

THE PREVALENCE OF OSTEOPOROSIS IN AN IRANIAN POPULATION

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Background - The present study was designed to determine the prevalence of osteoporosis in a representative group of healthy Iranian population.

Methods- The study population comprised of apparently healthy subjects who participated in the Iranian Multi-centric Osteoporosis Study (IMOS), a cross-sectional study carried out in urban areas of five great cities to assess the bone health in the country. Bone mineral density (BMD) values for the lumbar spine (L2-L4), the femoral neck and total hip were measured with a Lunar DPXMD densitometer (Lunar 7164, GE, Madison, WI) and used to identify the osteoporotic and osteopenic cases based on WHO categorization.

Results- A total of 4450 individuals (42.7% were male) with the mean age of 42.6 ± 13.9 years were studied. Some 522 of the studied females (20.5%) were menopause. Using the WHO definition, some 246 (6.5%) of the total studied subjects (4.8% of males and 7.7% of females) had osteoporosis (Table1). There was a significant difference between the frequency of osteoporosis among the two genders (P-value < 0.001).

Compared to pre-menopause women, osteoporosis assessed at different sites was more common among menopause women (neck of femur: 5.6% vs. 0.5%, total hip: 3% vs. 0.5%, spine: 18.4% vs. 3.5%; all the P-values were <0.001).

When the prevalence of osteoporosis was compared at different sites between genders, the condition was more prevalent among females aged more than 50. As for those aged less than 50, however, osteoporosis at different sites (except for spine) was more prevalent in men (Table 2).

Conclusion- Considering the high number of osteoporotic cases in the country, the early identification of low bone mass in both genders is of great concern. The considerable differences in BMD values reported in different populations also brings up the need for the development of a nationwide standardization of BMD measurements through the appropriate use of population-specific reference values.

ASSOCIATION BETWEEN DIFFERENT DOMAINS OF PHYSICAL ACTIVITY AND FRACTURES

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BACKGROUND: Epidemiological studies suggest for an inverse relationship between physical activity and risk of fractures. However, it is unclear how this association varies according to the domain of life in which the activity is undertaken.

METHODS: In the context of the European Prospective Investigation of Cancer- Norfolk study, total and domain-specific physical activity was assessed in 14,903 participants (6,514 men, mean age 62 yr) using a validated questionnaire (EPAQ2). After a median follow-up of 8 years, there were 504 fractures of which 164 were hip fractures. Metabolic equivalent measures were calculated according to frequency and duration of different activities for all participants.

RESULTS: The hazard ratios (95%CI) for any fracture due to physical activity undertaken at home, during exercise, at work, for transport, and in total were 1.14 (0.87-1.49), 0.91 (0.69-1.19), 1.31 (0.76-2.23), 1.33 (0.80-2.24), and 1.31 (0.99-1.74), respectively, after adjustment for baseline age, sex, history of fracture, body mass index, smoking status, alcohol intake, and heel broadband ultrasound attenuation in Cox proportional-hazards models. Hip fracture was inversely associated with moderate physical activity at home (HR=0.55, 95%CI 0.30-0.98) and for exercise (HR=0.52, 95%CI 0.29-0.93) among women. Sport/recreational activities were associated with highly reduced risk of hip fracture among men (HR=0.18, 95%CI 0.05-0.62; P for trend=0.004). Higher amounts of reported housework were associated with reduced risk of fracture among women and increased risk of fracture among men. Walking for leisure or transport for >90 min/week was associated with reduced risk of any fracture (HR=0.74, 95%CI 0.58-0.95) and hip fracture (HR=0.57, 95%CI 0.37-0.87) in both men and women. The associations between different domains of physical activity and fractures were more evident in younger participants (age <65 yr) and those without previous history of fracture.

CONCLUSION: This study suggests that physical activities at home and during exercise are associated with lower risk of hip fracture, whereas occupational and transportation-related activities are not. The interaction observed between age and physical activity suggests for a higher impact of activity on bones in the younger ages which might not be achievable for the elderly people. Further attention to the interactions between different domains of physical activity and known fracture risk factors among men and women is recommended.

PREVALENCE AND CORRELATES OF OSTEOPOROSIS IN US MEN

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While male osteoporosis has recently received attention as a growing public health concern, widely discrepant estimates of its prevalence exist, and relatively little is known about the characteristics of men with osteoporosis. The objectives of this study were to determine the prevalence of osteoporosis in US men using alternative definitions, and to describe correlates of low bone mass in men.

We used DXA data from the most recent (2005-2006) National Health and Nutrition Examination Survey to identify men with femoral neck osteoporosis (T-score ≤ -2.5), using both male and female normative references. Prevalence estimates based on bone mineral density (BMD) were compared with self-reported prevalence of osteoporosis. Corresponding national prevalence estimates were obtained using survey sample weights. Logistic regression was used to assess the association between subject characteristics and osteoporosis (based on female norms) among men aged 50 and older.

Based on female norms, estimates of osteoporosis ranged from 0.6% of men in their fifties to 8.8% of men eighty and older; corresponding estimates using male norms ranged from 2.0% to 11.6%. Projecting to the US population, this corresponds to 0.7 million (95% CI: 0.4-1.0 million) men with low femoral neck bone mass using female norms, and 1.2 million (95% CI: 0.8-1.7 million) men using male norms. A generational effect was noted between BMD-based and self-reported osteoporosis prevalence estimates. More subjects in their fifties reported having been diagnosed and treated for osteoporosis than met BMD criteria, while more men eighty and older met BMD criteria than reported diagnosis or treatment. After adjustment for age, a number of differences were noted between men 50 and older with and without osteoporosis. Osteoporotic men were shorter (mean height 166 vs. 175 cm, $p=0.01$), and more likely to report being unable to perform tasks around the home/yard (21.6% vs. 2.0%, $p=0.01$), walk or bicycle (23.4% vs. 1.4%, $p<0.01$), and engage in moderate activities (30.4% vs. 2.5%, $p<0.01$) than their non-osteoporotic peers.

Estimates of the number of US men with low femoral neck bone mass range from 0.7 to 1.2 million depending on the normative reference used. Men with osteoporosis are shorter than their non-osteoporotic peers and report greater functional disability than their peers. More research is needed to understand the functional consequences of male osteoporosis by different criteria.

DISTRIBUTION OF T-SCORES AND Z-SCORES IN A UNIVERSITY COHORT WITH AN EMPHASIS ON ELEVATED BONE MINERAL DENSITY (BMD)

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Introduction: Elevated BMD is currently not defined by the ISCD with a specific Z-score cutoff, however it has been suggested that a Z-score ≥ 2.5 is not normal.

Methods: IRB approval was obtained. We evaluated a University DXA database over 24 months to define T-score and Z-score distributions. A Z-score of equal to or greater than 2.5 was selected as the outcome event of interest in a logistic regression for adjusted odds ratio. The covariates were: height, weight, gender, menopausal status, use of female hormones, presence of insufficiency fractures after age 50, previous fractures, previous surgeries (back surgeries, vertebroplasty, or kyphoplasty), transplant history, presence of long term chronic conditions (asthma, lupus, rheumatoid arthritis, or cystic fibrosis), eating disorder, current use of glucocorticoids, smoking status, along with current and past usage of osteoporosis pharmacological therapies.

Results: The study included a total of 8,216 patients; 7212 (87.8%) were female and 1044 (12.2%) were male. In the total population, 13.6% had a Z-score of ≥ 2.5 at the lumbar spine, femoral neck, or total hip. Only 0.19% of the males and 0.76% of the females had a Z-score ≥ 2.5 at all 3 sites. The 97.5th percentiles for Z-scores in our population for men and women respectively were 3.4 and 3.9 at the lumbar spine, 1.5 and 2.1 at the femoral neck and 1.6 and 2.7 at the total hip. The 99th percentile for Z-scores for men and women respectively were 3.4 and 3.9 at the lumbar spine, 4.9 and 4.7 at the femoral neck and 2.4 and 2.7 at the total hip. At the lumbar spine, female gender and weight were found to be risk factors for an elevated Z-score (≥ 2.5). The use of steroids, bone-active medications, BMI, and smoking were significantly less likely to predict a lumbar spine Z-score ≥ 2.5 . An elevated total hip Z-score is predicted by increasing weight, while those patients using bone-active medications were less likely to have elevated BMD at the total hip. At the femoral neck, there were no significant risk factors related to a Z score ≥ 2.5 ; those taking bone-active medications were significantly less likely to have an elevated Z-score. Conclusion: This data suggests that an elevated Z-score is common at one or more sites and that further research about the Z-score cut point and whether multiple regions of interest need to have an elevated Z-score before making a diagnosis of high bone mineral density is warranted.

COORDINATE REGULATION OF BONE BIOMECHANICAL PERFORMANCE AND BONE SIZE IN MICE

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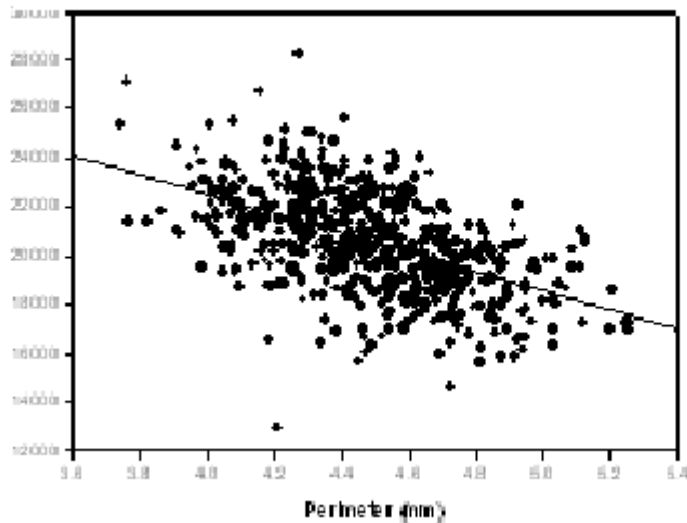
BACKGROUND: While DXA is the single best clinical tool for predicting fracture risk, it fails to reflect all aspects of biomechanical performance. These can't be studied systematically in the clinical setting since fractures are unique, unpredictable, and therefore unrecorded events. Animal models therefore offer the best approach to studying bones under load conditions similar to those that cause fractures.

METHODS: We studied the femora of 603 17 week old mice from a reciprocal F2 intercross between recombinant congenic mouse strains HcB-8 and HcB-23, performing DXA scans, 3-point bending tests, and imaging of the fracture surfaces, ultimately measuring 17 different mechanical and anatomical bone properties. We adjusted the measurements for sex and cross direction (8 female x 23 male or 23 female x 8 male). Following normalization and standardization of the raw data, we determined the correlations between each pair of properties. We mapped performed linkage analysis to map the genes responsible for variation in bone size and biomechanical performance.

RESULTS: HcB-23 mice have large diameter bones with high BMD, maximum load, low modulus, and low energy to failure. HcB-8 bones display opposite properties, with small bone size, low BMD, low maximum load, high modulus, and high energy to failure. The femoral ash percentage does not differ between these strains. BMD functions well as a surrogate for maximum load in 3-point bending tests, with $R = 0.77$, $p < 10^{-19}$. BMD is much less successful at predicting energy to failure, with $R = 0.35$, $p < 10^{-18}$, and was not correlated to deflection (the amount the bone bends while loaded). Linkage mapping reveals that in addition to BMD being correlated with maximum load, quantitative trait loci (QTLs) for BMD on chromosomes 4, 6, and 10 coincide with those for bone size, stiffness, and maximum load. However, not all biomechanical QTLs coincide with BMD QTLs. In some cases where QTLs for energy or displacement coincide with those for BMD, the alleles that improve BMD worsen displacement, and *vice versa*.

CONCLUSIONS: Our data illustrate several general principles regarding bone biomechanics. First, the single most important factor determining bone biomechanical performance is size. Second, there is an inverse correlation between bone size and bone modulus (tissue-level stiffness, see figure). Third, biomechanical QTLs can be identified that are unrelated to, or inversely related to BMD. Fourth, the success of DXA in predicting fracture risk arises in part from the fact that bone size is an important component of areal BMD.

Figure 1. Perimeter v Modulus



BODY WEIGHT DETERMINES DIRECTLY BONE MINERAL DENSITY IN AN IRISH REFERRAL POPULATION

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BACKGROUND: Obesity moderates the effect of osteoporosis by a number of ways: bone strength is augmented by an increase in bone mineral density (BMD) and by more robust bone geometry; padding at site of trauma dissipates the energy reducing fracture likelihood; but, lower level of activities lead to trauma and obese persons have more falls and higher impact of fall. We sought to evaluate the influence of age, gender, height, weight, and dietary calcium intake on BMD at spine and hip.

METHODS: In consecutive sample of patients referred to our DXA service (n=5999), we evaluated the relationship between BMD at both spine and femur with the following variables: age, gender, height, weight, body mass index; and calcium intake, correlation analysis, univariate analysis of variance, and forward multiple regression analyses using SPSS for Windows version 16.0 (SPSS, Chicago, IL).

RESULTS: Anthropometric indices (height, weight, BMI) had stronger correlation than age, sex or calcium intake with both lumbar BMD and femur BMD. Univariate analysis of variance identified weight as being the major factor accounting for variance in BMD at spine and femur. Forward multiple regression yielded a model for predicting both lumbar BMD and femur BMD with weight being the strongest predictor. The models accounted for 20% of variance of spine BMD, and for 37% of variance of hip BMD (Table 1).

CONCLUSION: Among a large sample of patients referred to our DXA service, body weight is the best determinant of BMD, with age have a substantially smaller effect, sex and height having a minimal effect, and calcium intake having no effect.

Forward Multiple Regression Analysis			
Dependent Variable	Predictors	standardised coefficient	r ²
Lumbar BMD	weight	0.344	0.201
	age	-0.156	
	height	0.080	
	sex	0.048	
Femur BMD	weight	0.512	0.373
	age	-0.232	
	sex	0.058	
	height	0.037	
	calcium	-0.028	

IMPACT OF SMOKING ON BONE MINERAL DENSITY IN ELDERLY MEN: THE FUJIWARA-KYO OSTEOPOROSIS RISK IN MEN (FORMEN) STUDY

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BACKGROUND: The impact of smoking on bone status in men has not been conclusively established.

METHODS: We examined how smoking and its cessation influence bone status in men. We analyzed 1,576 men among a baseline survey of Japanese men aged ≥ 65 years, the Fujiwara-kyo Osteoporosis Risk in Men Study, conducted during 2007-2008.

RESULTS: Lumbar spine (LS) bone mineral density (BMD) values among never, former, and current smokers were $1.045 \pm 0.194 \text{g/cm}^2$, $1.030 \pm 0.189 \text{g/cm}^2$, and $1.001 \pm 0.182 \text{g/cm}^2$ ($P=0.005$), respectively, while total hip (TH) BMD values were $0.888 \pm 0.120 \text{g/cm}^2$, $0.885 \pm 0.127 \text{g/cm}^2$, and $0.870 \pm 0.124 \text{g/cm}^2$ ($P=0.078$), respectively. The significant trend for LS BMD remained after adjusting for the covariates; age, height, weight, physical activity, milk consumption, and drinking habit ($P=0.036$). Among never and ever (current and former) smokers, LS and TH BMD decreased with the number of smoking years adjusted for those covariates. Among ever smokers, LS and TH BMD decreased with the number of smoking years after adjusting for age, height, weight, and number of cigarettes smoked daily.

CONCLUSION: The impact of smoking on bone status is mainly associated with the number of smoking years in elderly men.

LDL CHOLESTEROL LEVEL CORRELATE WITH URINARY DEOXYPYRIDINOLINE IN PRE-MENOPAUSAL JAPANESE WOMEN

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BACKGROUND: Many studies have investigated the association between bone mineral density and serum lipids; however, their findings have been discordant. Moreover, almost all the studies examined post-menopausal women and the elderly. Therefore, the objective of this study was to investigate whether serum lipid levels are associated with osteo-sono index (OSI) and bone turnover markers in pre-menopausal Japanese women.

METHODS: The subjects were 47 pre-menopausal Japanese women aged 46.11 ± 2.59 years old. We measured calcaneal OSI using the AOS-100 (ALOKA Co. Ltd., Japan). We also measured bone turnover markers [serum bone-specific alkaline phosphatase (BAP), urinary deoxypyridinoline (DPD)] and plasma lipids [total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and triglyceride (TG)].

RESULTS: Significant correlations were shown for DPD (LDL-C: $r=0.398, P<0.01$; TC: $r=0.341, P<0.05$); however, there was no correlation for BAP. OSI was correlated with height ($r=0.469, P<0.01$) and body weight ($r=0.397, P<0.01$), while there was no correlation with TC, LDL-C, HDL-C or TG.

CONCLUSION: We have found that the LDL-C level is correlated with DPD in pre-menopausal Japanese women. It is suggested that hyperlipidemia especially high LDL cholesterolemia may promote bone resorption.

CALCIDIOL AND iPTH SERUM LEVEL IN POSTMENOPAUSAL WOMEN TREATED WITH ERGOCALCIFEROL

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BACKGROUND: The therapeutic administration of Vitamin D is usually determined by empirical bases ruled by clinical criterion and not by seric dosage. The PTH response, in cases of low seric levels of calcidiol, can have a negative effect on bone health.

Objectives: Evaluation, before winter, of calcidiol levels in postmenopausal women (PMW) patients treated with ergocalciferol (800 UI/d average)

METHODS: 28 PMW of 72 years old (± 9.2 years old) have been studied, who were receiving doses of ergocalciferol 800 UI/d in average. The ergocalciferol was suspended a few days before the practice. The determinations made before winter, in 2007, included measurements of 25(OH) D with RIA (DIASORIN) and iPTH intact molecule with IRMA (DSL).

RESULTS: values of mean 25(OH) D were 44 ng/ml (± 18.4); from which the 50% of PMW showed values <40 ng/ml (< 10 ng/ml 0% PMW; 10 - 20 ng/ml en 14% PMW; 20 - 30 ng/ml 17% PMW; 30 - 40 ng/ml 17% PMW. Levels of iPTH = 42.9 ng/ml (± 21.7). Among the serum levels of iPTH and 25(OH) D, a negative correlation of a very significant difference was found ($r=-0.643$; $p<0.000$). **Discussion:** In the study group of patients treated with ergocalciferol 800 UI/d, the presence of low concentrations of 25(OH) D was important (<20 ng/ml 32% y <40 ng/ml 50%) and significant in relationship with iPTH. For this reason, it is questioned the dose usually provided to these patients with ergocalciferol in 800UI/d can be insufficient.

CONCLUSION: It has been proved low serum levels of 25(OH) D with iPTH response tested in patients treated with 800 UI/d of ergocalciferol.