



Original Research

Bone mineral density is lower in male than female patients with plaque-type psoriasis in Iran^{☆,☆☆}



V. Lajevardi, MD^a, R. Abedini, MD^a, M. Moghaddasi, MD^b, S.F. Nassiri, MD^a, A. Goodarzi, MD^{c,*}

^a Department of Dermatology, Tehran University of Medical Sciences, Razi Hospital, Tehran, Iran

^b Department of Rheumatology, Tehran University of Medical Sciences, Sina Hospital, Tehran, Iran

^c Department of Dermatology, Iran University of Medical Sciences, Rasool Akram Hospital, Tehran, Iran

ARTICLE INFO

Article history:

Received 16 December 2015

Received in revised form 22 April 2017

Accepted 30 July 2017

Keywords:

plaque-type psoriasis

bone mineral density

osteoporosis

osteopenia

T-score

ABSTRACT

Background: There are many similarities with regard to contributing cytokines in patients with psoriasis and osteoporosis. A theory of probable relationship between these two entities has been proposed but there is no concordant consensus. The aim of this study was to evaluate bone mineral density (BMD) in patients with psoriasis.

Method and materials: This cross-sectional study of BMD was conducted with 64 eligible patients with psoriasis who were referred to the dermatology clinic of Razi hospital in Tehran, Iran in between 2011 and 2012.

Results: The mean T score of femoral neck was -1.17 and -0.49 in men and women, respectively, which was statistically significant ($p = .047$). The mean T score of the lumbar spine was -0.93 and -0.30 in men and women, respectively, but not statistically significant ($p = .058$). In total except with the exclusion of the study site (femur or lumbar), men and women did not have a statistically significant difference with regard to osteoporosis or osteopenia in BMD ($p = .114$). The Pearson correlation coefficient demonstrated a moderate inverse relationship between age and T score of the femoral neck and lumbar spine ($r = -0.419$ and -0.406 , respectively), which was statistically significant ($p = .001$). Although there was no statistically significant relationship between the Psoriasis Area and Severity Index (PASI) and T scores of the femoral neck ($p = .596$), a positive and weak correlation was observed between the PASI and T scores for the lumbar spine, which was statistically significant ($r = 0.269$; $p = .03$).

Conclusion: Patients with psoriasis had decreased bone density, which was more significant in men. Prevalence of osteoporosis showed no statistically significant difference when compared with the healthy population in Iran.

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Introduction

Psoriasis is a chronic, inflammatory disorder of the joints, skin, and immune system with a prevalence of approximately 2% to 4% in the general population. Several recent studies have implicated systemic inflammatory cytokines with the pathogenesis of psoriasis and suggested that they are responsible for higher internal involvement such as cardiovascular disease, diabetes, and dyslipidemia. These studies show that psoriasis is a complex disorder (Langley et al., 2005; Neimann et al., 2006; Ridker, 2010; Schön and Henning-Boehricke, 2005).

At present, despite screening and prevention programs, osteoporosis remains a hidden problem that is less often detected (Poole and Compston, 2006). Many cytokines including interferon-gamma, interleukin-6, and TNF- α have been identified in the pathogenesis of osteoporosis and these are the same as those involved in the inflammation of psoriasis. Some studies have proposed a hypothesis of association between these two disorders (De Martinis et al., 2006; Kastelan et al., 2006).

A review of the literature revealed that there are few studies on the association between cutaneous psoriasis and osteoporosis and their results are inconsistent. Most of the existing research only focused on the impact of psoriatic arthritis on the generalized decrease in bone mineral mass (Frediani et al., 2001). Interestingly, in contrast with the usual higher average rates of osteopenia-osteoporosis among women in the health population, a few studies observed a prevalence among men with psoriasis (Dreiherr et al., 2009; Hofbauer et al., 2006).

[☆] Conflicts of interest: The authors have no conflict of interest to disclose.

^{☆☆} Funding sources: This study was funded by the Vice Chancellor of Research at the Tehran University of Medical Sciences in Iran.

* Corresponding Author.

E-mail address: azadeh_goodarzi1984@yahoo.com (A. Goodarzi).

This study was designed and conducted to evaluate the changes in bone density in patients with chronic plaque-type psoriasis (with or without arthritis) and probable gender-related predilection among a group of Iranian patients who were referred to a dermatology referral center at the Razi Hospital in Tehran, Iran.

Methods and materials

This cross-sectional study enrolled 64 patients with psoriasis who were referred to the Razi Dermatology Center in Tehran, Iran between 2011 and 2012. The patients did not have a history of other chronic inflammatory disorders, endocrine disorders (thyroid, parathyroid, and gonadal), chronic kidney disease, or liver disease. For each patient, a questionnaire on demographic data (age, sex), daily physical activity (subjective as acceptable or not), smoking, drug history recorded, and body indices including weight and height were measured. The severity of the skin disease on the basis of Psoriasis Area and Severity Index (PASI) score and the joint involvement on the basis of the number of joints were determined and recorded. Blood samples were tested for C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), 25-hydroxycholecalciferol (25 [OH]) vitamin D3 (Vit D3), calcium, phosphorus, and parathyroid hormone levels at the laboratory center of the Razi hospital.

Bone mineral density (BMD) using the dual-energy X-ray absorptiometry (DEXA) method of the lumbar spine (L1-L4) and femoral neck was performed at the Sina Hospital that is affiliated with the Tehran University of Medical Sciences and the results were recorded as T-scores and compared between male and female patients.

According to the World Health Organization's definition, T score values between -1 and -2.5 are considered osteopenia and values smaller than or equal to -2.5 as osteoporosis. Data were analyzed using SPSS (IBM, North Castle, NY) Version 18 and for the descriptive analysis, mean, standard deviation, and frequency were calculated with the *t* and analysis of variance (ANOVA) tests to compare different variable groups. Pearson's correlation coefficient or nonparametric equivalents were used for the quantitative data analysis. All tests were interpreted with a significance level of 5%, and in the case of insignificant results, we reported the power of each test.

The study protocol was approved by the Ethics Committee of the Tehran University of Medical Sciences and after a complete explanation of the study aims to patients, written informed consent forms were obtained.

Results

Of the 64 patients enrolled in the study, 34 patients (53.1%) were male and 30 patients (46.9%) were female with a mean age of 43.9 ± 16.8 years. The mean body mass index (BMI) of patients was 27.12 ± 4.93 kg/m². Forty patients (62.5%) were overweight (BMI >25). The demographic and laboratory data of patients are shown in Table 1.

Twenty-nine patients (45.3%) had femoral neck osteopenia and 6 patients (9.4%) had femoral neck osteoporosis. A BMD study of the lumbar spine showed that 18 patients (28.1%) had osteopenia and four patients (6.3%) had osteoporosis (Fig 1). A total of 28 patients (43.8%) had a decrease of bone mass (osteopenia) in either one of the two sites (femoral or lumbar), and 8 patients (12.5%) had osteoporosis in at least one of the two sites (Fig 2).

The mean T score of femoral neck was -1.17 and -0.49 in men and women, respectively. The difference was -0.68 (95% confidence interval (CI), -0.01 to -1.36), which was statistically significant ($p = .047$). The mean T score of the lumbar spine was -0.93 and -0.30 in men and women, respectively, and the mean difference was -0.63 (95 CI, -0.02 to -1.28) but not statistically significant ($p = .058$).

Table 1
Demographic and laboratory data of patients

	Value
Number	64
Sex	
Male	34 (53.1%)
Female	30 (46.9%)
Age (years)	
Mean \pm SD	43.9 ± 16.8
Min-Max	13-79
Body mass index (kg/m²)	
Mean \pm SD	27.12 ± 4.93
Min-Max	17-44
Activity	18 (28.1%)
Cigarette smoking	13 (20.3%)
Disease duration (years)	
Mean \pm SD	27.12 ± 4.93
Min-Max	1-40
PASI score	
Mean \pm SD	5.5 ± 4.7
Min-Max	0.4-26
Psoriatic arthritis	2 (3.1%)
Serum total calcium (mg/dl)	
Mean \pm SD	9.9 ± 0.5
Min-Max	7.6-10.9
Serum total phosphorus (mg/dl)	
Mean \pm SD	4.7 ± 0.8
Min-Max	2.7-6.7
Serum parathyroid hormone (ng/dl)	
Mean \pm SD	33.9 ± 16.4
Min-Max	7-84
25 (OH) Vit D3 (ng/dl)	
Mean \pm SD	17.2 ± 11.6
Min-Max	2.4-56
ESR	
Mean \pm SD	15.8 ± 6.2
Min-Max	5-30
CRP	
Positive	8 (12.5%)
Negative	56 (87.5%)

25 (OH) Vit D3, 25-hydroxycholecalciferol and vitamin D3; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; PASI, Psoriasis Area and Severity Index; SD, standard deviation.

A total of 17 male patients (50%) and 11 female patients (36.7%) had osteopenia. Six male patients (17.6%) and two female patients (6.7%) had osteoporosis. In these cases, there was no significant difference between the men and women ($p = .114$).

The Pearson correlation coefficient demonstrated a moderate inverse relationship between age and T score of the femoral neck and lumbar spine ($r = -.419$ and $-.406$, respectively), which was significant in both cases ($p = .001$). Table 2 shows the average density of bone mass in patients by age and sex.

No significant correlation was observed between BMI and T score of the lumbar spine and femoral neck ($p = .083$ and $p = .274$, respectively). The mean BMI of patients with osteopenia or osteoporosis also had no significant difference when compared with the BMI of health subjects ($p = .382$).

The mean T score of the femoral neck and lumbar spine in patients who smoke was lower than that of healthy subjects (mean difference, 0.35 and 0.63, respectively) although these differences were not statistically significant ($p = .413$ and $p = .124$, respectively). In addition, no significant differences were observed in the prevalence of smoking among osteoporotic, osteopenic, and normal subjects on the basis of BMD ($p = .572$).

Furthermore, no significant correlation was observed between disease duration and T score of the femoral neck and lumbar spine ($p = -.133$ and $p = .150$, respectively) and there was no statistically significant difference between the mean disease duration in patients with osteoporotic, osteopenic and normal BMD ($p = .859$).

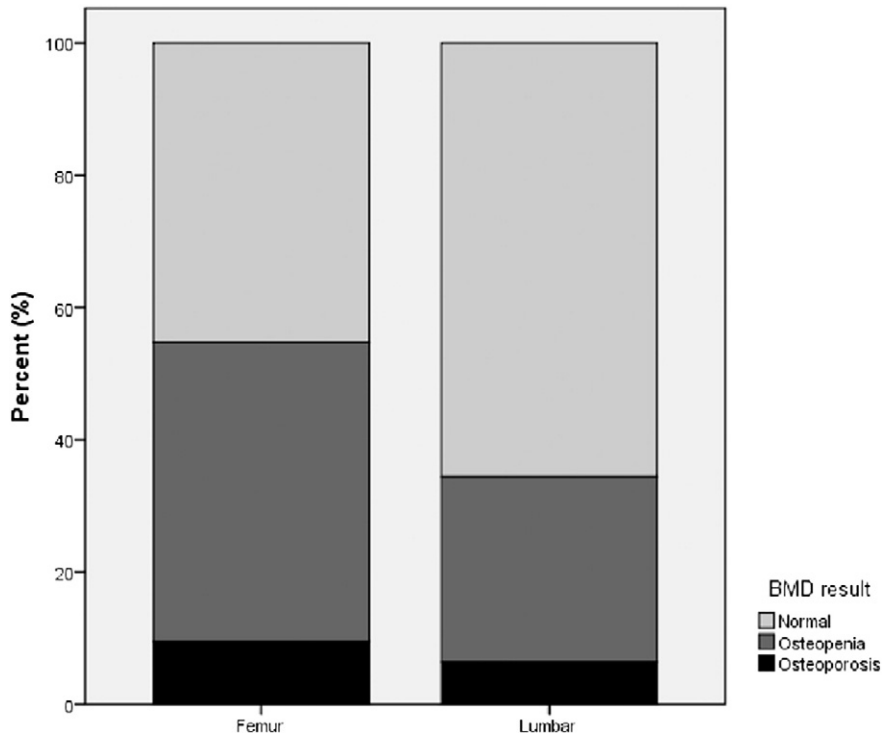


Fig. 1. Prevalence of osteoporosis and osteopenia in patients' femoral neck and lumbar spine.

Although there was no statistically significant relationship between PASI and T scores of the femoral neck ($p = .596$), a correlation was observed between PASI and T scores of the lumbar spine, which was positive and weak but significant ($r = .269, p = 0.03$). A significant difference was not observed between PASI scores of patients with osteoporotic, osteopenic, and normal BMD ($p = .159$).

With regard to inflammatory markers and cytokines, there was no significant correlation between ESR and T score of the femoral neck or lumbar spine ($p = .230$ and $p = .844$, respectively) and no significant difference was observed in the ESR of patients with an osteoporotic, osteopenic, or normal BMD ($p = .473$).

No significant difference was observed about the mean T score of the femoral neck and lumbar spine in patients with positive or negative CRP levels ($p = .589$ and $p = .608$, respectively). The prevalence

of positive CRP levels among patients with osteoporotic, osteopenic, and normal BMD was not different ($p = .520$).

During the investigation, no significant correlation between serum total calcium and T score of the femoral neck and lumbar spine ($p = .780$ and $p = .053$, respectively) was found. No difference in serum calcium levels between patients with osteoporotic, osteopenic, and normal BMD was observed ($p = .537$).

Serum phosphorus and bone density of the femoral neck and lumbar spine were not correlated ($p = .965$ and $p = .785$, respectively) and phosphorus serum levels among patients with osteoporotic, osteopenic, and normal BMD did not differ ($p = .920$).

A significant relationship between the level of parathyroid hormone and T score of the lumbar spine or femoral neck was not observed ($p = .816$ and $p = .785$, respectively) and the hormone levels

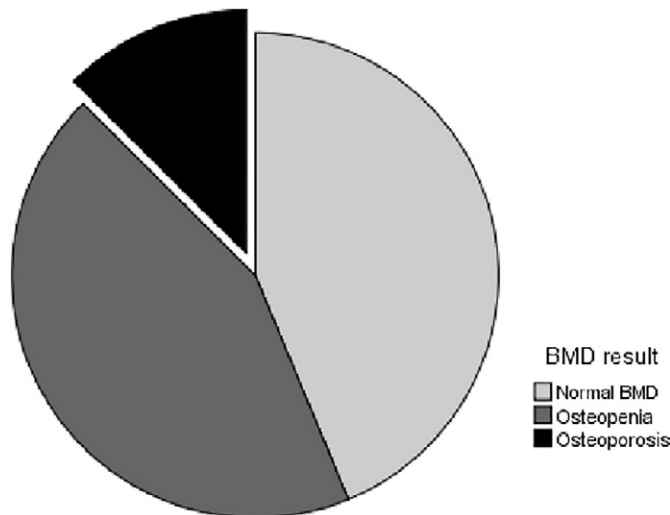


Fig. 2. Prevalence of osteoporosis and osteopenia in patients with psoriasis.

Table 2
Mean bone mineral density on the basis of age and sex

Age group	T score Femur		T score Lumbar	
	Male Patients (n = 34)	Female Patients (n = 30)	Male Patients (n = 34)	Female Patients (n = 30)
<20 years	-0.84 (1)	-0.10 (2)	-0.82 (1)	-0.74 (2)
20-29 years	-0.16 (3)	-0.66 (4)	-0.26 (3)	0.13 (4)
30-39 years	-0.56 (6)	0.02 (4)	0.06 (6)	0.53 (4)
40-49 years	-1.1 (14)	0.74 (13)	-0.74 (14)	0.40 (13)
50-59 years	-1.64 (7)	-1.21 (5)	-1.30 (7)	-0.93 (5)
60-69 years	-2.33 (2)	-3.68 (1)	-1.16 (2)	-0.60 (1)
≥70 years	-3.13 (1)	-1.55 (1)	-1.36 (1)	-1.59 (1)

between patients with osteoporotic, osteopenic, and normal BMD showed no significant difference ($p = .671$).

Finally, the levels of 25 (OH) and Vit D3 did not differ statistically significant with regard to T score of the femoral neck or lumbar spine ($p = .953$ and $p = .172$, respectively) and vitamin D levels were not significantly different between patients with osteoporotic, osteopenic, and normal BMD ($p = .636$).

Table 3 demonstrates the different variables that affect the correlation coefficient of the femoral neck and lumbar spine's T score. Table 4 shows the frequencies of these factors in patients with osteoporotic, osteopenic, and normal BMD.

Discussion

After observation of the similarities between cytokines that affect patients with psoriasis and osteoporosis, the theory of a probable relationship between these two entities has strongly emerged (Kastelan et al., 2006). The present study evaluated patients with psoriasis with regard to bone density and showed a decreased BMD, especially in men, although not statistically significant. Unfortunately, due to the lack of a control group, it was not possible to compare the results with healthy controls. However, when using the results of a national study on the general population of Iran and after matching the age and sex categories, we could determine that the BMD of patients with psoriasis on the basis of T scores shows a reduction. For example, in our study, the mean T scores of the femoral neck in 10 male patients of age 50 to 59 years old and 7 female patients of the same age group were -1.64 and -1.2, respectively. In a national Iranian study by Larijani et al. on osteoporosis in male and female patients of age 50 to 59 years old, these rates were 0.91 and 0.96, respectively (Bagheri et al., 2011; Larijani et al., 2004, 2005). These T scores are also available for other sex- and age-matched groups in Iran in studies on the femoral neck and lumbar spine (Bagheri et al., 2011; Larijani et al., 2004, 2005). It appears that the

amount of reduction in the bone density of patients with psoriasis compared with age- and sex-matched groups in a national study is not statistically significant and not in the range of osteoporosis.

In a large meta-analysis study on 21 related studies that analyzed 9657 cases, the prevalence of femoral neck and lumbar spine osteoporosis in Iran was approximately 18% (Bagheri et al., 2011), which was near the results of our study but not comparable because 12.5% of our patients had osteoporosis in at least one of these two areas.

Other studies on the association between psoriasis and BMD showed conflicting results. A study by Millard et al. (2001) on the Z score of patients with chronic plaque-type psoriasis compared with healthy controls showed no significant difference. Also, Balato et al. (2012) examined the prevalence of osteoporosis among patients with psoriasis in Italy and did not report a significant difference in BMD with the healthy population of Italy. One study (Keller et al., 2013) showed that patients with osteoporosis had a higher prevalence of psoriasis compared with patients without osteoporosis (1.5% vs. 0.87%). The prevalence of osteoporosis in Iranian studies has been reported generally lower than those in European and American studies (Larijani et al., 2004) but our study demonstrated a higher prevalence of osteoporosis in patients with psoriasis than in other studies (e.g., 5% in Balato et al., (2012) and 12.5% in our study), which shows the importance of demographic and climatic factors as well as races.

Overall, in most studies, women are at higher risk for osteoporosis, bone density loss, and fracture (Bagheri et al., 2011; Larijani et al., 2004) but in our study, a BMD reduction in men with psoriasis was higher than in women with psoriasis with 17.6% of men and 6.7% of women showing osteoporosis. The study by Dreier et al. (2009) also showed that the prevalence of osteoporosis in men with psoriasis was higher than that in women and even after controlling for confounding variables, osteoporosis had a higher and stronger association with the male sex (odds ratio [OR]: 1.35 in men; 0.90 in women).

Table 3
Pearson's correlation coefficient of the femoral neck and lumbar spine's T score and risk factors of osteoporosis

	Femur T score	Lumbar T score	Age	BMI	Disease Duration	PASI	Calcium	Phosphorus	Parathyroid Hormone	25(OH) Vit D3	ESR
Femur T score	1										
Lumbar T score	.665 ^a	1									
Age	-.419 ^a	-.406 ^a	1								
BMI	.219	.139	.203	1							
Disease Duration	-.133	.150	-.120	.057	1						
PASI	.068	.269	-.097	.079	.198	1					
Calcium	.040	.273	-.324 ^a	-.022	.040	.027	1				
Phosphorus	.006	.039	-.200	.069	-.146	-.013	.547 ^a	1			
Parathyroid Hormone	-.033	-.046	.137	-.043	-.021	-.056	-.260	-.224	1		
25(OH) Vit D3	-.008	-.194	.159	.150	-.101	-.120	.334 ^a	.103	-.284 ^a	1	
ESR	-.171	-.028	.137	-.161	-.049	.191	.004	.007	-.108	-.020	1

25 (OH) Vit D3, 25-hydroxycholecalciferol and vitamin D3; BMI, body mass index; ESR, erythrocyte sedimentation rate; PASI, Psoriasis Area and Severity Index.

^a p value < .05.

Table 4

Frequencies of factors that affect the bone density in patients with psoriasis and osteoporosis, osteopenia, and normal BMD

	Osteoporosis	Osteopenia	Normal BMD	p value
Number (%)	8 (12.5%)	28 (43.8%)	28 (43.8%)	
Age	57.2 ± 20.8	47.5 ± 16.1	36.5 ± 12.8	.002
Sex				
Male	6 (17.6%)	17 (50%)	11 (32.4%)	.114
Female	2 (6.7%)	11 (36.7%)	17 (56.7%)	
BMI	25.1 ± 3.3	26.9 ± 3.6	27.8 ± 6.2	.382
Activity	1 (5.6%)	10 (55.6%)	7 (38.9%)	.387
Cigarette smoking	2 (15.4%)	7 (53.8%)	4 (30.8%)	.572
Disease duration	8 ± 13.2	7.7 ± 9.1	6.7 ± 4.3	.859
PASI	2.9 ± 2.1	6.5 ± 4.1	5.3 ± 5.5	.159
Calcium	9.6 ± 1.4	9.9 ± 0.4	9.8 ± 0.4	.537
Phosphorus	4.6 ± 1.6	4.5 ± 0.8	4.4 ± 0.8	.920
Parathyroid Hormone	41.0 ± 11.0	33.1 ± 14.1	33.9 ± 19.8	.671
25(OH)Vit D ₃	19.8 ± 8.1	18.3 ± 13.4	15.4 ± 9.7	.636
ESR	14.7 ± 4.6	16.8 ± 5.4	14.7 ± 7.3	.473
CRP	2 (25%)	3 (37.5%)	3 (37.5%)	.520

25(OH)Vit D₃, 25-hydroxycholecalciferol and vitamin D₃; BMD, bone mineral density; BMI, body mass index; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; PASI, Psoriasis Area and Severity Index.

In the study by Hofbauer et al. (2006), 10.2% of men with psoriatic arthritis showed osteoporosis but this rate among women was only 1.75%. This can be explained perhaps by the fact that osteoporosis in women is usually due to an estrogen deficiency and postmenopausal women are generally at a higher risk for osteoporosis. In contrast, osteoporosis in men is usually caused by an underlying systemic disorder and much more a limitation of physical activities. In psoriasis, a great amount of inflammatory cytokines and immunological events can be an underlying cause of osteoporosis and women with psoriasis are typically at premenopausal age (Dreier et al., 2009).

The findings by Hofbauer and Dreier are comparable with those of our study with regard to different sex predilection of bone density loss in patients with psoriasis. In this study, none of the underlying factors (nutritional factors such as intake of calcium, phosphorus and vitamin D₃, personal habits such as daily exercise and smoking) showed a significant difference in the association of psoriasis and osteoporosis although the mean T score of the femoral neck and lumbar spine in patients who smoked was lower. In the study by Balato et al. (2012), patients with psoriasis and osteoporosis or osteopenia also had no significant difference with regard to these risk factors.

Logically, the greater severity of the skin involvement and the longer exposure to the inflammatory cytokines causes the higher degree of bone loss and higher risk of developing osteoporosis; however, our study found no association between disease duration and/or PASI score with the prevalence of osteopenia and osteoporosis in patients with psoriasis. The reduction of bone density in patients with psoriasis is associated with the number of involved joints. ESR and CRP levels are a sign of underlying inflammation but these factors did not show any increase in patients with psoriasis and osteoporosis comparable with the results of the Dreier and Hofbauer studies (Dreier et al., 2009; Hofbauer et al., 2006).

Limitations and recommendations

The most important limitation of this study was a lack of any age- and sex-matched healthy controls. We also did not exclude patients with older ages such as menopausal women, patients with a higher BMI, or smokers who could be confounders of our study. It is highly recommended that other, larger, and well-designed controlled studies are conducted with more focus on probable confounders.

Conclusion

In this study, patients with psoriasis had decreased BMD, which was more significant in men even though the prevalence of osteoporosis in patients showed no statistically significant difference with the health population of Iran (Bagheri et al., 2011; $p = .114$). However, the design of well-controlled studies that are matched for age, sex, and race are essential. Screening studies for osteoporosis should be considered in patients with psoriasis and especially in men with severe and widespread disease who also have other metabolic disorders.

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