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Original Article

An Association Between Respiratory Function and Bone Mineral Density in Women from the General Community: A Cross Sectional Study

S. Lekamwasam[1], D. P. Trivedi[2] and K. T. Khaw[2]

[1]Department of Medicine and [2]Clinical Gerontology, University of Cambridge School of Clinical Medicine, Addenbrooke's Hospital, Cambridge, UK

Abstract. Respiratory function has been associated with bone mineral density (BMD) in patients with respiratory diseases. We examined the relationship between bone density measured at the hip and respiratory function in women from the general community. A total of 4830 women aged 45–76 years were recruited from general practice age – sex registers in Cambridge between 1991 and 1995. At baseline survey, data collection included health questionnaires, measures of anthropometry, respiratory function, as well as bone mineral density BMD measured using dual energy X ray absorptiometry. BMD at total hip, femoral neck and trochanter significantly and positively correlated with FEV_1. This association was independent of age, weight, height, smoking habit, history of respiratory diseases, corticosteroids and use of hormone replacement therapy. After adjustment for these factors, an increase in FEV_1 of 1 l/s was associated with 0.026, 0.021 and 0.026g/cm^2 increase in bone mineral density at total hip, femoral neck and trochanter respectively. The association was consistent and similar in magnitude among current smokers and current non-smokers and across all age groups. The magnitude of the association was comparable to that associated with an age difference of 6 years or weight difference of 5 kg. Women in the bottom compared to top quartile of respiratory function had about double the risk of low bone density independent of other factors. Respiratory function measured using FEV_1 is positively and independently related to BMD in these middle-aged and older women across the whole normal distribution of these physiologic measures. This may reflect underlying common determinants such as physical activity. Even in healthy women, respiratory function may be a marker for women at increased risk of osteoporosis and associated fractures.

Keywords: Bone density; Community; Forced expiratory volume; Osteoporosis; Respiratory function; Women

Correspondence and offprint requests to: Professor K. T. Thaw, Clinical Gerontology Unit, Level 2, Box 251, University of Cambridge School of Clinical Medicine, Addenbrooke's Hospital, Cambridge CB2 2QQ, UK. e-mail: kk101@medschl.cam.ac.uk

Introduction

Osteoporosis and fragility fractures not only have considerable current medical and economic impact but are projected to increase exponentially world wide[1,2]. Bone mineral density (BMD) and fragility fractures in adults have been associated with numerous genetic, nutritional and environmental factors [3,4]. These include physical activity [5], alcohol intake [6], smoking habit [7], milk consumption [8] and parity [9] as well as early life factors such as weight and length at birth or at one year [3,4]. Some of these factors may help to explain the wide geographic variations and secular changes in bone health and fracture occurrence [10].

In clinical studies in patients with respiratory diseases such as cystic fibrosis and bronchial asthma, measures of respiratory function have correlated with bone mineral density [11,12]. In addition to compromised lung function, patients with these conditions are exposed to a variety of other factors that might impair their bone health. For example, cystic fibrosis is associated with pancreatic malabsorption and bronchial asthma is often treated with long-term corticosteroids. Conversely, in patients who have spinal osteoporotic fractures, reduced

pulmonary function is related to the severity of spinal deformity [13] where, again, there are obvious reasons for the association.

It is, therefore, not clear whether the observed association between respiratory function and BMD is simply restricted to patients with respiratory or other diseases or whether it occurs across the whole normal range of respiratory function.

In the current study we examined the relationship between respiratory function and bone mineral density in a population-based cross-sectional study of women living in the community.

Methods

The Cambridge General Practice Health Study invited women aged 45–76 years, resident in the community and identified using general practice age-sex registers, to participate in a health survey between 1991 and 1995. About 50% of those mailed agreed to participate. All those consenting completed a health and lifestyle questionnaire, which included questions on past medical history and social habits. They then attended for a health examination at Addenbrooke's Hospital, Cambridge.

At the health examination, height and weight was measured in light clothing without shoes. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Bone mineral density was measured at the total hip, femoral neck and trochanter by dual energy X-ray absorptiometry (DEXA), using the Hologic QDR –1000 densitometer (Hologic Inc., Waltham, MA, USA). The coefficient of variation for hip BMD measurement was 1.6% for femoral neck, 1.5% for trochanter and 3.0% for Ward's triangle [14]. In these analyses, results for total hip, femoral neck and trochanteric area are presented. Current smokers were defined as those who reported 'Yes' to the question 'Do you smoke cigarettes now?' Steroid users were defined as those who reported 'Yes' to the question 'Have you ever taken steroid tablets or injections for three months or more?' Women taking hormone replacement therapy (HRT) were defined as those who reported 'Yes' to the question 'Are you currently receiving any hormone replacement therapy (HRT)?'

Respiratory function was assessed by forced expiratory volume in 1 second, FEV_1, which was measured twice using a portable spirometer (Micromedical, UK) [15]. The higher reading of the two measurements was used in the analyses. Pulse rate was assessed as the average of two readings after the participant had been sitting resting for five minutes.

Statistical Analyses

Women were divided into quartiles according to respiratory function. Descriptive data are expressed as mean (SD) or percentages (number) in FEV_1 quartiles. Differences in BMD between FEV_1 quartiles were compared unadjusted and then adjusted for possible covariates using analysis of variance (ANOVA). Since FEV_1 and BMD are related to weight and height in different ways, we used weight and height independently in the models rather than the BMI. However, using BMI in place of height and weight in the analytical model did not change the salient findings. A linear regression model was fitted with BMD as the dependent variable and FEV_1 as independent variable with and without other covariates in the model. This analysis was repeated in women who had no previous history of respiratory (chronic obstructive airways disease or asthma), cardiovascular disease or cancer and had not taken steroids or hormone replacement therapy.

We arbitrarily defined low bone density as women in the bottom quintile of the bone density distribution (bottom quintile threshold points for total hip were $<=0.771$ g/cm^2 (estimated T-score -1.70), neck $<=0.634$ g/cm^2 and trochanter $<=0.570$ g/cm^2). We examined the prevalence of women with low bone density by quartile of respiratory function in the whole cohort and after excluding all women taking steroids, HRT or current smokers. Data were analyzed using SPSS software, version 10.0 for Windows. All significance tests were two sided.

Results

Descriptive Data

The baseline characteristics for 4830 women aged 45–76 years according to quartile of FEV_1 are shown in Table 1. Compared to the highest quartile of FEV_1, women in the lowest quartile were older, shorter and had lower bone mineral density. They were more likely to have taken steroids and report past history of respiratory disease, cardiovascular disease or cancer. Women in the lowest quartile were less likely to be current users of HRT compared to those in the highest quartile.

Association between BMD and FEV_1

Bone mineral density was continuously related with FEV_1, with mean bone mineral density increasing with increasing quartile of FEV_1 (Table 2). This association was apparent in all three sites, and remained significant after adjusting for age, weight, height, current smoking, and past history of disease, HRT and steroid use.

Table 3 shows the relationship between BMD and FEV_1 as continuous variables using multiple regression adjusted for age, weight, height, current smoking, current HRT, steroid use, past history of respiratory disease, cardiovascular disease or cancer.

We also analyzed the relationship in subgroups stratified by age (45–54 years, n=2047; 55–64 years, n=1588; and 65+ years, n=1195) adjusting for weight and height and stratified by smoking status (623 current

Table 1. Characteristics of 4830 women aged 45–76 years according to FEV_1 quartiles in the Cambridge General Practice Study

	Quartile 1 (0.51–1.98 l/s) *n*=1216 Mean (SD)	Quartile 2 (1.99–2.32 l/s) *n*=1167 Mean (SD)	Quartile 3 (2.33–2.67 l/s) *n*=1232 Mean (SD)	Quartile 4 (2.68–4.11 l/s) *n*=1215 Mean (SD)	Unadjusted *p* value
FEV_1	1.7 (0.28)	2.2 (0.10)	2.5 (0.10)	2.9 (0.23)	<0.001
Age (years)	64.4 (7.2)	59.7 (7.6)	54.8 (7.1)	51.5 (5.8)	<0.001
Height (cm)	157.9 (6.3)	159.9 (5.3)	161.8 (5.5)	161.5 (6.4)	<0.001
Weight (kg)	65.8 (11.8)	66.8 (11.8)	66.7 (11.9)	66.9 (9.8)	0.056
BMI (kg/m^2)	26.5 (4.5)	26.1 (4.4)	25.5 (4.3)	24.4 (3.3)	<0.001
Pulse (beats/min)	75.2 (12.4)	75.1 (11.7)	74.7 (14.1)	75.1 (11.8)	0.713
Total hip BMD (g/cm^2)	0.829 (0.136)	0.879 (0.139)	0.911 (0.133)	0.932 (0.123)	<0.001
Femoral neck BMD (g/cm^2)	0.686 (0.118)	0.728 (0.124)	0.763 (0.127)	0.791 (0.121)	<0.001
Trochanter BMD (g/cm^2)	0.616 (0.112)	0.656 (0.108)	0.681 (0.103)	0.703 (0.101)	<0.001
	Number (%)	Number (%)	Number (%)	Number (%)	
COAD/asthma	377 (31%)	250 (21.4%)	263 (21.3%)	208 (17.1%)	<0.001
History of cancer	96 (7.9%)	75 (6.4%)	60 (4.9%)	50 (4.1%)	<0.001
History of CVD	56 (4.6%)	27 (2.3%)	18 (1.5%)	2 (0.2%)	<0.001
Current HRT	118 (9.7%)	210 (17.9%)	317 (25.7%)	317 (26.1%)	<0.001
Ever taken steroid	80 (6.6%)	39 (3.3%)	47 (3.8%)	32 (2.6%)	<0.001
Current smoking	119 (9.8%)	150 (12.9%)	156 (12.7%)	118 (9.7%)	<0.001

FEV_1,Forced expiratory volume; BMD, Bone mineral density; COAD, chronic obstructive airway disease; CVD, cardiovascular disease; HRT, hormone replacement therapy.

Table 2. Crude and adjusted mean BMD values in FEV_1 quartiles in 4830 women aged 45–76 years in the Cambridge General Practice Study

		Quartile 1 (0.51–1.98 l/s) *n*=1216 Mean (SD)	Quartile 2 (1.99–2.32 l/s) *n*=1167 Mean (SD)	Quartile 3 (2.33–2.67 l/s) *n*=1232 Mean (SD)	Quartile 4 (2.68–4.11 l/s) *n*=1215 Mean (SD)	*p* value
Total hip BMD (g/cm^2)	*	0.829 (0.136)	0.879 (0.139)	0.911 (0.133)	0.932 (0.123)	<0.001
	**	0.865 (0.278)	0.888 (0.208)	0.896 (0.208)	0.904 (0.278)	<0.001
	***	0.854 (0.556)	0.873 (0.556)	0.879 (0.556)	0.887 (0.625)	<0.001
Femoral neck BMD (g/cm^2)	*	0.686 (0.118)	0.728 (0.124)	0.763 (0.127)	0.791 (0.121)	<0.001
	**	0.726 (0.278)	0.739 (0.208)	0.746 (0.208)	0.757 (0.278)	<0.001
	***	0.721 (0.556)	0.731 (0.556)	0.737 (0.556)	0.748 (0.556)	<0.001
TrochanterBMD (g/cm^2)	*	0.616 (0.112)	0.656 (0.108)	0.681 (0.103)	0.703 (0.101)	<0.001
	**	0.643 (0.208)	0.663 (0.208)	0.671 (0.208)	0.681 (0.208)	<0.001
	***	0.629 (0.486)	0.645 (0.486)	0.652 (0.486)	0.661 (0.486)	<0.001

FEV_1 = Forced expiratory volume, BMD=Bone mineral density
* Crude; ** Adjusted for age, height and weight; *** Adjusted for age, height, weight, smoking, hormone replacement therapy and steroid use, chronic obstructive airway disease, /asthma, cancer and cardiovascular disease.

smokers and 4207 current non-smokers) adjusting for age, weight and height. Finally we examined the relationship between bone mineral density and FEV_1 in 2692 women after excluding all women with a history of respiratory diseases, cancer, cardiovascular disease and steroid use, as well as women who were current HRT users, adjusting for age, weight and height in the model.

A unit increase in FEV_1 (1 l/s) was associated with an increase of 0.065–0.075 g/cm^2 ($p<0.001$) in BMD across three sites in the hip. After adjusting for age, weight and height the magnitude of relationship was reduced to between 0.023 and 0.03 g/cm^2 though still significant ($p<0.001$). The relationship remained significant after adjusting for other covariates including smoking, medication use and existing diseases. The gradients of the relationship between bone mineral density and FEV_1 were comparable not only across different age groups but also between current smokers and current non-smokers. Results were similar in women with no past history of diseases and those not taking steroids or HRT.

Table 4 shows the prevalence of women with low bone density (bottom quintile of BMD distribution) increased with decreasing quartile of respiratory function, with about three times the prevalence in the lowest compared to the highest quartile. Findings were similar

Table 3. Relationship of FEV1 and BMD in multiple regression analysis: Regression coefficients of BMD with FEV1 quartiles in the Cambridge General Practice Study

			Coefficient (per one 1 l/s)	SE	*p* value
Entire group	Total hip	*	0.026	0.004	<0.001
(*n*=4830)	Femoral neck	*	0.021	0.004	<0.001
	Trochanter	*	0.026	0.004	<0.001
Age 45–54	Total hip	**	0.034	0.006	<0.001
(*n*= 2047)	Femoral neck	**	0.031	0.007	<0.001
	Trochanter	**	0.033	0.006	<0.001
Age 55–64	Total hip	**	0.039	0.007	<0.001
(*n*=1588)	Femoral neck	**	0.032	0.007	<0.001
	Trochanter	**	0.032	0.006	<0.001
Age 65+	Total hip	**	0.039	0.008	<0.001
(*n*=1195)	Femoral neck	**	0.029	0.008	<0.001
	Trochanter	**	0.040	0.007	<0.001
Current smokers	Total hip	***	0.036	0.012	0.002
	Femoral neck	***	0.031	0.011	0.004
(*n*=620)	Trochanter	***	0.023	0.010	0.028
Current nonsmokers	Total hip	***	0.029	0.005	<0.001
	Femoral neck	***	0.021	0.004	<0.001
(*n*=4210)	Trochanter	***	0.030	0.004	<0.001
Excluding diseases	Total hip	***	0.029	0.006	<0.001
and drugs (*n*=2692)	Femoral neck	***	0.023	0.006	<0.001
	Trochanter	***	0.031	0.005	<0.001

FEV_1 = Forced expiratory volume, BMD=Bone mineral density.
* FEV_1 adjusted for age, height, weight, smoking, hormone replacement therapy, steroid use, chronic obstructive airways disease/asthma, cancer and cardiovascular diseases.
** FEV_1 adjusted for height and weight.
*** FEV_1 adjusted for age, height and weight.

Table 4. Risk of low bone density according to respiratory function in 4830 women aged 45–76 years in the Cambridge General Practice Study

Prevalence of low bone density[a] *n* (%)					Adjusted[b] odds ratio of low bone density in FEV_1 quartile 1 vs quartile 4 (95% CI)	*p* value
Quartile of FEV_1	Quartile 1 (0.51–1.98 l/s) *n*=1216	Quartile 2 (1.99–2.32 l/s) *n*=1167	Quartile 3 (2.33–2.67 l/s) *n*=1232	Quartile 4 (2.68–4.11 l/s) *n*=1215		
Total hip BMD	428 (35.2)	256 (21.9)	173 (14.0)	111 (9.1)	2.14 (1.57–2.92)	<0.001
Femoral neck BMD	429 (35.3)	271 (23.2)	165 (13.4)	100 (8.2)	1.83 (1.34–2.51)	<0.001
Trochanter BMD	434 (35.7)	253 (21.7)	170 (13.8)	104 (8.6)	2.22 (1.64–3.01)	<0.001

FEV_1=Forced expiratory volume; BMD, Bone mineral density.
[a]Low bone density = bottom quintile of bone density distribution.
[b]Adjusted for age, height, weight, pulse rate, smoking, hormone replacement therapy, steroid use, chronic obstructive airways disease/asthma, cancer and cardiovascular diseases.

for 2361 women with no past history of diseases, not taking steroids or HRT and were non-smokers. Table 4 also shows that women in the bottom compared to the top quartile of respiratory function had about double the risk of low bone density even after adjusting for covariates age, weight, height, pulse rate, smoking, medication use and past history of respiratory and cardiovascular disease or cancer.

Discussion

We found a positive and continuous relationship between FEV_1 and bone mineral density at the hip across the whole normal range of respiratory function in women in the community. After adjusting for possible confounding factors, the mean hip bone mineral density in women in the highest FEV_1 quartile was 3%–5%

higher than the mean BMD in women in the lowest quartile (Table 2). In multiple regression analyses, a unit change in FEV_1 (1 l/s) was associated with about 0.030 g/cm^2 change in total hip BMD independent of other covariates. Despite the differences in composition of bone in different skeletal sites, there was little variation in the BMD FEV_1 relationship at different sites. Within this study group, the magnitude of this relationship was comparable to a difference of 6 years in age or difference of 5 kg in weight on total hip bone mineral density. Random measurement errors in both FEV_1 and bone mineral density are likely to underestimate the magnitude of the relationship.

In our study population, both BMD and FEV_1 were positively related to weight and height. The age-adjusted partial correlation coefficients between BMD and weight at total hip, femoral neck and trochanter were $r = 0.46$, 0.37 and 0.36 ($p < 0.001$ for all), respectively. Partial correlations between bone mineral density and height at same sites were $r = 0.09$, 0.10 and 0.13, respectively ($p < 0.001$ for all). FEV_1 related more strongly to height ($r = 0.43$, $p < 0.001$) than weight ($r = 0.05$, $p < 0.001$). However, the correlation seen between BMD and FEV_1 remained significant even after adjusting for the effect of height and weight and the association appeared to be independent of these two measurements.

FEV_1, a commonly used lung function test in clinical practice, is reduced in both obstructive and restrictive lung diseases. Low BMD has been shown to occur in both obstructive and restrictive lung diseases [11,12]. Although the exact etiology of this is unclear, in patients with these respiratory diseases, chronic ill health, poor nutrition or medication such as steroid use could affect BMD. However, in the current cohort, the association between BMD and FEV_1 was apparent across the normal range of respiratory function even after excluding women with any history of respiratory disease.

The reason for this relationship is not clear. Cigarette smoking habit might plausibly explain the association. Smoking has a negative effect on bone metabolism [7] and is also a major cause of chronic obstructive airway disease resulting in impaired FEV_1 [16]. However, a similar correlation was observed in this cohort of women in both current smokers and current non-smokers; 68% of the latter group consisted of people who never smoked during their life. Smoking is therefore unlikely to explain this association.

Hypoxia has negative effects on bone mineralization [17] but whether the association is mediated through the degree of arterial oxygen saturation is unknown. Patients with chronic airflow limitation tend to be symptomatic by the time they develop chronic hypoxia and are not likely to remain undiagnosed. Patients with interstitial lung diseases tend to develop chronic hypoxia early and they can remain asymptomatic and undiagnosed for a variable period of time. Nevertheless, the low prevalence of interstitial lung diseases in the community [18] is unlikely to explain the above findings.

Low vitamin D levels have been documented among patients with cystic fibrosis, in whom the FEV_1 was correlated with bone mineral density [11]. Poor nutrition, limited sun exposure and pancreatic malabsorption can all contribute to hypovitaminosis D in these patients. Chronic hypovitaminosis D and resulting secondary hyperparathyroidism is known to impair bone mineralization [19]. Hypovitaminosis D is also known to be associated with skeletal muscle weakness [20] although the effect on respiratory muscles has not been documented. Whether low vitamin D status might contribute to the observed association remains to be established.

Physical activity is known to have a positive influence on bone mineral density [21]. FEV_1 depends on the strength of respiratory musculature and vital capacity, both of which are likely to improve with physical activity. Adjusting for self-reported physical activity did not change the findings (results not shown), but it is likely that we were unable to adjust adequately for physical activity in the statistical analysis, since our measurements of physical activity were crude. We used pulse rate as a surrogate marker of physical fitness but its inclusion in the regression model together with other covariates did not change the magnitude of the observed association.

The observed 3–5% difference in mean hip bone mineral density between top and bottom FEV_1 quartiles seen in this study may be of clinical and public health relevance. A difference in bone mineral density of similar magnitude was found when women reporting most frequent milk consumers were compared with least frequent milk consumers [8] and tea drinkers were compared with non-tea drinkers [22]. Tea drinking appears to be associated with lower hip fracture rates in both men and women in Europe [23,24]. Bone mineral density change of similar magnitude occurs following long-term HRT therapy, which has been shown to reduce the incidence of vertebral fractures by nearly 50%.

Although BMD is a major known determinant of future fracture risk of an individual, and pharmacologic interventions such as the bisphosphonates have been shown to reduce fracture risk, other factors which may influence the absolute risk of fracture are taken into consideration when making therapeutic decisions. Women in the bottom quartile of distribution for respiratory function had double the risk of low bone density. It would be of interest to know if respiratory function is an independent predictor of fracture risk. Among the patients with low BMD, the subgroup with poor respiratory function may form a special risk group for future fractures. Both low BMD and low FEV_1 have been shown to predict mortality in men and women [25–27].

The significant association between respiratory function and hip bone mineral density, found across all age groups in women living in the general community has, not to our knowledge, been previously reported. This relationship was independent of age, weight, height, smoking habit, medication use and clinical respiratory or bone diseases. The exact mechanism of this association is unclear but is likely to reflect some common

etiological factor or factors such as physical activity or nutritional status which need to be explored in future studies. In the interim, poor respiratory function may be a useful indicator of women at increased risk of osteoporosis.

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References

1. Ray NF, Chan JK, Thamer M, Melton LJ,III. Medical expenditures for the treatment of osteoporotic fractures in the United States in 1995: report from the National Osteoporosis Foundation. J Bone Miner Res 1997;12:24–35.
2. Cooper C, Campion G, Melton LJ, III. Hip fractures in the elderly: a world-wide projection. Osteoporos Int 1992;2:285–9.
3. Gale CR, Martyn CN, Kellingray S, Eastell R, Cooper C. Intrauterine programming of adult body composition. J Clin Endocrinol Metab 2001;86:267–72.
4. Cooper C, Cawley M, Bhalla A, et al. Childhood growth, physical activity, and peak bone mass in women. J Bone Miner Res 1995;10:940–7.
5. Bradney M, Pearce G, Naughton G, et al. Moderate exercise during growth in prepubertal boys: changes in bone mass, size, volumetric density, and bone strength: a controlled prospective study. J Bone Miner Res 1998;13:1814–21.
6. Clark K, Sowers MR. Alcohol dependence, smoking status, reproductive characteristics, and bone mineral density in premenopausal women. Res Nurs Health 1996;19:399–408.
7. Daniell HW. Osteoporosis of the slender smoker. Vertebral compression fractures and loss of metacarpal cortex in relation to postmenopausal cigarette smoking and lack of obesity. Arch Intern Med 1976;136:298–304.
8. Murphy S, Khaw KT, May H, Compston JE. Milk consumption and bone mineral density in middle aged and elderly women. BMJ 1994;308:939–41.
9. Murphy S, Khaw KT, May H, Compston JE. Parity and bone mineral density in middle-aged women. Osteoporos Int 1994;4:162–6.
10. Melton LJ, III, O'Fallon WM, Riggs BL. Secular trends in the incidence of hip fractures. Calcif Tissue Int 1987;41:57–64.
11. Elkin SL, Fairney A, Burnett S, et al. Vertebral deformities and low bone mineral density in adults with cystic fibrosis: a cross-sectional study. Osteoporos Int 2001;12:366–72.
12. Nishimura Y, Nakata H, Maeda H, Yokoyama M. [Bone mineral content in patients with bronchial asthma]. Nihon Kyobu Shikkan Gakkai Zasshi 1995;33:300–5.
13. Schlaich C, Minne HW, Bruckner T, et al. Reduced pulmonary function in patients with spinal osteoporotic fractures. Osteoporos Int 1998;8:261–7.
14. Laskey MA, Flaxman ME, Barber RW, et al. Comparative performance in vitro and in vivo of Lunar DPX and Hologic QDR-1000 dual energy X-ray absorptiometers. Br J Radiol 1991;64:1023–9.
15. Cox BD, Huppert FA, Whichelow MJ. The Health and Lifestyle Survey: 7 years on. Dartmouth, 1993.
16. Barnes PJ. Chronic obstructive pulmonary disease. N Engl J Med 2000;343:269–80.
17. Fujimoto H, Fujimoto K, Ueda A, Ohata M. Hypoxemia is a risk factor for bone mass loss. J Bone Miner Metab 1999;17:211–6.
18. Coultas DB, Zumwalt RE, Black WC, Sobonya RE. The epidemiology of interstitial lung diseases. Am J Respir Crit Care Med 1994;150:967–72.
19. Lamberg-Allardt CJ,Outila TA, Karkkainen MU, Rita HJ, Valsta LM. Vitamin D deficiency and bone health in healthy adults in finland: could this be a concern in other parts of Europe? J Bone Miner Res 2001;16:2066–73.
20. Glerup H, Mikkelsen K, Poulsen L, et al. Hypovitaminosis D myopathy without biochemical signs of osteomalacic bone involvement. Calcif Tissue Int 2000;66:419–24.
21. Welten DC, Kemper HC, Post GB, et al. Weight-bearing activity during youth is a more important factor for peak bone mass than calcium intake. J Bone Miner Res 1994;9:1089–96.
22. Hegarty VM, May HM, Khaw KT. Tea drinking and bone mineral density in older women. Am J Clin Nutr 2000;71:1003–7.
23. Kanis J, Johnell O, Gullberg B, Allander E, Elffors L, Ranstam J et al. Risk factors for hip fracture in men from southern Europe: the MEDOS study. Mediterranean Osteoporosis Study. Osteoporos.Int. 1999;9:45-54.
24. Johnell O, Gullberg B, et al. Risk factors for hip fracture in European women: the MEDOS Study. Mediterranean Osteoporosis Study. J Bone Miner Res 1995;10:1802–15.
25. Trivedi DP, Khaw KT. Bone mineral density at the hip predicts mortality in elderly men. Osteoporos Int 2001;12:259–65.
26. Browner WS, Seeley DG, Vogt TM, Cummings SR. Non-trauma mortality in elderly women with low bone mineral density. Study of Osteoporotic Fractures Research Group. Lancet 1991;338:355–8.
27. Ryan G, Knuiman MW, Divitini ML, James A , Musk AW, Bartholomew HC. Decline in lung function and mortality: the Busselton Health Study. J Epidemiol Community Health 1999;53:230–4.

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