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Body mass index and gynecological factors as determinants of bone mass in healthy Moroccan women

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Abstract

Several studies have shown that low body mass index (BMI) is associated with low BMD and fractures. However, the results that have been published from studies on reproductive factors and BMD are extremely controversial, with some demonstrating a beneficial effect, while others show a detrimental impact of these factors on bone mass.

Objective: To study the influence of several gynecological factors (years since menopause (YSM), age at menarche and gynecological age or reproductive life) simultaneously with anthropometric factors as determinants of bone mineral density (BMD) in healthy women older than 40.

Methods: BMD was determined by dual energy X-ray absorptiometry (DXA) at the lumbar spine and femurs in women aged >40 randomly chosen from the population of Rabat with a cluster sampling method.

Results: Four hundred and twenty-two healthy women older than 40 years were included in the study. The mean age was 57.2 years (8.4) [40–79] and the mean number of parities was 4.42 (2.9) [0–14]. Osteoporosis according to the classification of WHO (T-score ≤ -2.5) was observed in 133 women (32.2%). The increase in the number of parities was associated to a larger body mass index and a lower BMD as well in the hips and the lumbar spine after adjustment for age. The comparison of groups of patients according to the age at menarche, the age at menopause or the period of fertility did not highlight an association with BMD. BMD at the lumbar spine and the hips was correlated negatively with age, YSM and parity and positively with BMI. Multivariate analysis showed that the determinant of BMD are BMI (OR = 0.88; 95% CI: 0.83–0.92), parity (OR = 1.10; 1.01–1.56) and YSM (OR = 1.06; 1.03–1.10).

Conclusion: Bone loss in women older than 40 is a function of aging, parity and years since menopause; and there is a definite bone-protective effect of body mass weight. Further studies are required to evaluate the role of these parameters in the fracture risk.

Keywords: Bone mass; Body mass index; Gynecological age; Reproductive life; Age at menarche; Years since menopause

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1. Introduction

Osteoporosis is a metabolic bone disorder characterized by low bone mass and microarchitectural deterioration, with a subsequent increase in bone fragility and susceptibility to fracture [1]. Osteoporotic fractures, particularly of the hip, are associated with high mortality rates and loss of independence. Fracture incidence increases with age, and the predicted aging of populations will accentuate the burden of these fractures on health-care systems [2]. The risk of fracture increases proportionately with decrease in bone mineral density (BMD), and in 90% of all hip fracture cases, a fracture is sustained through a fall [3].

Several cross-sectional and longitudinal studies have shown that low body weight and low body mass index (BMI) are associated with low BMD and fractures [4–6]. However, the results that have been published from studies on reproductive factors and BMD are extremely controversial, with some demonstrating a beneficial effect, while others show a detrimental impact of these factors on bone mass [7–22]. Increasing parity might be expected to protect against bone loss because of pregnancy related increases in body weight, intestinal calcium absorption and cumulative estrogen exposure and a later age at menopause. Indeed, several reports have shown a positive correlation between parity and BMD [15,17,18,22] and a reduced hip fracture rate [20], although other studies have reported either no correlation between parity and BMD [5–11,23,24] or a negative correlation [12–14]. However, many studies have been conducted on women with low (e.g., 1–3) parity [5,8,10,15,23]. The few studies of parity and BMD conducted in relatively high parity (more than or equal to five live births) postmenopausal women have provided conflicting results. Among the other gynecological factors, Rosenthal et al. [25] identified late age of menarche as a risk factor for decreased spinal BMD and suggested that delayed menarche is indicative of inadequate sex hormone levels during adolescence, whereas delayed puberty is associated with osteopenia. Numerous studies suggested that age at menarche is associated with bone growth and bone density [25–29]. Hence, it has been observed that pubescent girls with an earlier onset of menarche are shorter and present stunted bone growth when compared to girls with an onset at the expected age [28]. Conversely, girls with late onset (>14) are more likely to be taller and slimmer and seem to have lower bone density [29]. A series of reports concerning postmenopausal women indicate that bone mass is more dependent on years since menopause than chronological age [30,31]. However, other authors [32] have shown that even though this is the case, the most important factor when it comes to postmenopausal bone mass is the duration of fertility (gynecological age or years between menarche and menopause). Thus, the following factors are thought to influence BMD: age, BMI, parity, age at menarche, years since menopause (YSM) and gynecological age. We aimed in this study to investigate the major determinant of BMD evaluated with DXA in normal women aged >40 years.

2. Materials and methods

2.1. Subjects

A total of 422 healthy Moroccan women aged >40 years living in the Rabat area participated in the present study. Rabat is the capital of Morocco with a diverse population representing most Moroccans. Morocco has a population of 29,891,708 (2004 population census), most of which are Caucasians and Rabat is a modern city of 627,932 inhabitants (50.2% of females). It is divided in multiple census districts by the census department of the Ministry of Health. Originally, a total of 659 subjects were randomly selected using a cluster sampling method from 30 census districts scattered around the city of Rabat from April to August 2005 to ensure that the average health status of the study group would reflect a normal adult population. Subjects who agreed to participate in the survey were asked to visit our department to be enrolled in a study with the objective to establish the Moroccan normal curve of BMD [33]. Our institutional review board approved this study. The procedures of the study were in accordance with the Declaration of Helsinki, and formal ethics committee approval was obtained for the study. All the participants gave an informed and written consent. Each subject completed a standardized questionnaire designed to document putative risk factors of osteoporosis. The questionnaire was administered during the home visit together with an invitation to enter the study. Lifestyle (alcohol consumption, gym-

nastics or jogging/walking, smoking) and diet (milk, yogurt, cheese) habits were also recorded. The women were asked whether they usually drank milk, coffee or alcohol; if they ate cheese or yogurt; if they did gymnastics or jogging/walking and if they smoked tobacco. If the answer was positive, they were asked to quantify their average current consumption (evaluated on the 7 day prior to the interview) of milk or yogurt (mL/day), cheese (g/day) and wine and/or spirits (mL/day). Tobacco smoking was quantified as average number of cigarettes (smoked/day) multiplied by the number of years of smoking, gymnastics as min/week, or jogging/walking as min/day. Finally, patients were categorized as never smokers, ex-smokers and current smokers; high, normal and low calcium intake (more than 1500 mg/day, between 800 and 1500 day^{-1} and below 800 mg/day, respectively); high, normal and low physical activity (more than 3, 2–3 and below 1 h/week, respectively). Menstrual and reproductive history were assessed. Postmenopausals were defined as those who had their last menstrual period >1 year ago in accordance with clinical definitions of the WHO. Height and weight were measured in our centre before DXA measurement, in light indoor clothes without shoes. Body mass index was calculated by dividing weight in kilograms by height in meters squared.

General exclusion criteria were non-Caucasian origin and diseases, drugs and other major determinants known to affect bone metabolism. Thus, we excluded subjects with gastrectomy, intestinal resection, recent hyperthyroidism or hyperparathyroidism, treatment with corticosteroids or recent severe immobilization. Subjects who had taken estrogens earlier during at least 2 years after menopause or who still were taking estrogens for more than 6 months were excluded as well as those who had taken oral corticosteroids for more than 6 months. We did not exclude individuals using inhalation steroids. Women using medications affecting calcium metabolism and those with medical conditions known to affect bone metabolism (e.g., amenorrhea, anorexia nervosa, premature ovarian failure) or with a history of any fracture or major systemic disorder were excluded. Also excluded were women who had experienced an early (before 40 years of age) menopause. We did not exclude subjects with life-style habits, such as heavy smoking, sedentary life-style, athletics, high or low calcium intake, etc., all of which are examples of voluntary factors which may have some impact on bone metabolism [34].

In total, 808 women were visited. Among them 178 individuals were excluded from the study according to predetermined exclusion criteria, whereas 630 met all inclusion criteria and were invited to BMD measurement. Finally, 569 (90.3% of participating females) responded and entered the reference population sample. Among them, 422 women were aged >40 years and their data were analysed in the current study. The BMD of their lumbar spine and proximal femurs was measured. All of them gave informed consent. All subjects were fully ambulatory. The age distribution, age at menarche, years since menopause and some other basic parameters are shown in Table 1.

2.2. BMD measurement

BMD was determined by a Lunar Prodigy Vision DXA system (Lunar Corp., Madison, WI). The DXA

Table 1
Characteristics of the study population

		Minimum	Maximum
Age (years), mean (S.D.)	57.2 (8.7)	40	79
Weight (kg), mean (S.D.)	71.7 (12.6)	40	115
Height (cm), mean (S.D.)	156.5 (6.1)	133	178
BMI (kg/m^2), mean (S.D.)	29.3 (5.1)	18.5	48.8
No. of children, mean (S.D.)	4.4 (2.9)	0	14
Age at menarche (years), mean (S.D.)	12.9 (1.2)	9	17
Postmenopausal, *n* (%)	359 (85.0)		
Age at menopause (years), mean (S.D.)	49.4 (5.1)	36	62
Years since menopause (years), mean (S.D.)	10.0 (7.4)	1	38
Low calcium intake, *n* (%)	213 (50.5)		
Low physical activity, *n* (%)	366 (86.7)		

Table 2
Comparison of patients with and without osteoporosis

	Patients with osteoporosis ($n = 136$)	Patients without osteoporosis ($n = 286$)	P value
BMI (kg/m^2), mean (S.D.)	27.6 (4.8)	30.0 (5.0)	<0.0001
No. of children, mean (S.D.)	5.2 (2.9)	4.0 (2.8)	<0.0001
Postmenopausal, *n* (%)	133 (97.3)	226 (52.3)	<0.0001
Age at menarche (years), mean (S.D.)	12.9 (1.1)	13.0 (1.2)	NS
Age at menopause (years), mean (S.D.)	49.1 (3.6)	49.5 (3.6)	NS
Gynecological age[a], mean (S.D.)	36.2 (3.8)	36.5 (3.9)	NS
Years since menopause, mean (S.D.)	12.3 (8.1)	8.7 (6.7)	<0.0001
Low physical activity, *n* (%)	123 (90.4)	243 (85.0)	NS
Low calcium intake, *n* (%)	67 (49.3)	146 (51.0)	NS
Spine *T*-score, mean (S.D.)	−3.20 (0.6)	−0.85 (1.1)	<0.0001
Spine BMD (g/cm^2), mean (S.D.)	0.783 (0.7)	1.061 (0.1)	<0.0001
Total hip *T*-score, mean (S.D.)	−1.74 (0.8)	−0.34 (1.0)	<0.0001
Total hip BMD (g/cm^2), mean (S.D.)	0.789 (0.1)	0.958 (0.1)	<0.0001

[a] Gynecological age or duration of fertility was defined as years between menarche and menopause.

scans were obtained by standard procedures supplied by the manufacturer for scanning and analysis. All BMD measurements were carried out by two experienced technicians. Daily quality control was carried out by measurement of a Lunar phantom. At the time of the study, phantom measurements showed stable results. The phantom precision expressed as the CV (%) was 0.08. Moreover, reproducibility has been assessed recently in clinical practice and showed a smallest detectable difference of 0.04 g/cm^2 (spine) and 0.02 (hips) [35,36]. Patient BMD was measured at the lumbar spine (anteroposterior projection at L1–L4) and the femurs (femoral neck, trochanter, ward and total hip).

2.3. Statistical analysis

The study was conducted on different steps:

- the first step consisted on the description of the study population. Results are presented as means (±S.D.) and categorical variables are expressed as frequencies;
- in the second step, we compared the women with and without osteoporosis defined as a *T*-score below −2.5 at any of the hips or the lumbar spine. Student's *t*-test and χ^2-test were used, respectively, for quantitative and qualitative variables (Table 2);

Table 3
Characteristics of studied women in relation to their body mass index

Variable	BMI			P value
	<25 ($n = 81$)	25–29 ($n = 162$)	≥30 ($n = 179$)	
Age (years), mean (S.D.)	57.2 (8.7)	56.3 (9.2)	57.9 (8.2)	NS
No. of children, mean (S.D.)	4.1 (2.5)	4.3 (3.0)	4.6 (2.8)	NS
Postmenopausal, *n* (%)	70 (86.4)	130 (80.2)	159 (88.8)	NS
Age at menarche (years), mean (S.D.)	13.0 (1.1)	12.8 (1.1)	13.0 (1.2)	NS
Age at menopause (years), mean (S.D.)	49.3 (3.3)	49.1 (3.9)	49.6 (3.5)	NS
Gynecological age[a], mean (S.D.)	36.2 (3.6)	36.3 (4.2)	36.5 (3.7)	NS
Years since menopause, mean (S.D.)	9.6 (7.1)	10.3 (7.7)	10.0 (7.4)	NS
Spine *T*-score, mean (S.D.)	−2.21 (1.5)	−1.52 (1.5)	−1.42 (1.5)	<0.0001
Spine BMD (g/cm^2), mean (S.D.)	0.903 (0.1)	0.982 (0.1)	0.994 (0.1)	<0.0001
Total hip *T*-score, mean (S.D.)	−1.36 (1.0)	−0.89 (1.1)	−0.44 (1.1)	<0.0001
Total hip BMD (g/cm^2), mean (S.D.)	0.832 (0.1)	0.891 (0.1)	0.947 (0.1)	<0.0001

[a] Gynecological age or duration of fertility was defined as years between menarche and menopause.

Table 4
Characteristics of studied women in relation to their parity

Variable	No. of children				*P* value
	0 (*n* = 43)	1–3 (*n* = 68)	4–5 (*n* = 170)	≥6 (*n* = 141)	
No. of children, mean (S.D.)	0 (0)	1.6 (0.4)	3.9 (0.7)	7.7 (1.8)	<0.0001
Age (years), mean (S.D.)	56.0 (8.3)	54.4 (9.0)	55.3 (8.2)	61.9 (8.0)	<0.0001
BMI (kg/m^2), mean (S.D.)	28.4 (4.6)	28.6 (4.3)	29.6 (5.3)	29.5 (5.3)	<0.0001
Postmenopausal, *n* (%)	34 (79.1)	51 (75.0)	139 (81.8)	135 (95.7)	<0.0001
Age at menarche (years), mean (S.D.)	13.2 (1.0)	13.3 (1.4)	12.8 (1.1)	12.9 (1.1)	0.02
Age at menopause (years), mean (S.D.)	49.6 (3.6)	49.4 (3.9)	49.1 (3.6)	49.5 (3.6)	NS
Gynecological age[a], mean (S.D.)	36.3 (4.0)	36.0 (4.4)	36.3 (3.6)	36.6 (4.0)	NS
Years since menopause, mean (S.D.)	9.3 (7.0)	8.7 (7.4)	8.6 (7.2)	12.3 (7.4)	<0.0001
Spine *T*-score, mean (S.D.)	−1.31 (1.3)	−1.06 (1.2)	−1.49 (1.5)	−2.12 (1.2)	<0.0001
Spine BMD, mean (S.D.)	1.004 (0.1)	1.040 (0.1)	0.987 (0.1)	0.910 (0.1)	<0.0001
Total hip *T*-score, mean (S.D.)	−0.73 (1.1)	−0.51 (1.0)	−0.62 (1.2)	−1.15 (1.0)	<0.0001
Total hip BMD, mean (S.D.)	0.907 (0.1)	0.934 (0.1)	0.925 (0.1)	0.862 (0.1)	<0.0001

[a] Gynecological age or duration of fertility was defined as years between menarche and menopause.

- comparison according to BMI category (WHO classification) was made in the third step using analysis of variance ANOVA;
- in the fourth step, we compared women according to number of parity using analysis of variance ANOVA after separating them in four categories: nulliparous, 1–3 children, 4–5 children and >6 children. Analysis was also done with three separate sets of adjustments: one for age only; a second for age and BMI; a third for age, BMI and other reproduction-related variables;
- we looked for correlations between hip and spine BMD in the fifth step and all the potential determinants of bone mass using the spearman test;
- and finally, we realised a forward multiple regression analysis including in the equation these parameters to evaluate their respective weight on the osteoporotic status. The odds ratios (OR) were computed for the various factors considered, together with their 95% approximate confidence intervals (CI).

The level for significance was taken as $P < 0.05$. SPSS 13.0 were used for the statistical analysis.

3. Results

The number of children among the study population ranged from 0 to 14, with a mean (S.D.) parity of 4.4 (2.9) live births. Women with osteoporosis were older, weighted more, had more children and more YSM (Table 3). There were no difference in age at menarche, age at menopause and gynecological age. When separating the study group according to BMI, BMD and *T*-scores were significantly lower in women with

Table 5
Correlation study in the overall group of women between BMD and age, BMI and gynecological factors

	Hip BMD	Lumbar spine BMD
Age		
r	−0.467[a]	−0.526[a]
p	0.0001	0.0001
BMI		
r	0.190[a]	0.055
p	0.0001	0.191
Gynecological age		
r	0.054	0.023
p	0.307	0.665
Number of parity		
r	−0.325[a]	−0.402[a]
p	0.0001	0.0001
Years since menopause		
r	−0.357[a]	−0.274[a]
p	0.0001	0.0001
Age at menarche		
r	0.061	0.053
p	0.144	0.208
Age at menopause		
r	0.056	0.021
p	0.291	0.688

[a] Correlation is significant at the 0.01 level (two-tailed).

Table 6
Results of multivariate logistic regression analysis for risk factors of osteoporosis

	T-score below −2.5		
	Lumbar spine	Total hip	Any
Body mass index	0.88 (0.84–0.92)	0.81 (0.73–0.90)	0.88 (0.83–0.92)
Number of parity	1.70 (1.06–2.73)	1.17 (1.00–1.36)	1.10 (1.01–1.56)
Years since menopause	1.05 (1.02–1.09)	1.14 (1.07–1.21)	1.06 (1.03–1.10)

Numbers are presented as odds ratio (95% confidence intervals in parentheses).

low BMI. Comparison of women according to their number of children showed that multiparous women are at highest risk of low BMD and *T*-scores at the lumbar spine and hips. The effects of parity on BMD are shown in Table 4. There was a significant negative correlation between hip and lumbar spine BMD and age, number of parity and YSM and a positive correlation with BMI (Table 5). Multiple regression analysis showed that the three variables having an effect on BMD when all of the incriminated parameters are included are BMI, number of parity and YSM (Table 6).

4. Discussion

Our study demonstrated that the major determinants of low BMD in a randomly chosen sample of Moroccan healthy women older than 40 are BMI, number of parity and YSM.

Overweight women were at diseased risk of low bone density. This finding agrees with several previous studies showing thinner women to have less bone mass [4–6] and a greater risk for fractures than heavier ones [7]. Overweight may protect women against bone loss after menopause by increasing the amount of biologically available estrogens (that is, conversion of androstenedione to estrone in adipose cells and decrease in the concentration of sex hormone binding globulins). However, a positive relation between body size and bone density has been also reported in men and premenopausal women, thus stimulating the search for other mechanisms. Obesity can protect the skeleton through two mechanisms: the mechanical stimulation exerted by corporal weight and greater fat. In view of the above, a series of important roles can be ascribed to the adipose compartment. First of all, fat tissue is a source of conversion of androgens to estrogen (aromatization). Fat also influences estrogen conversion from the more potent to the less potent catechol estrogens and alters the binding capacity of estrogen and sex-hormone binding globulin. And finally, fat tissue acts as a storage unit of steroid hormones [37].

During pregnancy mineralization of fetal skeleton increases a reabsorption of calcium from maternal bone stores. Otherwise estrogen levels are elevated during pregnancy. These findings have suggested that parity may affect the risk of osteoporosis [38–40]. Clinical and epidemiological data are inconsistent, showing both an increased and a reduced risk in parous women of osteoporosis. The Moroccan population offers numerous strengths for evaluating the relationship between parity and osteoporosis. The most important of these is the high parity characteristic of this population. The high parity in Moroccan women may indeed reveal parity–BMD associations that might not be apparent in studies of women of lower parity. Second, the Moroccan lifestyle tends to be very homogeneous among women: for example, Moroccan women rarely smoke or drink alcohol, have little outdoor activities and rarely use oral contraceptives or postmenopausal estrogen replacement therapy. Our study showed the strong negative effect of multiparity on BMD persisting significantly after adjusting for age, BMI and YSM.

Several studies conducted on women less than 50 years old [9,11] and on women over 70 years old [7] found no parity–BMD correlation. Among those studies that have reported a positive association between increasing parity and increasing BMD, most [16–18,22,34], but not all [15], included large significant proportions of women aged in their 50s. Thus, it is possible that some of the conflicting results reported in the literature may be attributable to differences in the ages of the populations studied. Few studies have evaluated the relationship between parity and BMD in postmenopausal women with very high parity [14,17,30,31]. In Hispanic women from Columbia

characterized by high parity, parous women were found to have higher BMD at the hip than nulliparous women, but among parous women, and especially those with two or more children, there was no consistent trend between number of deliveries and BMD (not adjusted for BMD) [17]. The relationship between parity and BMD has also been evaluated among postmenopausal women from Turkey [14]. Also consisting with our own findings, these investigators reported an inverse correlation between parity and BMD of the hip and spine (i.e., increasing parity associated with decreasing BMD). Recently, in contrast with our results, a study conducted in Amish population characterized by very high parity revealed that parity is associated with increased hip BMD, although this association appears to be largely mediated by an accompanying increase in BMI seen with high parity [24].

Age at menarche and gynecological age did not show any influence on bone mass in our sample population, when studied as a whole or according to age, YSM, parity or BMI. Nonetheless, the effects of both age at menarche and gynecological age are highly controversial in the medical literature.

The results of the present analysis confirm the well-recognized role of YSM on the risk of osteoporosis. This finding is consistently reported in populations from different countries [5]. Estrogen deficiency is responsible for one-third to one-half of the bone loss during a woman's lifetime, the fact being directly correlated with an increased risk of bone fracture in aged women. Estrogens inhibit the production and the action of the cytokines. In postmenopause, the inhibitory effect is removed resulting in a predominant osteoclast activity which is responsible for increased bone resorption and bone loss.

A major strength of our study is that the study population was extracted from the general healthy population of a big city using a cluster sampling system. Moreover, the Moroccan practice of avoiding alcohol and tobacco minimizes the potential confounding effects of these variables.

In summary, the principal conclusions of this study are the following: bone loss in Moroccan women older than 40 is a function of aging, parity and years since menopause; there is a definite bone-protective effect of body mass weight. Further studies are required to evaluate the role of these parameters in the fracture risk.

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