0.046	1.11	1.02 - 1.20	0.018
u-NTx in 2000 (nmolBCE/mmol/Cr)	1.00	0.98 - 1.02	0.979	1.00	0.98 - 1.01	0.894
BMD(YAM%) of lumbur spine in 2000 (%)	0.96	0.93 - 1.00	0.026	0.97	0.95 - 1.00	0.035
Height reduction for 3 years (cm/year)	0.67	0.19 - 2.43	0.543	0.61	0.21 - 1.75	0.355
BMI reduction for 3 years (kg/m^2/year)	0.89	0.40 - 1.98	0.783	1.06	0.59 - 1.90	0.852

〔B〕〔Model 2〕

	high u-NTx in 2003			high u-DPyr in 2003		
	relative risk	95%CI	p	relative risk	95%CI	p
Age in 2000 (year)	0.99	0.93 - 1.06	0.776	0.99	0.94 - 1.03	0.550
Height in 2000 (cm)	1.04	0.95 - 1.13	0.393	1.01	0.95 - 1.08	0.721
BMI in 2000 (kg/m^2)	1.12	1.00 - 1.26	0.050	1.11	1.02 - 1.22	0.019
u-NTx in 2000 (nmolBCE/mmol/Cr)	1.00	0.98 - 1.02	0.972	1.00	0.98 - 1.01	0.865
BMD(YAM%) of femoral neck in 2000 (%)	0.97	0.93 - 0.99	0.045	0.98	0.95 - 1.01	0.114
Height reduction for 3 years (cm/year)	0.61	0.17 - 2.14	0.440	0.56	0.20 - 1.61	0.285
BMI reduction for 3 years (kg/m^2/year)	0.96	0.42 - 2.19	0.921	1.13	0.62 - 2.06	0.681

Footnote: High levels of bone resorption, as dependent variables, were determined by dichotomous classification into normal (<55 nmoleBCE/mmol) and high (>=55) for u-NTx, and into normal (<5.9 pmol/μ mol/cr) and high (>=5.9) for u-Dpyr in the model.

References

1) Soda MY, Mizunuma H, Honjo S, Okano H, Ibuki Y and Igarashi M: Pre- and postmenopausal bone mineral density of the spine and proximal femur in Japanese women assessed by dual-energy x-ray absorptiometry: a cross-sectional study. J. Bone Miner Res., 8(2): 183-189, 1993
2) Iki M, Kajita E, Dohi Y, Nishino H, Kusaka Y, Tsuchida C, Yamamoto K and Ishii Y: Age, menopause, bone turnover markers and lumbar bone loss in healthy Japanese women. Maturitas, 25(1): 59-67, 1996
3) Frangolias DD, Pare PD, Ken2dler DL, Davidson AG, Wong L, Raboud J and Wilcox PG: Role of exercise and nutrition status on bone mineral density in cystic fibrosis. J. Cyst. Fibros., 2(4): 163-170, 2003
4) Tschopp O, Boehler A, Speich R, Weder W, Seifert B, Russi EW and Schmid C: Osteoporosis before lung transplantation: association with low body mass index, but not with underlying disease. Am. J. Transplant, 2(2): 167-172, 2002
5) Yasumura S, Haga H, Nagai H, Suzuki T, Amano H and Shibata H: Rate of falls and the correlates among elderly people living in an urban community in Japan. Age Ageing, 23(4): 323-327, 1994
6) Nguyen TV, Center JR and Eisman JA: Osteoporosis in elderly men and women: effects of dietary calcium, physical activity, and body mass index. J. Bone Miner Res., 15(2): 322-331, 2000
7) Yamamoto I, Takada M, Yuu I, Ohnaka Y, Kigami Y, Yamamoto Y, Hamazu H and Morita R: Radioimmunoassay for the pyridinoline cross-linked carboxy-terminal telopeptide of Type 1 collagen(1CTP) -Some basic aspects of the RIA kit and clinical evaluation in various bone diseases [Jpn]. Kaku Igaku, 30: 1411-1417, 1993
8) Baba H, Hashizume M, Matsuura T and Uemura A: Evaluation of a Specific Immunoassay for Cross-linked N-telopeptides of Type I Collagenn (Ntx) in Urine. J. Med. Tech., 42: 477-481, 1998
9) Yoshimura N: Incidences of fast bone losers and factors affecting changes in bone mineral density. A cohort study in a rural Japanese community. J. Bone Miner Metab., 14: 171-177, 1996
10) Jones G, Nguyen T, Sambrook P, Kelly PJ and Eisman JA: Progressive loss of bone in the femoral neck in elderly people: longitudinal findings from the Dubbo osteoporosis epidemiology study. BMJ, 1994 Sep 17, 309(6956): 691-5, 1994
11) Fukumoto S: Clinical utility of metabolic bone markers. J. Ana. Bio-sci., 22(2): 107-114, 1999
12) Ozdemir F, Demirbag D and Rodoplu M: Reproductive factors affecting the bone mineral density in postmenopausal women. Tohoku J. Exp. Med., 205(3): 277-85, 2005
13) Saito T, Nakamura K, Okuda Y, Nashimoto M, Yamamoto N and Yamamoto M: Weight gain in childhood and bone mass in female college students. J. Bone Miner Metab., 23(1): 69-75, 2005
14) Consensus Development Conference: diagnosis prophylaxis, and treatment of osteoporosis. Am. J. Med., 94: 646-650, 1993
15) Li S, Wagner R, Holm K, Lehotsky J and Zinaman MJ: Relationship between soft tissue body composition and bone mass in perimenopausal women. Maturitas, 47(2): 99-105, 2004
16) Miller PD, Hochberg MC, Wehren LE and Ross PD: Wasnich RD. How useful are measures of BMD and bone turnover?. Curr. Med. Res. Opin., 21(4): 545-54, 2005
17) Minisola S, Pacitti MT, Ombricolo E, Costa G, Scarda A, Palombo E and Rosso R: Bone turnover and its relationship with bone mineral density in pre- and postmenopausal women with or without fractures. Maturitas, 29(3): 265-270, 1998
18) Schneider DL and Barrett-Connor EL: Urinary N-telopeptide levels discriminate normal, osteopenic, and osteoporotic bone mineral density. Arch. Intern. Med., 157(11): 1241-1245, 1997
19) Lueken SA, Arnaud SB, Taylor AK and Baylink DJ: Changes in markers of bone formation and resorption in a bed rest model of weightlessness. J. Bone Miner Res., 8(12): 1433-8, 1993
20) Frangolias DD, Pare PD, Kendler DL, Davidson AG, Wong L, Raboud J and Wilcox PG: Role of exercise and nutrition status on bone mineral density in cystic fibrosis. J. Cyst. Fibros., 2(4): 163-170, 2003
21) Tschopp O, Boehler A, Speich R, Weder W, Seifert B, Russi EW and Schmid C: Osteoporosis before lung transplantation: association with low body mass index, but not with underlying disease. Am. J. Transplant., 2(2): 167-72, 2002
22) Nguyen TV, Center JR and Eisman JA: Osteoporosis in elderly men and women: effects of dietary calcium, physical activity, and body mass index. J. Bone Miner Res., 15(2): 322-331, 2000
23) Hatori M, Hasegawa A, Adachi H, Shinozaki A, Hayashi R, Okano H, Mizunuma H and Murata K: The effects of walking at the anaerobic threshold level on vertebral bone loss in postmenopausal women. Calcif. Tissue Int., 52(6): 411-414, 1993