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Predictors of Bone Mineral Density in Men

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Objective: It is well known that men loose bone density with aging and are at risk for osteoporosis. The risk factors for osteoporosis in men remain controversial. The objective of the study is to assess determinants of bone mineral density (BMD) in middle aged Turkish men.

Materials and Methods: A cross-sectional study was conducted. One-hundred and ninety-three aged men between 35-65 years were evaluated. Bone density was measured using dual-energy X-ray absorptiometry (DEXA). Patients were interviewed using a questionnaire which included variables such as age, weight, height, formal education status, co-morbidity that might cause osteoporosis and as well as for malignancy or rheumatological or neurological diseases, and medications that affect bone metabolism (anticonvulsants, diuretics, thyroid hormone, corticosteroids, heparin, warfarin, methotrexate, and cyclosporine), smoking history, physical activity and calcium intake.

Results: According to the lumbar BMD values, 33.7% of them were osteoporotic. According to the hip BMD values, only 13% of were within osteoporotic range. Regression analysis indicated that calcium and alcohol consumption, smoking history, testosterone and cholesterol levels were significant predictors of hip and lumbar bone mineral density. We found a negative correlation between bone loss and calcium, alcohol consumption, testosterone and cholesterol levels. A positive correlation was found between smoking history and osteoporosis.

Conclusion: Smoking is one of the major causes of bone loss in Turkish males. We suggest that all of these parameters must be taken into account during the evaluation of diagnosis of osteoporotic patients.

Key Words: *Male, osteoporosis, risk factors.*

Erkeklerde Kemik Mineral Dansite Belirteçleri

Amaç: Erkeklerin yaşlanmakla kemik yoğunluklarının azaldığı ve osteoporoz açısından risk altında oldukları iyi bilinmektedir. Erkeklerde osteoporoz için risk faktörleri halen tartışmalıdır. Bu çalışmanın amacı orta yaşlı Türk erkeklerinde kemik mineral yoğunluğu (KMY) belirleyicilerinin değerlendirilmesidir.

Gereç ve Yöntem: Kesitsel bir çalışma yapılmıştır. Yüz doksan üç, 35-65 yaş arasında erkek değerlendirilmiştir. Kemik yoğunlukları dual-enerji X-ray absorpsiyometri (DEXA) kullanılarak ölçüldü. Hastalar, yaş, boy, kilo, eğitim durumu, osteoporoza neden olabilecek malignansi, nörolojik, romatolojik hastalıklar gibi komorbidite ve kemik metabolizmasını etkileyen ilaçlar (antikonvülzanlar, diüretikler, tiroid hormonu, kortikosteroidler, heparin, varfarin, metotreksat ve siklosporin), sigara öyküsü, fiziksel aktivite ve kalsiyum alımını içeren bir anket kullanılarak görüşülmüştür.

Bulgular: Lomber KMY değerlerine göre, % 33.7'si osteoporotikti. Kalça KMY değerlerine göre, sadece % 13'ü osteoporotik sınırlar içinde idi. Regresyon analizinde kalsiyum ve alkol tüketimi, sigara öyküsü, testosteron ve kolesterol düzeyleri kalça ve lomber kemik mineral yoğunluğunun anlamlı bir yordayıcısı olduğunu göstermiştir. Kemik kaybı ve kalsiyum, alkol tüketimi, testosteron ve kolesterol düzeyleri arasında negatif korelasyon bulundu. Sigara öyküsü ve osteoporoz arasında positif bir korelasyon saptandı.

Sonuç: Sigara, Türk erkeklerinde kemik kaybının önemli nedenlerinden biridir. Biz tüm bu parametrelerin osteoporotik hastalarının tanı değerlendirmesi sırasında dikkate alınması gerektiğini önermekteyiz.

Anahtar Kelimeler: *Erkek, osteoporoz, risk faktörleri***.**

Introduction

Osteoporosis in men is now recognized as an increasingly important public health issue. About 30% of hip fractures occur in men, and one out of eight men older than 50 years will have an osteoporotic fracture. Although the prevalence of hip fractures is less in men than in women, male hip fractures, which account for about 30% of all hip fractures, are associated with a higher degree of chronic disability as well as a higher mortality rate, and these patients are also less likely to be started on the appropriate osteoporotic medical management than female patients. Treatment data and criteria is

also quite limited regarding men with osteoporosis. Treatment plans should address the need for weight bearing and resistance training exercise modified according to the patent's physical ability. Nutritional education, focusing on calcium and vitamin D intakeand supplementation, should be stressed. It has been noted that 50-60% of older adults do not consume the recommended daily intake of calcium, and older adults are more susceptible to vitamin D deficiency (1). Many risk factors are associated with osteoporotic fracture, hormonal factors, the use of certain drugs, tobacco smoking, low physical activity, low intake of calcium and vitamin D, race, small body size, and a personal or a family history of fracture (2).

The aim of this study was to determine the predictors of BMD in Turkish men.

Material and Methods

The study was carried out in Ankara. Patients were enrolled into the study from the outpatient department of Physical Medicine and Rehabilitation Clinic of the Diskapi Yildirim Beyazit Education and Research Hospital. One-hundred and ninety-three healthy men, who have admitted for various reasons, aged between 35-65 years old were recruited to the study. All of them voluntarily participated in the study. Patients were interviewed using a questionnaire which included variables such as age, weight, height, formal education status of patients, co-morbidity that might cause osteoporosis (i.e., endocrine disorders like hyperthyroid, hypothyroid, hyperparathyroid diseases, or hyperprolactinemia, etc.) and as well as for malignancy or rheumatological or neurological diseases, and medications that affect bone metabolism (anticonvulsants, diuretics, thyroid hormone, corticosteroids, heparin, warfarine, methotrexate, and cyclosporine), smoking history, physical activity and calcium intake. The subjects who use calcium or vitamin D supplementation for any reason; and current or past history for anti-osteoporotic drugs were excluded from the study. We have grouped patients according to the smoking history; non-smokers and smokers. Never smokers and ex-smokers who have not smoked for the last two years have been recorded as non-smokers. The amount of cigarette smoking was calculated by this formula: Number of cigarette packets smoked daily* the number of years = n packet/years. Physical activity has been classified as follows; sedentary that means they didn't do any exercises, they were only active at home, mild physical activity that means they walk 30 minutes everyday, excessive physical activity means they do weight bearing exercises. Calcium intake was assessed semiquantitavily (never, sometimes, everyday) from reported current consumption of each of these foods: milk (more than 250 ml), cheese (more than 50g) and yogurt (more than 125 g). Alcohol consumption was assessed semiquantitavily (never, less than once a month, once or twice a month, twice a week, three or four times a week, everyday) from reported current consumption. Body mass index (BMI) was calculated in kg/m^2. Body mass index (BMI) was categorized according to WHO criteria as underweight (BMI 18.49 kg/ m^2), normal (BMI between 18.5 and 24.9 kg/ m^2), overweight (BMI 25-29.9 kg/ m^2), and obese (BMI 30 kg/ m^2). Lateral and anterior/posterior thoracic and lumbar radiographics of the study participants were taken. Their history of low-trauma fracture was obtained. Low-trauma fracture was defined as a fracture occurring from a trivial/minor injury. They then enquired as to how it had occurred. It was only included if it occurred from low-trauma injuries. Fractures such as those sustained as result of a car accident or fall from a major height were excluded.

BMD was measured from hip (femur neck, trochanter, total) and lumbar spine (L1,2,3,4 and total) by DEXA (Hologic QDR 4900W, Hologic Inc., Bedford, Massachusetts, USA), which has a mean precision error of 1% for the lumbar spine and hip. Values for results of DEXA measurements were expressed as BMD (g/cm^2) and T score of young adult healthy reference population, as supplied by the manufacturer because there is still no internationally accepted consensus for osteoporosis in men. The results were recorded as g/cm^2 and T score. T scores >-1 SD were classified as normal, the T scores ≤-1 SD were classified as low BMD (3). 1) Men whose T score 0 to -1 Standard Deviation (SD) on L1-4 or femur neck or total femur were accepted as men with normal BMD; 2) Individuals with T score in these regions between -1 SD and -2.5 SD were accepted as osteopenic men; 3) Individuals whose T score on L1-4 or femur neck or total femur were less than -2.5 SD were accepted as osteoporotic men. Laboratory; Fasting blood samples were collected in the morning between 08:00 and 09:00 from all subjects. Routine biochemical parameters including sodium, potassium, calcium, phosphorus, creatinine, transaminases, cholesterol, triglycerides, serum magnesium (Mg) were determined by standard laboratory techniques. Serum osteocalcin (OC), total estradiol (E), testosterone (T), growth hormone (GH), parathyroid hormone (PTH) and 25 (OH) vitamin D_2 levels were determined using commercially available radioimmunoassay kits. SPSS for Windows 12.0 package statistical software (SPSS Inc., Chicago, IL) was used in the statistical analysis. All measurements were given as mean -SD. Comparisons among groups were analyzed using one-way analysis of variance (ANOVA). Predictors of lumbar spine and hip BMD were determined using logistic regression analysis. The independent variables entered in the regression model were; age; body mass index (BMI); smoking history; alcohol intake; calcium consumption and serum concentrations of 25 (OH) vitamin D_2, osteocalcin, parathyroid hormone (PTH), total estradiol, testosterone, growth hormone, cholesterol and magnesium. Statistical significance level was set to 0.05.

Results

Socio-demographic variables, laboratory results, and BMD results are summarized in Table 1, 2 and 3. Thirty three point seven percent of the subjects had osteoporosis and 28.5% of them had osteopenia at spine, while 13.0% of them had osteoporosis and 46.1% of them had osteopenia at hip. Sixty two point two

percent of the subjects had low BMD values at spine and 59.1% of them had low BMD at hip. Eighty four percent of the patients were smoking. The maximum cigarette smoking value was 144 packet-years. Their calcium consumption was investigated and it was seen that 25 of them were accustomed to drinking a glass of milk everyday, 110 of them accustomed to eating cheese everyday, 91 of them eat a bowl of yogurt everyday. Seventy eight patients were using alcohol. Only 20 patients were regular users and most of the patients were moderate alcohol users. When we evaluated their physical activity; 67.35% of them were in mild activity group. Only 3.62% of them were in heavy activity group. Fifty six of the patients were in sedentary group. We evaluated the fracture history and found that; out of 45 patients 44 of them had previous traumatic fractures and only one of them had a low-traumatic fracture. This patient was a smoker, heavy alcohol user, had diabetes mellitus and hypertension and his calcium consumption was very low. Most of the patients were graduated primary school, 30 of them secondary school, 28 of them high school and only 4 of them graduated university. Two of the patients had chronic renal disease, one was ankylosis spondylitis, 33 of them were diabetes mellitus, seven were rheumatoid arthritis, and 3 of them had celiac disease. Logistic regression analysis was revealed a negative correlation between low BMD and calcium consumption, alcohol consumption, testosterone and cholesterol levels, and a positive correlation between low BMD and smoking habits ($p<0.05$) (Table 4).

Table 1 Demographic features of patients.

	n	minimum	maximum	mean	Std. Deviation
Age (years)	193	35	65	52,69	6,66
Height (cm)	193	146,00	186,00	169,56	6,047
Weight (kg)	193	50,00	105,00	76,43	12,29
Body mass index (kg/m^2)	193	18,34	36,33	26,53	3,72

Table 2. The results of lumbar and femoral neck BMD.

Femoral Neck BMD	n	Percent %
Normal	79	40,9
Osteopenic	89	46,1
Osteoporotic	25	13,0
Low Femoral BMD	114	59,1
Lumbar Vertebra BMD		
Normal	73	37,8
Osteopenic	55	28,5
Osteoporotic	65	33,7
Low Lumbar BMD	120	62,2

Table 3. Laboratory results of the subjects

PTH (pg/ml)	54.74 ± 26.3
25OHD (ng/ml)	34.23 ± 17.4
OC (ng/ml)	9.20 ± 5.8
Cholesterol (mg/dl)	186.11 ± 55.3
Triglyceride (mg/dl)	140.68±68.2
Magnesium (mg/dl)	2.17 ± 0.5
Testosterone (ng/ml)	474.67 ± 357.6
Estradiol (pg/ml)	36.92 ± 27.1
GH (ng/ml)	0.65 ± 2.2
Femur total BMD (gr/cm2)	0.91 ± 0.2
Spine BMD (gr/cm2)	0.92± 0.2

PTH: parathyroid hormone, 25OHD: 25 hydroxy vitamin D2, OC: osteocalcin, GH: growth hormone, BMD: Bone mineral density.

Table 4. Results of logistic regression analysis.

	B	P value	Odds ratio
Cheese Consumption	-1.82	0.01	0.16
Alcohol Consumption	-0.43	0.05	0.65
Smoking	0.08	0.00	1.09
Testosterone	-0.01	0.00	0.99
Cholesterol level	-0.04	0.00	0.96

Discussion

Osteoporosis is a growing health problem not only in women but also in men (4). Therefore the evaluation of predictors of osteoporosis in men is essential in clinical medicine for early diagnosis. Izumotani et al. (5) examined 686 healthy middle aged (40-59) men and found that 9.5% of them were osteoporotic according to the lumbar vertebra BMD results. In our study 33.7% of the patients were osteoporotic and 28.5% of them had osteopenia at spine, while 13.0% of them had osteoporosis and 46.1% of them had osteopenia at hip. These ratios were very high contrary to literature. Because the male osteoporosis is presently both understudied and underreported, with only about 5% of existing literature on osteoporosis relating to men we don't know the real prevalence. Although prevalence estimates vary, approximately one third to one half of men in the United States 50 years of age and older have clinically detectable osteopenia, whereas 5% to 20% have osteoporosis (6). The increased rate of osteoporosis at spine in our subjects may be due to the age range extending to 65 years old, or due to less number of patients in study. Diagnosis of osteoporosis in men was based on WHO criteria established for osteoporosis in women because there is still no internationally accepted consensus for osteoporosis inTurkish men.

Clarke et al. (7) studied 45 healthy men whose age ranges were between 20-80 years. They found femoral neck BMD decreased with age, but remained stable at the other sites measured. There were few patients in their study, but age range was very wide. Also Krassas et al. (8) studied 366 males. Contrary to our study sample number of patients was too much. They found a negative correlation between age and BMD. In our study correlation between BMD and age could not been demonstrated. The age range of the patient in our study was close to each other. It could have been resulted from the age range involving only the presenil aged men.

Various studies have shown a positive relation between body weight and BMD in both men and women (9, 10). In Turkey Cankurtaran et al. (9) found men with low body weight (< 57 kg), physically inactive, and poorly educated were significantly more osteoporotic. Krassas et al. (8) found a positive correlation between BMI and BMD. Cheung et al. (11) studied Chinese men aged 50 years and above; in the linear regression model, weight, age, BMI, were found to be significant determinants of total hip BMD. Toth et al. (12) found a strong positive association between BMI and femur neck BMD. In another study, weight (positively) and age (negatively) were associated with bone density (13). In our study, we found a negative correlation between BMI and low BMD with univariant analysis, but when multivariate analysis applied correlation could not be demonstrated.

Smoking is recognized as a risk factor for low BMD. Although the exact mechanism is not clearly understood, cigarette smoking is a risk factor for osteoporosis. Vogel and colleagues examined bone density and bone loss rates among 1303 Japanese-American men 51-82 years old. Twenty percent were current smokers. Results indicated that compared with never smokers, current and past smokers had significantly less bone density, especially in the cancellous calcaneus and trabecular distal radius. Also, the magnitude of the smoking effect was strongly associated with the duration of smoking (14). These findings were consistent with the Rotterdam study in which a statistically significant higher rate of bone loss was seen in both elderly men and women who currently smoked cigarettes (15). In the meta-analysis by Ward and Klesges (16) it was estimated that smoking increases the lifetime risk of developing a vertebral fracture by 32% and hip fracture by 40% in men. It is stated that smoking had an independent, dose-dependent affect on bone loss, which increases fracture risk, and might be partially reversed by smoking cessation (16). In our study 84% of patients were smoking, and the logistic regression analysis showed that smoking was a negative predictor for BMD among males, consistent with the previous studies. Like osteoporosis ratios; smoking patient ratio was very high contrary to the literature (14).

Alcohol has been demonstrated to reduce bone formation and to decrease the proliferation of osteoblastic cells (17). On the other hand, studies demonstrating alcohol-induced bone loss and increased fracture rate in population-based studies are controversial (18-22). Kanis et al. (23) found that alcohol intake was associated with osteoporosis and increased hip fracture risk, but the effect was nonlinear. Alcohol induced osteopenia identified that it is the result of mainly from decreased bone formation rather than increased bone resorption (22). On the other hand Orwoll et al. (13) studied 355 men and they found positive correlation between alcohol consumption and vertebra, femur and radius BMD's. However, in this study patients were divided into two groups, as alcohol users and non users,

and the total amount of alcohol consumption was not evaluated (13). In another study drinking alcohol but not binge drinking was found to be beneficial to bone health of men and possibly postmenopausal women (24). In a prospective study of Holbrook and Barrett (25) social drinking have been associated with higher BMD in men and women. In our study, only 20 patients were regular alcohol users and 58 patients were moderate users. Logistic regression analysis showed that moderate consumption of alcohol protects from osteoporosis and it is a positive predictor of BMD.

Laboratory studies have suggested a role for cholesterol in the pathogenesis of osteoporosis (5). But the clinical studies evaluating the relation of cholesterol and BMD are also controversial (26, 27). In a prospective study of Tanko et al. (26) 340 postmenopausal women have been followed up for 8 years but a correlation between BMD and cholesterol could not have demonstrated. Brownbill and Ilich (27) have demonstrated that higher levels of serum cholesterol are positively associated with BMD. The hypothesis that increased total cholesterol may adversely affect BMD was suggested by previous epidemiologic and laboratory investigations indicating a link between atherosclerosis and osteoporosis (28). Severe osteoporosis in the hip may indicate advanced atherosclerosis and thereby an increased risk for not only hip fractures but also for coronary heart disease (29). In our study we have found a correlation between cholesterol level and BMD values, consistent with the Brownbill's study. Cholesterol levels might be a positive predictor of BMD in Turkish men. However the mechanism of this association is not clear and studies are needed to clarify this relationship.

Increased awareness of patients and public is needed to decrease the risk of morbidity and mortality resulting from osteoporotic fractures (30). Cindaş and Savaş (31) found that Turkish men who are at risk of osteoporosis do not have sufficient knowledge about osteoporosis and its consequences.

We are all aware of that; our study which is composed of 193 males, is not a representative of the whole country, but it can be taken into consideration as a study leading to further community based studies.

We suggest that all of these parameters must be taken into account during the evaluation of diagnosis of osteoporotic patients.

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