

## Influence of Smoking on Bone Mineral Density in Elderly Men

### Abstract

**Background:** Smoking has deleterious effects on bone mass and is associated with the subsequent development of osteoporosis, particularly in elderly participants. The purpose of this study was to determine the influence of smoking in the elderly male smokers. **Methods:** All male participants aged 60 years and older of the Amirkola cohort who performed bone densitometry entered the study. Bone mineral density (BMD) was measured at the lumbar spine (LS) and femoral neck (FN) using the dual-energy X-ray absorptiometry method. In statistical analysis, the smokers and nonsmokers were compared according to BMD, frequency of low bone mass defined as BMD T-score  $<-1$  at either LS or FN, and the number of bone fractures. SPSS software version 18 was used for analysis. **Results:** A total of 203 smokers with mean smoking duration of  $21.67 \pm 17.7$  years and the mean number of  $36.4 + 15.8$  cigarettes per day were compared with 408 nonsmokers. The mean BMD values in LS ( $0.90 \pm 0.14$  vs.  $0.94 \pm 0.19$ ) and FN section ( $0.87 \pm 0.13$  vs.  $0.89 \pm 0.15$ ) and also the frequency of bone fractures were significantly lower, and the frequency of low bone mass at either LS and FN was significantly higher in smokers ( $P = 0.014, 0.038, 0.003, \text{ and } 0.004$ , respectively). In multiple logistic regression analysis, smoking was independently associated with low bone mass by odds ratio of  $= 2.27$  (95% confidence interval:  $1.49-3.44$ ). **Conclusions:** These findings indicate a significant association between low bone mass and bone fracture at either LS or FN in the elderly male smokers.

**Keywords:** Association, bone mineral density, elderly men, smoking

### Introduction

Low bone mass and osteoporosis are prevalent in the general population and are an important cause of fracture.<sup>[1,2]</sup> Osteoporotic hip fracture, particularly in elderly men is a major reason of morbidities, disability as well as mortality and social costs.<sup>[3]</sup>

Various factors such as age, gender, inadequate intake of calcium (Ca), lack of Vitamin D, physical activity, and chronic diseases such as endocrine, gastrointestinal, rheumatic and blood disorders, certain medications, genetics, environmental factors, lifestyles, lack of estrogen, parity, and smoking may affect bone mineral density (BMD).<sup>[4-8]</sup> Recent studies have shown that cigarette has destructive effects on bone mass through its toxic effect on osteoblasts (bone constructive cells) with increasing bone destructive osteoclast cells.<sup>[9,10]</sup> In addition, smoking is related to the low levels of parathyroid hormone and decreases BMD with an unknown mechanism.<sup>[11,12]</sup>

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Relationship between smoking and BMD has been addressed in several studies, but the results are inconsistent. While the negative influence of smoking on bone mass has been shown,<sup>[13-18]</sup> nonetheless, the results vary according to site and severity of bone loss. Several factors such as age, body mass index, the number, and duration of smoking can differently affect the outcome.<sup>[13,17]</sup> In addition, coexistence of several underlying conditions such as obesity and metabolic syndrome in smokers may counteract the influence of smoking on bone mass.

To overcome this problem, we conducted the present case-control study in a homogeneous group recruited from a general population with similar ethnic, lifestyle, demographic features, diet, and physical activity. Both patients and controls were recruited from the same source, and so the results were expected to be associated with minimal confounding effect. The aim of this study was to determine the influence of smoking on bone mass of the elderly male smokers aged 60 years and older.

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## Methods

### Study design and participants

This nested case-control study comprised all male participants of the Amirkola Health and Ageing Project. This project was carried out in Amirkola, Babol, a city located on the Southern coast of the Caspian Sea, North of Iran. This research was a grant by the Research and Technology Chancellery of Babol University of Medical Sciences conducted in 2011 and 2012 participated by elderly aged 60 years and over of whom 72.3% of the invited participants took part and completed the project.<sup>[19]</sup> All male participants who agreed to perform bone densitometry entered this study. Patients with the respiratory, gastrointestinal, and chronic musculoskeletal problems and those who were receiving antiosteoporosis treatment were excluded from the study. Informed consent was obtained from all patients, and the proposal of this study was approved by the Ethics Committee of Babol University of Medical Sciences (No: 4232), Babol, Iran.

### Variables

The primary objective of this study was to compare BMD and to determine the prevalence of low bone mass (osteoporosis + osteopenia) at either lumbar spine (LS) or femoral neck (FN) in 203 smoker and 408 nonsmoker male participants.

All current and former smokers were included irrespective of the number of cigarettes per day or duration of smoking. Information about the number of cigarette per day and duration of smoking was provided through an interview. Further data were collected regarding physical activity, BMI, level of education, and presence of underlying clinical condition as well as serum Vitamin D. Details of patients selection and methods of data collection for all variables were described elsewhere.<sup>[19]</sup>

BMD was measured in the LS at L2-L4 regions and FN by dual-energy X-ray absorptiometry method using Lexxos densitometer. Findings were reported as BMD g/cm<sup>2</sup>, BMD *T*-score, and BMD *Z*-score. Osteoporosis was defined according to the International Society for Clinical Densitometry criteria as *T*-score  $\leq -2.5$  at either FN or LS measurement sites.<sup>[20]</sup> Osteopenia was diagnosed BMD *T*-score between  $-1$  and  $-2.5$  ( $> -2.5 < -1$ ). BMD measurements for all participants were performed in a single center by an experienced technician under the supervision of a radiologist. All data were accessible to researchers.

In statistical analysis, smokers and nonsmokers were compared according to BMD parameters and the frequency of low bone mass defined as BMD *T*-score  $< -1$  (osteoporosis + osteopenia at either LS or FN). In addition, the number of bone fractures in each group and

the association of low bone mass with other factors were determined. Data regarding osteoporotic vertebral and no vertebral fractures were provided by medical record review, history, and interview. Traumatic fractures due to accidents were excluded from the study.

### Statistical analysis

The normality of the data was indicated by Kolmogorov-Smirnov test. While Student's *t*-test was used to compare quantitative variables and Chi-square test for categorical variables. Multiple logistic regression analysis was applied to determine the independent association between smoking and low bone mass. SPSS software version 18 (SPSS Inc., Chicago, Illinois, USA) was used for analysis.

## Results

Two hundred and three smoker and 408 nonsmoker males with a mean age of  $68.57 \pm 16.7$  and  $69.2 \pm 7.2$  years, respectively, were compared. Data regarding demographic and laboratory characteristics are shown in Table 1. The mean values for age, anthropometric indices, and physical activity level score were almost the same in smokers and nonsmokers. Besides, there were not significant differences between serum Ca and Vitamin D levels in smokers in comparison with the counterpart group (9.26 vs. 9.22 for Ca and 31.39 vs. 32.80 for Vitamin D, respectively) [Table 1].

A total of 72 current smokers (35.5%) and 131 (64.5%) ex-smokers entered the study. The mean duration of smoking was  $21.67 \pm 17.7$  years and the mean number of cigarettes was  $36.4 \pm 15.8$ . In statistical analysis, mean lumbar spine bone mineral density (LSBMD) and femoral neck bone mineral density (FNBMD) in smokers were significantly lower than nonsmokers ( $P = 0.014$  and  $0.038$ , respectively) [Table 2 and Figure 1]. The means of the BMD *T*-score and BMD *Z*-score in both LS and FN sites were also significantly lower in smokers as compared with nonsmokers [Table 2].

**Table 1: Comparison of the demographic, biochemical, and clinical characteristics in smoker and nonsmoker elderly men of the Amirkola cohort study**

Variable	Smoker (n=203) Mean±SD	Non smoker (n=408) Mean±SD	P
Age (year)	68.5±16.7	69.20±7.25	0.31
Height (cm)	163.56±5.98	162.46±6.52	0.04
Weight (kg)	69.32±12.37	69.53±12.40	0.84
BMI (kg/m <sup>2</sup> )	25.86±4.08	26.27±4.02	0.23
WC (cm)	95.29±10.42	95.31±10.31	0.98
HC (cm)	99.95±8.36	100.34±7.73	0.75
No. of chorionic diseases	2.31±1.77	2.70±1.70	0.11
Physical activity score	99.07±57.06	9.22±0.42	0.27
Serum Ca (mg/dl)	9.26±0.45	9.22±0.42	0.27
Serum Vit D (ng/ml)	31.39±25.59	32.80±30.33	0.57

WC=Waist circumference, HC=Hip circumference, BMI=Body mass index, SD=Standard deviation

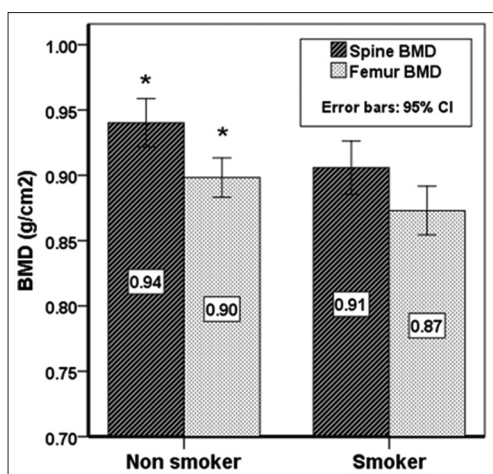


Figure 1: Comparison of lumbar spine (spine) and femoral neck (femur) bone mineral density in smoker and nonsmoker elderly men of the Amirkola cohort study

Osteoporosis at either FN or LS was found in 31 (15.3%) smokers versus 71 (17.4%) nonsmokers ( $P = 0.58$ ) and osteopenia in 132 (65%) and 211 (51.7%), respectively (odds ratio [OR] = 1.73, 95% confidence interval [CI]: 1.22–2.45,  $P = 0.004$ ) [Table 3]. Vertebral and no vertebral fractures were observed in 78 (38.4%) smokers and 107 (26.2%) nonsmokers ( $P = 0.003$ ). In multiple logistic regression analysis, considering low bone mass (combination of osteoporosis and osteopenia) as dependent variable, there was an independent significant association between low bone mass and smoking. After adjusting the levels of education, serum Vitamin D, BMI, and age, the odds of having low bone mass in smokers was significantly higher than nonsmokers (OR = 2.27, 95% CI: 1.49–3.44,  $P = 0.04$ ). With increasing age, the odds of low bone mass increase by a dose-response pattern relationship, whereas, by increasing BMI, compared with BMI <25 kg/m<sup>2</sup>, the odds of having low bone mass decreased significantly from 0.15 (95% CI: 0.097–0.23,  $P = 0.001$ ) to 0.07 (95% CI: 0.041–0.13,  $P = 0.001$ ) [Table 4]. However, serum Vitamin D and educational level were not associated with significant changes in the risk of low bone mass.

## Discussion

The results of this study indicate significantly lower BMD in smokers versus nonsmokers. BMD at both measurement sites decreased significantly in smokers, and the deleterious effect of smoking on bone mass has been confirmed by comparisons of all BMD parameters. Proportion of low bone mass at either LS or FN in smokers was 2.27 times greater than in nonsmokers. Moreover, bone fracture in the elderly male smokers was significantly higher in smokers.

The findings of this study provide support in earlier studies and consistency with other studies as regards sites of BMD loss.<sup>[13,16,18,21]</sup>

Table 2: Bone mineral density in smokers versus nonsmokers of the Amirkola Health and Aging Project according to bone mineral density parameters and sites of bone mineral density measurements

Bone mineral density	Smokers (n=203)	Nonsmokers (n=408)	P
LSBMD (g/cm <sup>2</sup> )	0.90±0.14	0.94±0.19	0.014 <sup>#</sup>
FNBM (g/cm <sup>2</sup> )	0.87±0.13	0.89±0.15	0.038 <sup>#</sup>
LSBMD Z-score	-0.52±1.03	-2.161.3±3	0.002 <sup>#</sup>
FNBM Z-score	-0.65±0.88	-0.41±1	0.003 <sup>#</sup>
LSBMD T-score	-1.26±0.92	-1.01±1.3	0.011 <sup>*</sup>
FNBM T-score	-1.28±0.92	-1.07±1.10	0.012 <sup>*</sup>

<sup>#</sup>Student's *t*-test and <sup>\*</sup>Mann-Whitney U-tests were used for comparison. LSBMD=Lumbar spine bone mineral density, FNBM=Femoral neck bone mineral density

Table 3: Frequency of osteoporosis and osteopenia at either femoral neck or lumbar spine in elderly smoker and nonsmoker men of the Amirkola cohort study

Bone scan	Smoker (%)	Nonsmoker (%)	P
Vertebrae and femur			
Normal	40 (19.7)	126 (30.9)	0.003
Osteopenia	132 (65)	211 (51.7)	0.004
Osteoporosis	31 (15.3)	71 (17.4)	0.58

Table 4: Independent association between low bone mass (osteoporosis + osteopenia at either lumbar spine or femoral neck) with smoking, age, body mass index, and education levels in smoker and nonsmoker elderly men of the Amirkola cohort study after logistic regression analysis with calculation of adjusted odds ratio with 95% confidence interval

Variables	OR (95% CI)	P
Smoking		
Nonsmokers	1	
Smokers	2.27 (1.49-3.44)	0.04
Age		
60-64	1	
65-65	1.22 (0.72-2.2)	0.5
70-74	2.34 (1.04-4.95)	0.003
75-79	2.55 (1.37-4.26)	0.003
80-84	3.83 (1.49-9.54)	0.005
>85	5.77 (1.44-23.1)	0.001
BMI (kg/m <sup>2</sup> )		
<25	1	
25-30	0.15 (0.097-0.23)	0.001
≥30	0.07 (0.041-0.13)	0.001
Levels of education		
Illiterate	1	
Primary school	1.26 (0.81-2.03)	0.28
Secondary school	0.62 (0.22-2.21)	0.54
High school	0.39 (0.18-0.90)	0.028
University	0.93 (0.39-2.20)	0.87

OR=Odds ratio, CI=Confidence interval, BMI=Body mass index

In a study of Chinese men, cigarette smoking was inversely associated with BMD at both total hip and spine.<sup>[16]</sup> Similarly, Tamaki *et al.* found decreased BMD in the hip and spine both in current and former smokers. Reduction of BMD was associated with the number of pack-years or duration of smoking years<sup>[13]</sup> In another study of postmenopausal women, BMD did not differ between never, former, and current smokers, and there was a negative association between FNBMD and smoking with a dose-dependent manner of cigarette consumption but not with the duration of smoking.<sup>[19,21]</sup> In a study by Szulc *et al.*, BMD was similar between current and former smokers and the former smokers had lower BMD than nonsmokers; the levels of urinary bone resorption markers were higher in present rather than former smokers and nonsmokers. In this study, the participants with moderate smoking and low body weight had a higher rate of bone loss, and the bone resorption was discordant to bone formation.<sup>[22]</sup>

Krall and Dawson-Hughes found greater bone loss from the FN and total body in smokers, whereas there was no difference in bone loss between smokers and nonsmokers at the LS.<sup>[23]</sup> In the Hordaland study, heavy smoking increased the risk of hip fracture in the elderly women and men, and the deleterious effect of smoking was stronger in lean smokers, whereas fat mass was associated with lower fracture risk. These observations indicate that obesity exerts protective effects against bone loss in smokers.<sup>[18]</sup>

In contrast, Kuo *et al.* in healthy Taiwanese middle-aged men found significantly lower LSBMD in current smokers compared with never smokers, but no significant reduction was found in FNBMD.<sup>[17]</sup> In a study on 140 Finnish men aged 54–63 years who were randomly selected, smoking had no effect on BMD.<sup>[2]</sup>

Influence of smoking on bone mass may be confounded by several associated coexisted clinical conditions in smokers. Factors such as age of study population, sex, the number and duration of smoking, and presence of comorbidities such as obesity, metabolic syndrome, and Vitamin D deficiency may differently affect the interaction between smoking and BMD loss. For example, lean body mass increases bone resorption in smokers whereas fat mass decreases bone loss<sup>[18,22]</sup> In the geographic region of this study, obesity, metabolic syndrome, and Vitamin D deficiency are common even in adolescence and childhood periods.<sup>[24,25]</sup> Both obesity and metabolic syndrome exert beneficial effects against bone loss.<sup>[8,26]</sup>

Deleterious effect of smoking on bone mass has been attributed to its independent influence on bone metabolism. Cigarette smoking decreases intestinal absorption of Ca. Furthermore, smoking alters circulating levels of adrenal cortical hormones as precursors of estrogen and testosterone.<sup>[23]</sup>

The results of this study should be interpreted with limitations. Although the performance of BMD measurement is associated with some technical errors, particularly in the FN region, in the present study, the possibility of technical errors is expected to be minimal because BMD measurement in both smokers and nonsmokers was assessed similarly; so, the results are subjected to be biased minimally.

Data regarding osteoporotic vertebral or nonvertebral fractures were provided by history and the review of medical records. The possibility of overdiagnosis cannot be ignored. The magnitude and duration of smoking on bone mass have not been shown in this study as the sample size was not adequately large enough to address this issue. Consequently, this topic requires prospective longitudinal studies.

In the current study, the prevalence of osteoporosis in smokers was comparable to nonsmoker. It may be explained by insufficient sample size or underestimation of osteoporosis in the elderly because of coexistent osteoarthritis. A significant proportion of elderly people have osteoarthritis.<sup>[27]</sup> In the elderly participants, the presence of osteoarthritis results in false elevation of BMD and underestimation of osteoporosis, particularly in the LS. Therefore, the real number of participants with osteoporosis might be higher than that observed in this study. This issue suggests using BMD Z-score rather than BMD T-score for the evaluation of spine osteoporosis in elderly participants.<sup>[28]</sup> Nevertheless, this study is cross-sectional, and the association between smoking and low BMD does not indicate causality.

The strength of this study is dependent to the characteristics of the study population which has been recruited among a general population with unique ethnic background and similar lifestyles. Many associated factors of bone loss are expected to be distributed across the two study groups alike. Hence, the findings of this study were anticipated to be less confounded. The strength of this study is related to similar technic of BMD measurement in all participants in a single center.

## Conclusions

This study indicates significantly lower LSBMD and FNBMD in current smokers as well as the elderly male ex-smokers. The observed association between low bone mass and smoking in the elderly men supports the results of earlier studies and highlights preventive measures.

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## Conflicts of interest

There are no conflicts of interest.

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