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RESEARCH

EVALUATION OF RISK FACTORS FOR OSTEOPOROSIS AND OSTEOPENIA IN MALE PATIENTS AGED OVER 60 YEARS OF AGE

ABSTRACT

Introduction: Osteoporosis in men is often underdiagnosed and neglected compared to postmenopausal women. Major risk factors should be determined to prevent this disease, which has potential risk of mortality and morbidity for elder men. This study's purpose was to determine the risk factors for osteoporosis and osteopenia in male patients aged >60 years.

Materials and Method: Between January 2015 and June 2017, male patients aged >60 years admitted to our centers who underwent dual energy x-ray absorptiometry (DXA) were included in this retrospective study. Patients' age, body mass index, site of residence (village/city), smoking status, and systemic diseases were examined through our records. Patients were divided into control, osteopenia, and osteoporosis groups according to DXA measurements. Serum vitamin D measurements also were evaluated. Multivariate analysis was performed to determine major risk factors for osteoporosis and osteopenia.

Results: Compared with the control group, patients in the group categorized as having osteoporosis or osteopenia had a significantly lower body mass index and more commonly resided in the city (p<0.001 and p<0.005, respectively). Serum vitamin D levels were significantly lower in the osteoporosis and osteopenia groups than in the control group (p=0.001). According to multivariate analysis, insufficient or deficient serum vitamin D levels were determined to be a major risk factor for osteoporosis and osteopenia (p=0.001).

Conclusion: According to our results, men aged >60 years with deficient serum vitamin D levels (<20 ng/mL) were six times more likely to have osteopenia and 80 times more likely to have osteoporosis.

Keywords: Osteoporosis; Bone diseases, Metabolic; Bone density; Risk factors; Vitamin D

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ARAŞTIRMA

ALTMIŞ YAŞ ÜZERİ ERKEK HASTALARDA OSTEOPOROZ VE OSTEOPENİ RİSK FAKTÖRLERİNİN DEĞERLENDİRİLMESİ

ÖZ

Giriş: Erkeklerde osteoporoz postmenopozal kadınlara kıyasla çoğunlukla az tanı alır ve ihmal edilir. Yaşlı erkeklerde potansiyel mortalite ve morbidite riski taşıyan bu hastalığı önlemek için başlıca risk faktörleri belirlenmelidir. Bu çalışmanın amacı, 60 yaş üzerindeki erkek hastalarda osteoporoz ve osteopeni için risk faktörlerini belirlemektir.

Gereç ve Yöntem: Ocak 2015- Haziran 2017 tarihleri arasında merkezlerimize başvuran ve Dual Enerji X-ray Absorptiometri (DXA) ölçümleri yapılan 60 yaş üzeri erkek hastalar bu retrospektif çalışmaya dahil edildi. Hastaların yaşı, beden kütle indeksi (BKİ), yerleşim yeri (köy-şehir), sigara içme durumu ve sistemik hastalıkları kayıtlarımızdan incelendi. Hastalar DXA ölçümlerine göre kontrol, osteopeni ve osteoporoz olarak 3 gruba ayrıldı. Hastaların serum vitamin D ölçümleri de değerlendirildi. Osteoporoz ve osteopeni için temel risk faktörlerini belirlemek için çok değişkenli analiz uygulandı.

Bulgular: Kontrol grubuyla karşılaştırıldığında, osteoporoz veya osteopeni grubundaki hastalarda VKİ anlamlı derecede düşüktü ve bunlar daha çok şehirde yerleşikti (sırasıyla p<0.001 ve 0.005). Serum vitamin D seviyeleri osteoporoz ve osteopeni gruplarında kontrol grubuna göre anlamlı düşüktü (p=0.001). Çok değişkenli analize göre, yetersiz veya eksik serum vitamin D seviyeleri osteoporoz ve osteopeni için temel risk faktörleri olarak belirlendi (p=0.001).

Sonuç: Sonuçlarımıza göre, serum vitamin D düzeyleri yetersiz olan 60 yaşın üzerindeki erkeklerde (<20 ng / mL) osteopeni tanısı olasılığının 6 kat, osteoporoz tanısı olasılığının 80 kat fazla olduğu görülmüştür.

Anahtar sözcükler: Osteoporoz; Kemik hastalıkları; metabolik; Kemik dansite; Risk faktörleri; Vitamin D

INTRODUCTION

Osteoporosis is the most common metabolic bone disease, characterized by decreased bone mass and microarchitectural deterioration of the bone tissue, with consequent increases in bone fragility and fracture susceptibility (1,2). The prevalence of osteoporosis in male patients aged >60 years was reported at 13%, which increases to 70% at age ≥80 years (3-5). Of the 9.0 million new osteoporotic fractures that occurred worldwide in 2000, 39% occurred in men, and 45% of these fractures occurred in the areas frequently affected by osteoporosis (6).

Various risk factors for osteoporosis have been reported, including race, heredity, age, gender, family history, low bone mineral density (BMD), vitamin D deficiency, smoking, low physical activity, and body mass profile (7). Investigators attempt to decrease the number of male patients with osteoporosis using the appropriate strategies and early intervention for preventable factors. Although, there are numerous studies about male osteoporosis exist in the literature; some studies reported that osteoporosis in elder men is still underdiagnosed and neglected (8-11).

Dual energy X-ray absorbtiometry (DXA) is recommended for osteoporosis in men aged 70 years and older but supportive data is limited (12,13). Male osteoporosis is becoming an increasingly common condition with subsequent mortality and mortality (14). Healthcare providers should consider annual screening for osteoporosis in men as equal as routine prostate and colorectal screening. In addition to that, independent major risk factors should be determined for elder men to prevent this disease, which has potential risk of mortality and morbidity. Therefore, the aim of this study was to determine the main risk factors for osteoporosis in male patients aged >60 years.

MATERIALS AND METHOD

This multicenter retrospective study was conducted with the approval of the institutional ethical review board (University Clinical Researches Ethical Review Board, ID=42914) and performed in accordance with the Declaration of Helsinki. To obtain a standardized data evaluation, this study was performed at two centers using the same manufacturer's DXA devices and located in the same areas of sun exposure. Male patients aged >60 years who were admitted to the two centers from January 2015 to June 2017 and underwent DXA and laboratory tests were reviewed from our electronic medical records. Patients with known history of metabolic bone diseases, taking any form of medication for osteoporosis or osteopenia, under follow-up at the endocrinology department due to secondary osteoporosis or osteomalacia were excluded. After exclusions, the data of 460 patients were evaluated in this study.

Patients' age, gender, body mass index (BMI), site of residence (village or city), smoking status, and systemic diseases were reviewed from our electronic medical records. Patients' BMIs were classified according to World Health Organization classification as underweight (<18.5 kg/m^2), normal (18.5–24.5 kg/m^2), overweight (25–29.9 kg/m^2), class-I obesity (30–34.9 kg/m^2), class-II obesity (35–39.9 kg/m^2), and class-III extreme obesity (>40 kg/m^2). Systemic comorbid diseases were hypertension, hyperlipidemia, cardiovascular system disease (coronary artery disease and congestive heart failure), respiratory system disease (asthma, chronic obstructive lung disease), diabetes mellitus, gastrointestinal system disease (peptic ulcus, irritable bowel syndrome, celiac disease), neurological system disease (cerebrovascular disease, Parkinson

disease, epilepsy, Alzheimer disease, depression), and rheumatological disease (rheumatoid arthritis, ankylosing spondylitis).

All subjects underwent measurement of BMD (kg/cm^2) using the same DXA devices (*STRATOS dR*, DMS, Maugio, France) at the anteroposterior lumbar spine (L1-L4) and at the femoral neck as per standard protocol stated by the manufacturer. Patients' were primarily divided into one of three groups according to T scores established by World Health Organization classification as control (>−1), osteopenia (−1 to −2.5), and osteoporosis (<−2.5). Serum levels of vitamin D [25(OH) D] were measured by radio-immune-assay (RIA) method by using the same kits in both two centers. Serum vitamin D levels classified as adequate (>30 ng/mL), insufficient (21–29 ng/mL), or very deficient (<20 ng/mL). Serum calcium (Ca) and phosphor (P) levels were also reviewed for all patients, which were analyzed by calorimetric method. The normal laboratory ranges for serum Ca was 8.8-10.6 mg/dl and for serum P was 2.3-5 mg/dl. Those with impaired serum Ca and P values were routinely consulted to endocrinology department and excluded from the study to keep apart osteomalacia and secondary osteoporosis as mentioned above.

Statistical analysis was performed using SPSS 20.0 (*SPSS Inc.*, IBM, NY, USA). Numeric variables were given as means and standard deviation; categorical variables were given as frequency and percentage. The comparison of the three study groups was performed using One-way analysis of variance (ANOVA) for means, and with Chi-square test for frequencies.

Bonferroni or Tamhane's t^2 tests were used for comparison between groups. P values of <0.05 were considered statistically significant. Finally, multivariate regression analysis was performed to determine the main risk factors for osteoporosis and osteopenia.

RESULTS

The demographics of the three study groups as well as of systemic comorbid diseases, serum vitamin D levels, and BMD values are shown in *Table 1*. No significant difference was observed among the three groups in terms of age, smoking status, and systemic comorbid diseases. The osteoporosis and osteopenia groups had significantly lower BMI values than the control group (p=<0.001 and p=<0.001, respectively). In addition, patients diagnosed with osteoporosis and osteopenia were significantly more likely to be living in a city than patients in the control group (p=0.005). Serum vitamin D levels, BMD values, and t scores were significantly lower in patients in the osteoporosis and osteopenia groups than in patients in the control group, as expected.

According to multivariate regression analysis, insufficient and deficient serum vitamin D levels were determined as the main risk factors for osteoporosis and osteopenia in male patients aged >60 years (Table 2). According to our results, males aged >60 years with deficient serum vitamin D levels (<20 ng/mL) were six times more likely to have osteopenia and 80 times more likely to have osteoporosis.

Table 1. Demographics and clinical characteristics of study groups.

	Normal (n=179)	Osteopenia (n=201)	Osteoporosis (n=80)	p
Age (years)	67.0±8.5	68.8±9.7	68.7±9.2	0.154
BMI (kg/m²)	29.6±4.3	27.9±4.2	26.5±5.1	**<0.001**
BMI (WHO Classification)				**<0.001**
Underweight	1 (0.5%)	2 (1%)	7 (8.7%)	
Normal	35 (19.6%)	66 (32.9%)	32 (40%)	
Overweight	69 (38.5%)	78 (38.8%)	24 (30%)	
Class I	40 (22.4%)	28(13.9%)	9 (11.2%)	
Class III	31 (17.3%)	24 (11.9%)	6 (7.5%)	
Class III	3 (1.7%)	3 (1.5%)	2 (2.6%)	
Site of Residence				**0.005**
City	95 (53%)	127 (63.2%)	59 (73.7%)	
Village	84 (47%)	74 (36.8%)	21 (26.3%)	
Smoking Status				0.363
None	137 (76.5%)	153 (76.1%)	55 (68.7%)	
Smoking	42 (23.5%)	48 (23.9%)	25 (31.3%)	
Systemic Comorbid Disease (+/-)				
Hypertension	88 / 91	106/95	42/38	0.764
Hyperlipidemia	10/169	5/196	1/79	0.126
Cardiovascular disease	19/160	16/185	6/74	0.589
Respiratory system disease	41/138	47/154	25/55	0.309
Diabetes mellitus	18/161	12/189	6/74	0.332
Gastrointestinal system disease	2/177	9/192	4/76	0.115
Neurologic system disease	16/163	17/184	7/73	0.986
Rheumatologic disease	1/178	3/198	0/80	0.405
Serum Vitamin D Level				**<0.001**
Adequate	118	41	5	
Insufficient	42	115	26	
Deficient	19	45	49	
BMD (kg/cm²)	1.08±0.07	0.88±0.05	0.72±0.07	**<0.001**
T score (lumbar)	0.1±1.1	(-)1.4±0.7	(-)2.9±0.6	**<0.001**
T score (femur neck)	(-)0.2±1.0	(-)1.3±0.9	(-)1.9±1.2	**<0.001**

BMD: bone mineral density, BMI: body mass index, WHO: world health organization

Table 2. The major risk factors for osteopenia and osteoporosis according to multivariate regression analysis.

Study Group	Variable	Level	Multivariate regression analysis		
			Odds ratio	(95% Confidence Interval)	p
Osteopenia	Vitamin D	Insufficient		8.1 (4.8-13.6)	**<0.001**
	Vitamin D	Deficient		6.8 (3.5-13.2)	**<0.001**
Osteoporosis	Vitamin D	Insufficient		17.6 (5.7-54.2)	**<0.001**
	Vitamin D	Deficient		80.5 (25.4-254.5)	**<0.001**

DISCUSSION

The most significant finding of our study was that insufficient or deficient serum vitamin D levels are the major risk factors for osteoporosis or osteopenia in male patients aged >60 years. Previous clinical studies widely investigated the risk factors for osteoporosis in men. Cheung et al. evaluated the determinants of BMD in Chinese men and authors reported that age, weight, BMI, cigarette smoking and exercise were significant determinants of total hip BMD. Authors found that body weight was the most important determining factor (15). The positive correlation of low BMI and low BMD for post-menopausal women has also been reported in previous clinical studies (16). Villareal et al. observed that diet-induced weight loss in elderly adults increased bone turnover and decreased hip BMD (17). In another study by Boyanov et al., BMD values for 80 male patients diagnosed with metabolic syndrome were found to be significantly higher than values for a control group (18). Yang et al. also emphasized the importance of diet as determinant of BMD values in their study evaluating 2305 male aged 50 to 79 years (19). Despite having higher BMI values in our country compared to eastern countries such as China and Korea; we also found significantly lower BMI values in osteopenia and osteoporosis groups compared with a control group, similar to results from reported studies. Our results showed

that 80% patients were overweight or obese in the control group; however, 50% patients were overweight or obese in the osteoporosis group.

Smoking is another risk factor, which has been found to correlate with decreased BMD (20,21). Oncken et al. investigated smoking cessation and found a significant increase in femur neck BMD measurements 1 year after cessation of smoking cigarettes (22). According to our results, smoking status did not differ among groups; however, we did not have data about number of cigarette smoked per day and duration of smoking, which may influence the results.

Pagonis et al. reported that osteoporotic fracture patterns in urban patients are more severe, which is explained by decreased activity level and poor quality of life (23). In the same study, the authors stated that people living in rural areas had a later diagnosis of osteoporosis, and had better treatment outcomes (23). Men aged >60 years living in rural areas are more active than their urban counterparts, because of work and environmental conditions (24). Consistent with results from the literature, our findings indicated that 74% male patients diagnosed with osteoporosis lived in the city, while the remaining 26% lived in villages. However, in the control group, half of the patients lived in the city.

Clinical studies about systemic comorbid diseases and drug use revealed that 90% patients with osteoporosis have a chronic disease and one-third of them use a drug that can cause osteoporosis (25). In studies evaluating systemic comorbid diseases related to osteoporosis, hypertension and diabetes were found as most commonly associated with osteoporosis (26). In our study, the most common systemic comorbid disease was found to be hypertension in both groups. Respiratory system disease such as chronic obstructive lung disease and asthma were the second-most common systemic comorbid diseases in both groups. We found no relationship between systemic comorbid diseases and lower BMD values. Our study had no data about the drug use that may also cause secondary osteoporosis. Most studies in the literature investigated male osteoporosis by excluding systemic comorbid diseases. However, we believe that rather than evaluation of healthy elder people, evaluation of elder people with systemic comorbid diseases may give valuable information about the real incidence of disease and may demonstrate the main characteristics of population accurately.

To our knowledge, vitamin D provides an important contribution to skeletal calcium balance by increasing intestinal and renal calcium absorption. It was stated that the shade of clothing, duration of exposure to direct sunlight, and regional climatic characteristics could affect vitamin D levels. A positive correlation also was found between duration of sunshine exposure and vitamin D level (27). However, the prevalence of vitamin D deficiency is high worldwide even in tropical regions (28). Most studies about male osteoporosis have indicated that vitamin D deficiency is a substantial risk factor for the reduction of BMD and the development of osteoporosis. Moreira et al evaluated healthy men in Brazil and authors found a high prevalence of vitamin D deficiency and its relation to increased osteoporosis (28). Khashayar et al reported significant correlation of vitamin D deficiency and BMD in healthy Iranian men (29). Sundh et al emphasized that serum vitamin D is associated with higher cortical porosity in elderly men (30). Other studies also revealed the importance of vitamin D deficiency in male osteoporosis (12,15,19,31). The provinces where our study was performed are disadvantaged areas in terms of climate characteristics and insufficient sun exposure, when evaluated with regard to vitamin D synthesis. According to multivariate regression analysis, we found insufficient and deficient serum vitamin D levels to be the main predictive factors for the diagnosis of osteopenia and osteoporosis in our study. Our results also are consistent with previous community-based studies. Considering data obtained from our study, clinicians should attempt to prevent osteoporosis and osteopenia by investigating serum vitamin D levels in elderly patients.

The main limitation of our study was its retrospective design, which may strongly influence determining risk factors accurately. However, we evaluated a relatively large homogenous (>60 years old male patients) patient data collected from two centers with a standardized method. In addition, we performed a multivariate regression analysis to determine the major risk factors for osteopenia and osteoporosis with odds ratios. The most important strength of our study was that it is the first study in our country reporting major risk factors for osteoporosis and osteopenia in male patients aged >60 years. In addition, the importance of serum vitamin D level deficiency was also shown in this study.

According to our results, males aged >60 years with deficient serum vitamin D levels (<20 ng/mL) were six times more likely to have osteopenia and 80 times more likely to have osteoporosis. Physicians should take into account the importance of serum vitamin D deficiency in elderly men and its significant relation with osteoporosis which can cause mortality and morbidity.

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