Bone Mineral Density and Clinical Hand Osteoarthritis in Elderly Men and Women: The Rancho Bernardo Study

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ABSTRACT. ***Objective.*** Many studies have found increased bone mineral density (BMD) in patients with osteoarthritis (OA). As a result, clinicians may not consider osteoporosis in patients with OA. We examined the relation between hand OA and BMD levels among 1779 community-dwelling, ambulatory white adults aged 50–96 years.

Methods. BMD was measured by dual energy x-ray absorptiometry at the hip, lateral and anteroposterior (AP) lumbar spine, and total body. Both hands of each subject were systematically examined for bony enlargement, swelling, and deformity.

Results. Using the American College of Rheumatology criteria for epidemiologic studies, the clinical diagnosis of hand OA was made in 6.6% of men and 14.5% of women. In women, BMD measurements adjusted for age, body mass index, smoking, alcohol, exercise, and current estrogen use were significantly lower only at the hip in those with versus those without hand OA. In contrast, men with hand OA had higher multiply-adjusted mean BMD levels at all sites compared to those without hand OA. These differences were statistically significant only at the AP spine; the absent difference for lateral spine BMD suggests that degenerative changes may explain the higher AP spine BMD levels. Patterns in both men and women were similar in those with isolated hand OA or hand OA in the presence of knee or hip OA.

Conclusion. OA was not associated with increased BMD levels in men or women. Contrary to expectations the only significant difference was that women with hand OA had lower hip BMD. Thus evaluation for osteoporosis should not be overlooked in women with hand OA. (J Rheumatol 2002;29:1467–72)

Key Indexing Terms:
HAND OSTEOARTHRITIS
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In 1972, Foss and Byers observed the absence of osteoarthritic changes in patients with osteoporosis who sustained hip fractures[1]. Several studies have shown a positive association between radiographic evidence of large joint osteoarthritis (OA) and bone mineral density (BMD) at the hip, lumbar spine, total body, or distal radius[2-6]. However, these findings have not been consistent in all studies and gender differences have been observed[7-9].

Studies have also reported conflicting results in persons with hand OA. Three longitudinal studies reported no association of hand OA with bone mass at appendicular sites in men or women[10-12]. One study of women ages 45 to 64 found a significant positive association of hand OA with lumbar spine and femoral neck BMD; however, other studies of axial sites found no association[2,13]. Two large epidemiologic studies[3,13] reported a significant positive association of hand OA and total body BMD, while a small study found no association[2].

All the above studies used radiographic findings to define OA. Many older persons have radiographic evidence of hand OA, but most are asymptomatic. The National Health Examination Survey reported radiographic changes indicative of hand OA in older men and women: 63% ages 55–64, 74.5% ages 65–74, and 84.5% ages 75–79[14]. The present study used symptoms and clinical findings for case definition of hand OA based on the American College of Rheumatology (ACR) standard criteria for epidemiologic studies[15]. We examined the relation between clinically defined hand OA and BMD levels among 1779 community-dwelling, ambulatory men and women aged 50–96 years.

MATERIALS AND METHODS

From May 1992 to December 1996, 1779 ambulatory older white adults (698 men, 1081 women) aged 50–96 years from a geographically defined middle-class community, Rancho Bernardo, California, participated in a study of osteoporosis. The University of California Institutional Review Board approved the study. At the clinic visit, all participants completed a

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standardized questionnaire that included medical history, health habits, dietary supplements, and medications. Self-reported arthritis was ascertained from the question: "Have you ever been told by a doctor that you had arthritis which requires medicine or limits activity?" Alcohol use was categorized as drinking 3 or more days per week, and regular exercise was defined as exercise 3 or more times per week. Reported aspirin and nonsteroidal antiinflammatory drug use was validated by the clinic nurse, who examined all pills and prescriptions brought to the clinic for that purpose.

Height and weight were measured with subjects wearing light clothing and no shoes. As a measure of obesity, body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters (kg/m^2). BMD (g/cm^2) was measured at the hip, anteroposterior (AP) and lateral lumbar spine, and total body by certified radiology technicians using dual energy x-ray absorptiometry [Hologic QDR-1000 (hip and AP spine) and QDR-2000 (lateral spine, total body), Bedford, MA, USA]. Scans were standardized daily against a calibration phantom; the precision error was ≤ 1.5% for the hip, and ≤ 1.0% for the spine. Osteoporosis was defined by BMD levels, according to the World Health Organization (WHO) criteria, as ≥ 2.5 standard deviations (SD) below young adult mean[16].

Two trained nurse examiners systematically evaluated 16 joints of each hand in all subjects for hard bony tissue enlargement, swelling, and joint deformity. The joints included the distal interphalangeal (DIP), proximal interphalangeal (PIP), metacarpophalangeal (MCP), first carpometacarpal (CMC), radioscaphoid, ulnar styloid-carpal area, and the mid-dorsal wrist. The algorithm for diagnostic criteria of symptomatic hand OA developed by the ACR as standard criteria for epidemiologic studies[15] was used for case definition, as shown in Table 1. The examiners also evaluated each knee and hip using the ACR clinical criteria alone for classification of OA of the knee and hip[17,18]. In a small subset of subjects (n = 13) who were examined by both a rheumatologist (MW) and the trained nurse examiners, concordance of OA diagnosis was 85%.

All analyses were performed using the Statistical Analysis System (SAS Institute Inc., Cary, NC, USA). Age adjusted differences in proportions were calculated using the Mantel-Haenszel statistic with a 2 tailed test of significance (alpha = $p \leq 0.05$). Analyses were sex-specific and stratified by the presence of hand OA. All BMD levels were normally distributed, making transformations unnecessary. Analysis of covariance was calculated to determine differences in mean BMD levels by hand OA categories while controlling for age, BMI, smoking, alcohol, and exercise for the total sample, with the addition to the model of current estrogen use for women only.

RESULTS

Eleven percent of these older adults had OA of the hand defined by ACR criteria. Hand OA was twice as common in women than men (14.5% vs 6.6%). As shown in Table 2, both men and women with hand OA were significantly older than those without hand OA: mean age for men was 78.7 versus 70.3 years, respectively ($p < 0.001$), and for women 78.1 versus 67.8 years ($p < 0.001$). Mean BMI for all women was < 25 and similar by OA status. The mean BMI was lower in men with hand OA compared to men without hand OA (24.9 vs 26.4 kg/m^2; $p < 0.01$). There were no significant differences in health habits or medication use by OA status in men or women, except that men with hand OA were significantly less likely to drink alcohol 3 or more times per week.

Table 1. ACR algorithm for clinical hand OA.

1. Hand pain, aching, or stiffness
and
2. Hard tissue enlargement of 2 or more of 10 selected joints
and
3. Fewer than 3 swollen MCP joints
and either
4a. Hard tissue enlargement or 2 or more DIP joints
or
4b Deformity of 2 or more of 10 selected joints

The 10 selected joints are the second and third distal interphalangeal (DIP), the second and third proximal interphalangeal (PIP), and the first carpometacarpal (CMC) joints of both hands. The second and third DIP joints may be counted in both item 2 and 4a. This classification method yields a sensitivity of 92% and a specificity of 98%. MCP: metacarpophalangeal.

Both men and women with hand OA were 2 times as likely to report a history of arthritis at any site in comparison to those without hand OA. Women with hand OA reported arthritis nearly twice as often as men with hand OA (44.6% vs 24.4%). Using ACR defined criteria based on examination of the hip and knee, similar proportions of women and men with hand OA also had hip or knee OA (women 38.9% and men 37.0%). Both men and women with hand OA were twice as likely to be classified as having knee or hip OA compared to men and women without hand OA.

Osteoporosis at the total hip, defined as BMD ≥ 2.5 SD below the young adult mean, was present in roughly one-fifth of the women with hand OA and one-quarter of those without hand OA. About one-tenth of men with and without hand OA had osteoporosis at the hip.

As shown in Table 3, women with hand OA had lower age adjusted BMD levels than women without hand OA at all sites, and the differences were significant at the femoral neck, total hip, and lateral lumbar spine. After controlling for age, BMI, smoking, alcohol, exercise, and current estrogen use, women with hand OA still had significantly lower BMD levels at the femoral neck and total hip. In contrast, men had higher age adjusted BMD levels at all sites in comparison to men without hand OA, but these differences were not significant at any site (Table 4). However, after adjusting for age, BMI, smoking, alcohol, and exercise, mean BMD levels were significantly higher only at the AP spine in men with hand OA, compared to men without hand OA.

To examine isolated hand OA, men and women with hand OA were stratified by presence or absence of knee or hip OA. No mean BMD level in men or women differed significantly between those with isolated hand OA or hand OA in the presence of knee or hip OA (data not shown).

Data for women stratified by current estrogen status are shown in Table 5. Women taking estrogen had higher BMD levels at all sites, but there was no difference in BMD between current estrogen users by hand OA status.

DISCUSSION

As expected, women were more likely than men to have hand OA: about one in 7 women and one in 15 men met the

Table 2. Age adjusted characteristics for men and women by clinical hand OA status.

Variable	Women, n = 1081		Men, n = 698	
	OA+, n = 157	OA–, n = 924	OA+, n = 46	OA–, n = 652
Age, yrs, mean (95% CI)	78.1 (69.3, 86.9)	67.8*** (64.1, 71.5)	78.7 (75.6, 81.8)	70.3*** (69.5, 71.1)
BMI, kg/m^2, mean (95% CI)	24.5 (23.8, 25.2)	24.9 (24.6, 25.2)	24.9 (23.9, 25.9)	26.4* (26.1, 26.7)
Height, in, mean (95% CI)	62.8 (62.4, 63.2)	63.2 (63.0, 63.4)	68.5 (67.7, 69.3)	68.8 (68.6, 69.0)
		Proportions		
Current smokers	6.4	7.8	4.4	6.6
Alcohol 3+ times per week	40.8	38.1	52.5	67.4*
Exercise 3+ times per week	72.0	67.3	82.2	75.2
Current estrogen use	38.2	44.7	—	—
Aspirin use	26.4	29.9	43.5	44.9
NSAID use	30.2	24.1	28.3	21.6
Self-reported OA	44.6	19.9***	24.4	13.4*
Knee or hip OA†	38.9	20.4***	37.0	18.1**
Hip osteoporosis††	21.3	26.1	8.7	10.9

* $p < 0.05$, **$p < 0.01$, *** $p < 0.001$ (reference group = sex-specific OA+).
† ACR defined criteria for knee or hip OA. †† Total hip BMD ≥ 2.5 SD below young adult mean.

Table 3. Adjusted BMD by clinical hand OA status in women.

Measurement Site	Women	
	OA+, n = 157	OA–, n = 924
Femoral neck		
Age	0.638	0.670**
Age and BMI	0.640	0.671**
All covariates†	0.642	0.670**
Total hip		
Age	0.779	0.809*
Age and BMI	0.781	0.809*
All covariates	0.784	0.809*
Lumbar spine (AP)		
Age	0.919	0.927
Age and BMI	0.923	0.926
All covariates	0.927	0.925
Lumbar spine (lateral)		
Age	0.594	0.618*
Age and BMI	0.595	0.618*
All covariates	0.597	0.618
Total body		
Age	0.941	0.960
Age and BMI	0.942	0.959
All covariates	0.947	0.961

* $p < 0.05$, ** $p < 0.01$ (reference group = sex-specific OA+). †All covariates = age, BMI, smoking, alcohol, exercise, and current estrogen use. Hologic 1000 used for femoral neck, total hip and AP lumbar spine; Hologic 2000 used for total body and lateral lumbar spine.

Table 4. Adjusted BMD by clinical hand OA status in men.

Measurement Site	Men	
	OA+, n = 46	OA–, n = 652
Femoral neck		
Age	0.782	0.767
Age and BMI	0.794	0.766
All covariates†	0.785	0.767
Total hip		
Age	0.972	0.960
Age and BMI	0.983	0.959
All covariates	0.984	0.959
Lumbar spine (AP)		
Age	1.127	1.079
Age and BMI	1.144	1.077*
All covariates	1.139	1.077*
Lumbar spine (lateral)		
Age	0.728	0.693
Age and BMI	0.733	0.693
All covariates	0.733	0.692
Total body		
Age	1.141	1.110
Age and BMI	1.150	1.109
All covariates	1.148	1.111

*$p < 0.05$ (reference group = sex specific OA+). † All covariates = age, BMI, smoking, alcohol, and exercise. Hologic 1000 used for femoral neck, total hip and AP lumbar spine; Hologic 2000 used for total body and lateral lumbar spine.

criteria for ACR defined hand OA. However, these numbers are substantially lower than OA defined radiographically[14]. Contrary to expectations, Rancho Bernardo women with hand OA had lower mean BMD levels at all sites than women without hand OA. Differences at the hip sites remained significant after adjustment for age, BMI, smoking, alcohol, exercise, and current estrogen use. In contrast, Rancho Bernardo men with hand OA had higher BMD levels than men without hand OA; multiply-adjusted differences were statistically significant only at the AP spine. Given the absent difference for lateral spine BMD, the BMD levels of the AP lumbar spine may have been

Table 5. Multiply-adjusted† BMD by clinical hand OA status stratified by estrogen use in women.

Measurement Site	Women OA+, n = 157	Women OA–, n = 924
Femoral neck		
No estrogen	0.646	0.643
Current estrogen	0.677	0.696
Total hip		
No estrogen	0.780	0.776
Current estrogen	0.834	0.842
Lumbar spine (AP)		
No estrogen	0.892	0.887
Current estrogen	0.989	0.972
Lumbar spine (lateral)		
No estrogen	0.587	0.594
Current estrogen	0.634	0.645
Total body		
No estrogen	0.940	0.920
Current estrogen	0.988	1.008

† All covariates = age, BMI, alcohol, exercise, smoking. Hologic 1000 used for femoral neck, total hip and AP lumbar spine; Hologic 2000 used for total body and lateral lumbar spine.

falsely elevated due to degenerative disease of the posterior elements, including hypertrophy of the spinous processes, osteophytes, degenerated discs, and extraosseous calcifications[19,20]. Overall, the results for the Rancho Bernardo men were consistent with an absence of association of hand OA and BMD. Although nearly 40% of both men and women with hand OA also had large joint OA, mean BMD levels were not significantly different between those with isolated hand OA versus those with hand OA and knee or hip OA. Therefore, the axial BMD levels were not likely due to arthritic immobility.

This is the first study to report significantly lower hip BMD levels in women with hand OA. The Baltimore Longitudinal Study of Aging[10,11] found no association of bone mass (percentage cortical area of the second left metacarpal in men and women and the distal radius BMD in women) and the presence or severity of hand OA. In 79-year-old Swedes, no correlation was found between hand OA and decreased bone mineral content at the heel[12]. In the Chingford Study[4], women with radiographic OA at any site had higher BMD at the AP lumbar spine than controls; and at the femoral neck, BMD was significantly higher in those with only thumb base, knee, or lumbar spine OA. In contrast, an EPIDOS study of 300 women found no association of radiographic hand OA with BMD at the hip, but did find a positive correlation with total body BMD[13]. Also in premenopausal women from the Michigan Bone Health Study[3], hand OA was positively associated with total body BMD.

Over one-fifth of Rancho Bernardo women with hand OA had osteoporosis at the hip as defined by the WHO criteria, and therefore were at high risk for fractures. These results are supported by data from the Tecumseh Community Health Study[21]. Using measures of metacarpal bone mass and OA based on hand radiographs, women with hand OA had higher bone mass at baseline, but after 20 years had more bone loss than normal subjects. Other studies have directly evaluated risk of fracture in the presence of OA. In the Study of Osteoporotic Fractures, women with hand OA did not have significantly lower osteoporotic fracture risk despite significantly higher BMD levels compared with controls[22]. These findings were thought to be due, in part, to increased fall risk. In an assessment of fractures in the EPIDOS study, Marcelli and associates[13] found that elderly women with a high hand radiographic score for OA were unlikely to report a history of osteoporotic fractures; however, women with a history of hip fractures were not included in this substudy. In the Chingford study of younger women, ages 45 to 64 years, no association was observed with fractures and hand OA[23].

The reason for conflicting data most likely represents radiographic versus clinical definition of hand OA. Other factors that may play a role include multijoint versus isolated hand OA, hormonal influences, or misdiagnosis of hand OA. Hand radiographs appear to overdiagnose OA, since practically all elderly men and women are found to have radiographic evidence of hand OA[14]. In contrast to studies of hand OA and osteoporosis that used radiographs, the ACR clinical criteria, which incorporate symptoms and physical findings, were used to classify OA status in our study. The ACR clinical criteria[15] were derived from 199 patients with hand pain, half of whom had hand OA, and yielded a sensitivity of 92% and specificity of 98%. Radiographic findings were less sensitive and less specific for the diagnosis of hand OA. Therefore, differences in case definitions for hand OA may explain different results.

Hand OA may be an isolated disorder or a subset of polyarticular disease. The presence of hand OA has been described as an indicator for a systemic tendency to OA at the hips and knees[24,25]. In the Baltimore Longitudinal Study of Aging[26], bilateral disease involving one or more digits of each hand was significantly associated with knee OA in both men and women. The Chingford Study[27,28] reported that multiple joint involvement in hand OA represented a generalized form of OA. In several studies, patients with large joint OA had increased appendicular and axial bone mass compared with normal controls[6,7,9,29]. However, 2 small studies[30,31] using forearm measurements found women with generalized OA had levels similar to controls after adjustment for covariates. Although nearly 40% of the Rancho Bernardo men and women with hand OA had clinical evidence of knee or hip OA, their BMD levels at all sites were like those observed with isolated hand OA. Only a few studies evaluated the presence of large joint involvement, therefore comparisons of a heterogeneous disorder may have contributed to conflicting results.

Some women rapidly develop hand OA at the time of menopause, suggesting a role for estrogen deficiency[32]. If low estrogen levels are related to OA and osteoporosis, then decreased BMD levels should be associated with high prevalence of OA. However, the role of estrogen in OA has been studied, with conflicting results. In experimental animals, estrogen administration suppressed collagen syntheses through an estrogen receptor mechanism and induced OA[33,34]. In postmenopausal women with knee OA, higher synovial estradiol levels and estrogen receptor binding were found in comparison to women with no OA[35]. In the Study of Osteoporotic Fractures, no association of radiographic hand OA and serum levels of estrone, testosterone, or androstenedione was found[36]. However, some epidemiologic studies report lower prevalence of OA in women who take estrogen than women not taking estrogen[37-40]. The majority of the studies on BMD and hand OA did not report use of estrogen. In Rancho Bernardo, a lower proportion of women with hand OA were current estrogen users in comparison to women without hand OA, but the difference was not statistically significant. Estrogen use also did not explain the gender differences in the relation between hand OA and BMD or the low hip BMD in women with hand OA observed in this study.

The ACR clinical criteria we used have been recommended for uniform reporting of hand OA in epidemiological studies[15]. Because all participants in this study were not seen by a rheumatologist, we cannot exclude misdiagnosis of hand OA. However, the ACR clinical criteria were found to have high interrater agreement between the rheumatologist and the nurse examiners. In contrast, comparison of the physician's "gestalt" diagnosis (without careful examination of all joints) with the diagnosis using ACR clinical criteria yielded only 43% agreement. Therefore, the systematic examination of all the hand joints was more likely to correctly identify persons with hand OA.

In summary, clinically defined hand OA was present in 14.5% of women and 6.6% of men in this population of ambulatory older white adults. Previous studies have shown that men and women with hand OA do not have greater appendicular bone mass, but may have higher hip, spine, or total body BMD. In contrast, this study found an inverse association of clinical hand OA with the hip BMD in women only. Men with clinical hand OA had increased BMD levels at the AP spine, which were likely due to artifacts since there was no apparent difference at the lateral spine. The associations or lack of associations were similar in the presence or absence of large joint OA. By WHO criteria, nearly one in 10 men and one in 5 women with hand OA had osteoporosis at the hip. These findings based on hand OA defined by the ACR clinical criteria[15] may be more clinically meaningful, in contrast to other studies using radiographic defined hand OA. Therefore, these findings suggest that women with clinical hand OA should be considered to be at risk for osteoporosis, and evaluation of bone mass should not be overlooked.

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