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Appendicular bone mass and knee and hand osteoarthritis in Japanese women: a cross-sectional study

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Abstract

Background: It has been reported that there is an inverse association between osteoarthritis (OA) and osteoporosis. However, the relationship of bone mass to OA in a Japanese population whose rates of OA are different from Caucasians remains uncertain.

Methods: We studied the association of appendicular bone mineral density (second metacarpal; mBMD) and quantitative bone ultrasound (calcaneus; stiffness index) with knee and hand OA among 567 Japanese community-dwelling women. Knee and hand radiographs were scored for OA using Kellgren-Lawrence (K/L) scales. In addition, we evaluated the presence of osteophytes and of joint space narrowing. The hand joints were examined at the distal and proximal interphalangeal (DIP, PIP) and first metacarpophalangeal/carpometacarpal (MCP/CMC) joints.

Results: After adjusting for age and body mass index (BMI), stiffness index was significantly higher in women with K/L scale, grade 3 at CMC/MCP joint compared with those with no OA. Adjusted means of stiffness index and mBMD were significantly higher in women with definite osteophytes at the CMC/MCP joint compared to those without osteophytes, whereas there were no significant differences for knee, DIP and PIP joints. Stiffness index, but not mBMD, was higher in women with definite joint space narrowing at the CMC/MCP joint compared with those with no joint space narrowing.

Conclusions: Appendicular bone mass was increased with OA at the CMC/MCP joint, especially among women with osteophytes. Our findings suggest that the association of peripheral bone mass with OA for knee, DIP or PIP may be less clearcut in Japanese women than in other populations.

Background

Osteoarthritis (OA) and osteoporosis are both common conditions in elderly women [1,2]. It would be anticipated that the conditions frequently coexist due to their high prevalence, but some studies have suggested that there is an inverse association between the occurrence of OA and osteoporosis [3–12]. Increased bone mass has been proposed as a risk factor for OA independent of age and other factors, because higher bone mass may increase bone stiffness and thereby increase loading of articular cartilage and lead to cartilage damage [13,14]. Alternatively, OA and osteoporosis may only be indirectly related through weight, mechanical stress, genetic factors, or other factors that affect both bone mass [15,16] and the risk of OA [17,18].

Recent reviews reported that bone mass or bone mineral density (BMD) (measured with various techniques at different skeletal sites) was significantly increased in the OA cases compared with age- and sex-matched controls [19–22]. A recent large epidemiologic study showed higher bone density at both central (hip and lumbar spine) and peripheral (radius and calcaneus) sites in elderly women with moderate-severe radiographic grades of hip OA after adjusting for age, weight and other anthropometric characteristics [11]. Population-based epidemiologic studies have shown that women with radiographic changes of knee [5,9,12,23] or hand OA [5,10,12] have increased bone mass after adjustment for age and other covariates, compared to those without OA.

Most previous studies reported the association of OA with bone mass among Caucasian populations, and there are few data among Asian populations. One study reported that Japanese patients with knee OA had greater bone mass at the hip and lumbar spine compared to age and weight matched controls [24]. We reported elsewhere that, compared to Caucasians, Japanese women appear to have a substantially higher prevalence of knee OA, but much lower prevalence of hand OA except distal interphalangeal (DIP) joint [25]. This suggests that the prevalence and/or types of risk factors for OA may differ between Japanese and Caucasian populations.

Although BMD declines throughout the skeleton with age, there is significant variation between skeletal sites, even within an individual. Therefore, we hypothesized that bone measurements at the heel might be more strongly related to OA at the knee, since both sites are weight-bearing, whereas hand BMD measurements might be more strongly related to hand OA. Furthermore, it has been suggested that certain features of OA (such as osteophytes) may be reparative in nature, whereas other features (such as joint cartilage damage) are destructive, and may therefore have a different relationship with bone mass at nearby (or distant) skeletal sites. To investigate these issues, as well as the general issue of whether bone density is associated with OA in Japanese, we examined the cross-sectional association between radiographic knee or hand OA and appendicular bone mass at weight-bearing and non-weight-bearing sites among a community-based sample of Japanese women. More specifically, we examined the association between bone mass and different severity levels of radiographically defined knee and hand OA.

Subjects and Methods

The Hizen-Oshima Study is a prospective population-based cohort study of musculoskeletal conditions (i.e., osteoporosis and osteoarthritis). We recruited community-dwelling women aged 40 years or over in Oshima town, Nagasaki prefecture, Japan. The women were identified by the municipal electoral list and contacted through mailings. As of March 31, 1999, the town of Oshima had a population of 5817 (2840 male and 2977 female), in which the population of women aged 40 or over was 2006. The proportion of women aged 40 or over in Oshima (2006/5817 = 34%) was somewhat higher than the national average of 27%, based on the 1995 Census for all of Japan. All women aged 40 or over were invited to participate. The baseline examination was performed at the Oshima Health Center between 1998 and 1999. A total of 586 women (approximately 30% of eligible women) participated in the study. The response rates in the age groups 40–49, 50–59, 60–69, 70–79, and 80 years or over were 10, 28, 45, 39, and 15%, respectively. The low response among younger women may reflect time constraints of work or family, or they may have not been interested in their musculoskeletal health. Low response among the oldest women may reflect difficulty attend the study site because of poor health or lack of transportation. We compared the age distribution of participants vs. non-participants. In total, the mean age of participants (63.9 years) was significantly higher than that of non-participants (61.1 years). Despite having a shipyard in the town, Oshima is a mainly rural (farming/fishery) district. Approximately half of the women who participated in the study continue to grow rice and vegetables by manual labor, sometimes using machinery. All participants were noninstitutionalized, living independently at baseline, and were able to ambulate independently (with or without a cane), and all women except one were able to go up and down stairs. All subjects gave written informed consent before examination. This study was approved by the local Ethics Committee.

Antero-posterior weight-bearing knee radiographs were obtained with the subjects' knees in full extension, according to the protocol by Framingham Osteoarthritis Study [25]. Postero-anterior hand radiographs were obtained with the central ray focused on the 3rd metacarpophalan-

Table 1: Characteristics of the subjects (N = 567).

Characteristic	Mean	SD	Range
Age (years)	64.2	9.6	40–89
Height (cm)	149.8	6.0	129.0–166.5
Weight (kg)	52.4	8.8	31.6–98.8
Body mass index (kg/m^2)	23.3	3.4	15.6–42.8
Stiffness index[a]	70.1	13.3	38–123
mBMD[b] (mmAl)	2.23	0.34	1.41–3.07

a: Stiffness index was measured in 557 women. b: metacarpal bone mineral density

geal (MCP) joint; each hand film was taken separately. Radiographs were graded according to the criteria described by Kellgren and Lawrence (K/L) [26]. In addition, since the K/L system of radiographic grading for OA does not differentiate between osteophytic and joint space narrowing changes of OA [23,27], we separately evaluated the presence of osteophytes and of joint space narrowing for each subject, without regard to the K/L grade; first, we evaluated the osteophytes for all subjects, after that the joint space narrowing. Each joint was scored for the severity of both osteophytes and joint space narrowing, using categories of none (0), questionable (1), or definite (2). Each subject was classified according to the most severe grade within a given joint group for each of the radiographic findings (K/L grade, osteophytes or joint space narrowing). We examined the following joint groups: the knees, the second and third distal interphalangeal (DIP), the proximal interphalangeal (PIP), and the metacarpophalangeal /carpometacarpal (MCP/CMC) joints of the hands. We reported earlier the prevalence of radiographic OA of the knee and hand between Japan and the United States [25]. To standardize readings between the studies, the Japan reader (S.Y.) trained with the primary reader of the Framingham Osteoarthritis Study prior to reading the Japanese films, and used the same atlas and grading scheme. To evaluate interrater reliability for OA grade, we randomly selected 40 subjects from each population and had the Framingham and Japan readers read each set of films. In testing whether OA was present or absent, the kappa statistic was 0.77 ($p < 0.001$) for knee and 0.68 ($p < 0.001$) for hand (combining all joints), indicating good agreement between readers. Intrarater reliability (Kappa) for OA grade was 0.77 for the knee ($p < 0.001$), but was not evaluated separately for the hands. Spearman correlation coefficients between osteophytes and joint space narrowing were 0.59 ($p < 0.001$) for knee, 0.63 ($p < 0.001$) for DIP, 0.38 ($p < 0.001$) for PIP and 0.59 ($p < 0.001$) for MCP/CMC. Our radiograph reader (S.Y.) was blinded to the subject's age, bone mass and anthropometric characteristics.

Quantitative ultrasound of the right calcaneus (heel) bone was determined by measurement of broadband ultrasound attenuation (BUA) and the speed of sound (SOS) using the Achilles ultrasound bone densitometer (Lunar Corp., Madison, WI). Stiffness index, a function of BUA and SOS measurements, was calculated according to the manufacturer's equation. Measurements of the right second metacarpal bone mineral density (mBMD) were obtained from hand radiographs using an optical densitometer, the Bonalyzer II (Teijin Ltd., Tokyo). The reproducibility expressed as coefficient of variation (CV), measured on 5 times consecutively within 1 h with repositioning between each measurement, was 1.71% for stiffness index calculated in 17 healthy volunteers, and 0.56% for mBMD measurements calculated in a random sample of 20 of the subjects.

Height (m) and weight (kg) were measured with the subject in light clothing and without shoes, and body mass index (BMI) was calculated as weight (kg)/height (m^2).

Analysis

Data were analyzed using the Statistical Analysis System Version 6.12. (SAS Institute Inc. Cary, NC). For reasons of poor technical quality, the radiographs of 19 women did not allow reliable OA definition, leaving 567 women for the analyses. The relation of stiffness index and mBMD, after adjustment for age and BMI, with OA grade (0–4), osteophyte status (none, questionable, definite) or joint space narrowing status (none, questionable, definite) was evaluated by linear regression analysis using PROC GLM in SAS with testing of differences in least-square means between women with radiographic findings and those with no OA or with no osteophyte or no joint space narrowing.

Results

Characteristics of the subjects are shown in Table 1. Age and BMI adjusted means with standard errors for bone mass (stiffness index and mBMD) by radiographic grade

Table 2: Age and body mass index adjusted means (SEM) of bone mass (stiffness index[a] and mBMD[b]) by osteoarthritis (OA) grade at the knee, distal interphalangeal (DIP), proximal interphalangeal (PIP), carpometacarpal/metacarpophalangeal (CMC/MCP) joints.

OA grades	No.	Stiffness index[a]	P value*	No.	mBMD[b]	P value*
Knee						
0	261	70.7 (0.7)		267	2.25 (0.02)	
1	110	69.7 (1.0)	0.40	112	2.20 (0.02)	0.09
2	103	69.8 (1.0)	0.46	104	2.21 (0.02)	0.20
3	69	70.5 (1.3)	0.90	70	2.28 (0.03)	0.44
4	14	63.3 (2.7)	0.01	14	2.16 (0.07)	0.22
		Test for trend	0.18		Test for trend	0.63
DIP						
0	122	71.2 (1.0)		125	2.25 (0.02)	
1	98	70.0 (1.0)	0.36	98	2.20 (0.03)	0.11
2	214	69.3 (0.7)	0.11	219	2.23 (0.02)	0.43
3	59	69.5 (1.3)	0.30	59	2.23 (0.03)	0.52
4	64	71.5 (1.3)	0.87	66	2.27 (0.03)	0.69
		Test for trend	0.82		Test for trend	0.65
PIP						
0	355	70.5 (0.5)		363	2.23 (0.01)	
1	106	69.1 (1.0)	0.24	107	2.27 (0.02)	0.14
2	88	70.0 (1.1)	0.73	89	2.22 (0.03)	0.73
3	5	63.6 (4.5)	0.13	5	2.27 (0.11)	0.72
4	3	72.7 (5.8)	0.70	3	2.08 (0.14)	0.29
		Test for trend	0.39		Test for trend	0.91
CMC/MCP						
0	420	70.1 (0.5)		428	2.24 (0.01)	
1	47	67.6 (1.5)	0.11	48	2.16 (0.04)	0.05
2	55	69.8 (1.4)	0.84	55	2.25 (0.03)	0.80
3	32	73.9 (1.8)	0.04	33	2.26 (0.04)	0.58
4	3	72.9 (5.8)	0.63	3	2.26 (0.14)	0.86
		Test for trend	0.26		Test for trend	0.80

a: Stiffness index values were missing for 10 women. b: metacarpal bone mineral density. *P value versus women with no OA.

of OA (grade 0–4) at the knee, DIP, PIP and CMC/MCP joints are shown in Table 2. Stiffness index was significantly lower in women with grade 4 at knee than those in no OA, but was not different in women with OA grades (1–4) at DIP and PIP from those with no OA. On the other hand, stiffness index was significantly higher in women with grade 3 at CMC/MCP joint compared with those with no OA. Metacarpal BMD was not significantly different in women with OA grades (1–4) at all joints evaluated from those with no OA. Bone mass (stiffness index and mBMD) did not show a significant trend with grade of OA at each joint.

Adjusted means of bone mass (stiffness index and mBMD) were significantly higher in women with definite osteophytes at the CMC/MCP joint compared to those with no osteophytes, whereas there were no significant differences for the knee, DIP and PIP joints (Table 3). Stiffness index, but not mBMD, was significantly higher in women with definite joint space narrowing at CMC/MCP joint compared to those with no joint space narrowing (Table 4).

Because of the relatively low prevalence of radiographic changes of definite OA in women below age 60 and the possible hormonal effects on both bone mass and OA in perimenopausal women, the above analyses were repeated in the 405 women aged 60 years or over. Similar results were obtained in this age group (Tables 5,6,7). Stiffness index was significantly lower in women with grade 1 at CMC/MCP joint than those in no OA. Metacarpal BMD was significantly lower in women with grade 1 at knee than those in no OA (Table 5); the same was observed for women with questionable knee joint space narrowing (Table 7). Metacarpal BMD tended to be higher in women with definite osteophytes at CMC/MCP joint compared to those with no osteophytes (Table 6).

We also compared bone mass (stiffness index and mBMD) between women with OA (K/L grades 1–4) and no

Table 3: Age and body mass index adjusted means (SEM) of bone mass (stiffness index[a] and mBMD[b]) by osteophyte status at the knee, distal interphalangeal (DIP), proximal interphalangeal (PIP), carpometacarpal/metacarpophalangeal (CMC/MCP) joints.

Osteophyte status	No.	Stiffness index[a]	P value*	No.	mBMD[b]	P value*
Knee						
None	344	70.3 (0.6)		351	2.24 (0.01)	
Questionable	86	71.4 (1.1)	0.36	87	2.24 (0.03)	0.93
Definite	127	68.8 (0.9)	0.19	129	2.22 (0.02)	0.41
DIP						
None	158	70.0 (0.8)		161	2.23 (0.02)	
Questionable	257	70.4 (0.6)	0.70	261	2.22 (0.02)	0.73
Definite	141	69.6 (0.8)	0.80	144	2.26 (0.02)	0.30
PIP						
None	400	70.2 (0.5)		410	2.23 (0.01)	
Questionable	148	69.9 (0.8)	0.80	148	2.25 (0.02)	0.38
Definite	9	68.8 (3.4)	0.68	9	2.15 (0.08)	0.33
CMC/MCP						
None	437	70.1 (0.5)		446	2.23 (0.01)	
Questionable	81	68.2 (1.1)	0.10	81	2.19 (0.03)	0.11
Definite	39	73.7 (1.6)	0.04	40	2.32 (0.04)	0.04

a: Stiffness index values were missing for 10 women. b: metacarpal bone mineral density. * P value versus women with no osteophytes.

Table 4: Age and body mass index adjusted means (SEM) of bone mass (stiffness index[a] and mBMD[b]) by joint space narrowing status at the knee, distal interphalangeal (DIP), proximal interphalangeal (PIP), carpometacarpal/metacarpophalangeal (CMC/MCP) joints.

Joint space narrowing status	No.	Stiffness index[a]	P value*	No.	mBMD[b]	P value*
Knee						
None	374	70.6 (0.5)		381	2.24 (0.01)	
Questionable	85	67.8 (1.1)	0.02	87	2.17 (0.03)	0.02
Definite	98	70.3 (1.1)	0.84	99	2.27 (0.03)	0.31
DIP						
None	214	70.6 (0.7)		219	2.24 (0.02)	
Questionable	214	69.1 (0.7)	0.14	217	2.22 (0.02)	0.37
Definite	126	70.8 (0.9)	0.90	128	2.25 (0.03)	0.71
PIP						
None	442	70.1 (0.5)		450	2.23 (0.01)	
Questionable	107	70.3 (1.0)	0.89	109	2.23 (0.02)	0.99
Definite	8	67.1 (3.6)	0.40	8	2.19 (0.09)	0.66
CMC/MCP						
None	480	69.8 (0.4)		488	2.23 (0.01)	
Questionable	36	70.4 (1.7)	0.74	37	2.18 (0.04)	0.21
Definite	41	73.4 (1.6)	0.03	42	2.26 (0.04)	0.49

a: Stiffness index values were missing for 10 women. b: metacarpal bone mineral density. * P value versus women with no joint space narrowing.

Table 5: Age and body mass index adjusted means (SEM) of bone mass (stiffness index[a] and mBMD[b]) by osteoarthritis (OA) grade at the knee, distal interphalangeal (DIP), proximal interphalangeal (PIP), carpometacarpal/metacarpophalangeal (CMC/MCP) joints, ages 60 years over.

OA grades	No.	Stiffness index[a]	P value*	No.	mBMD[b]	P value*
Knee						
0	151	65.8 (0.8)		154	2.14 (0.02)	
1	82	65.8 (1.1)	0.99	83	2.06 (0.03)	0.03
2	88	66.7 (1.0)	0.50	89	2.11 (0.03)	0.48
3	65	66.3 (1.3)	0.75	66	2.14 (0.03)	0.90
4	13	59.5 (2.8)	0.03	13	2.03 (0.07)	0.16
		Test for trend	0.71		Test for trend	0.89
DIP						
0	50	65.8 (1.4)		51	2.11 (0.04)	
1	61	64.9 (1.3)	0.61	61	2.07 (0.03)	0.37
2	174	66.0 (0.7)	0.93	178	2.13 (0.02)	0.68
3	52	65.6 (1.4)	0.90	52	2.09 (0.03)	0.69
4	62	67.0 (1.2)	0.54	63	2.14 (0.03)	0.48
		Test for trend	0.43		Test for trend	0.29
PIP						
0	227	66.0 (0.7)		231	2.11 (0.02)	
1	85	65.8 (1.1)	0.90	86	2.15 (0.03)	0.17
2	79	66.2 (1.1)	0.89	80	2.10 (0.03)	0.73
3	5	58.9 (4.4)	0.11	5	2.14 (0.11)	0.75
4	3	68.2 (5.6)	0.70	3	1.95 (0.14)	0.28
		Test for trend	0.80		Test for trend	0.73
CMC/MCP						
0	278	65.9 (0.6)		282	2.12 (0.01)	
1	40	62.5 (1.5)	0.04	41	2.04 (0.04)	0.06
2	49	66.3 (1.4)	0.79	49	2.13 (0.04)	0.86
3	29	70.0 (1.8)	0.03	30	2.16 (0.05)	0.40
4	3	68.5 (5.6)	0.63	3	2.16 (0.14)	0.79
		Test for trend	0.16		Test for trend	0.64

a: Stiffness index values were missing for 6 women. b: metacarpal bone mineral density. *P value versus women with no OA.

OA, adjusting for age and BMI, but there was no significant difference at any joint in all women (Table 8), and in ages 60 and older (Table 9).

Discussion

We did not detect a consistent association of peripheral bone mass with radiographic features of OA in the knee, DIP and PIP joints. However, we found that OA at the CMC/MCP was associated with higher bone mass: stiffness index was significantly higher in women with grade 3, definite osteophyte or definite joint space narrowing, compared with those with no OA, no osteophyte or no joint space narrowing, respectively, and mBMD was higher in women with definite osteophytes, compared with those with no osteophytes. Since it is well known that age and obesity are related both to OA and bone mass, and are potential confounders [15–18], our analyses were adjusted for age and BMI.

Several studies reported that radiographic knee OA was associated with increased femoral neck or spine BMD independently of age and BMI [5,9,23], whereas knee OA was not associated with radius or metacarpal BMD [23,28]. Furthermore, several studies reported that radiographic hand OA was associated with increased lumbar spine or total body BMD [5,10,12], but not with radius or metacarpal BMD [29,30]. It has been reported that in cases with generalized OA, the width of the radius and the metacarpal is significantly larger than in controls, and bone width can influence bone mass results expressed as BMD or % cortical area [22]. In the current study, metacarpal width in women with OA (grade 1–4) at CMC/MCP joint was greater than that in women without OA (grade 0) at the CMC/MCP joint, but this difference was not significant (p = 0.28). These findings may in part explain why we did not find an association of mBMD with OA grade and joint space narrowing status at the CMC/MCP joint despite finding an association of stiffness index with these measures of OA.

Table 6: Age and body mass index adjusted means (SEM) of bone mass (stiffness index[a] and mBMD[b]) by osteophyte status at the knee, distal interphalangeal (DIP), proximal interphalangeal (PIP), carpometacarpal/metacarpophalangeal (CMC/MCP) joints, ages 60 years over.

Osteophyte status	No.	Stiffness index[a]	P value*	No.	mBMD[b]	P value*
Knee						
None	216	65.5 (0.7)		219	2.12 (0.02)	
Questionable	74	67.7 (1.1)	0.10	75	2.12 (0.03)	0.89
Definite	109	65.4 (1.0)	0.95	111	2.11 (0.02)	0.77
DIP						
None	78	64.2 (1.1)		79	2.07 (0.03)	
Questionable	192	66.8 (0.7)	0.06	195	2.11 (0.02)	0.26
Definite	129	65.6 (0.9)	0.32	131	2.14 (0.02)	0.05
PIP						
None	257	65.8 (0.6)		263	2.11 (0.02)	
Questionable	133	66.2 (0.8)	0.76	133	2.14 (0.02)	0.29
Definite	9	64.5 (3.2)	0.68	9	2.02 (0.08)	0.32
CMC/MCP						
None	291	65.9 (0.6)		296	2.12 (0.01)	
Questionable	71	64.2 (1.1)	0.18	71	2.06 (0.03)	0.10
Definite	37	69.6 (1.6)	0.03	38	2.20 (0.04)	0.06

a: Stiffness index values were missing for 6 women. b: metacarpal bone mineral density. * P value versus women with no osteophytes.

Table 7: Age and body mass index adjusted means (SEM) of bone mass (stiffness index[a] and mBMD[b]) by joint space narrowing status at the knee, distal interphalangeal (DIP), proximal interphalangeal (PIP), carpometacarpal/metacarpophalangeal (CMC/MCP) joints, ages 60 years over.

Joint space narrowing status	No.	Stiffness index[a]	P value*	No.	mBMD[b]	P value*
Knee						
None	243	66.3 (0.6)		247	2.13 (0.02)	
Questionable	65	63.9 (1.2)	0.08	66	2.04 (0.03)	0.01
Definite	91	66.3 (1.1)	0.97	92	2.14 (0.03)	0.73
DIP						
None	113	65.9 (0.9)		115	2.11 (0.02)	
Questionable	166	65.3 (0.8)	0.62	169	2.11 (0.02)	0.86
Definite	117	66.5 (0.9)	0.65	118	2.12 (0.02)	0.83
PIP						
None	303	65.8 (0.6)		307	2.12 (0.01)	
Questionable	88	66.7 (1.0)	0.43	90	2.12 (0.03)	0.99
Definite	8	62.4 (3.4)	0.34	8	2.07 (0.09)	0.63
CMC/MCP						
None	330	65.5 (0.5)		334	2.11 (0.01)	
Questionable	32	65.6 (1.8)	0.98	33	2.07 (0.04)	0.37
Definite	37	69.5 (1.6)	0.02	38	2.15 (0.04)	0.41

a: Stiffness index values were missing for 6 women. b: metacarpal bone mineral density. * P value versus women with no joint space narrowing.

In our study, the associations with OA were inconsistent, suggesting they may simply be due to chance. The cross-sectional nature of our study and the use of peripheral bone mass measurements may have affected our ability to detect an association with OA. A recent review [31] reported that higher BMD as measured by DXA at the spine and hip was associated with OA at hip, spine or knee, but weaker associations were observed with hand OA. Measuring BMD at skeletal sites distant from the site evaluated for OA might provide a general indication of skeletal bone

Table 8: Age and body mass index adjusted means (SEM) of bone mass (stiffness index[a] and mBMD[b]) by osteoarthritis (OA) grade at the knee, distal interphalangeal (DIP), proximal interphalangeal (PIP), carpometacarpal/metacarpophalangeal (CMC/MCP) joints. (n = 567)

OA grades	No.	Stiffness index[a]	P value*	No.	mBMD[b]	P value*
Knee						
0		70.6 (0.6)			2.25 (0.02)	
1–4		69.6 (0.6)	0.28		2.22 (0.01)	0.15
DIP						
0		71.3 (1.0)			2.26 (0.02)	
1–4		69.8 (0.5)	0.18		2.23 (0.01)	0.29
PIP						
0		70.5 (0.5)			2.23 (0.01)	
1–4		69.4 (0.7)	0.26		2.24 (0.02)	0.46
CMC/MCP						
0		70.1 (0.5)			2.24 (0.01)	
1–4		70.0 (0.9)	0.92		2.22 (0.02)	0.52

a: Stiffness index values were missing for 10 women. b: metacarpal bone mineral density. *P value versus women with no OA.

mass, whereas measurements closer to the sites evaluated for OA might provide an indication of local bone effects. If local bone factors are more important, this might partly explain why heel BMD was not consistently associated with OA at other sites. On the other hand, being a weight-bearing site, one would expect that heel bone mass would reflect the physical loads borne by the knees, but not necessarily loading of bones in the hand. If so, heel bone mass might be more strongly associated with knee OA than hand OA, but this was not seen. Likewise, hand BMD was not strongly associated with hand OA in our study. The composition of measured bone might also play a role. The heel and spine have high proportions of trabecular bone than other sites such as the hip and metacarpal. However, there is no convincing evidence that the associations with OA might be stronger (or weaker) for BMD measurements at sites with high proportions of trabecular bone.

Several environmental or cultural (lifestyle) characteristics may contribute to site-specific OA occurrence [18]. Knee bending and squatting were strongly associated with OA of the knee [32,33]. However, these were retrospective case control studies, and as such provide weaker evidence of a causal relationship than prospective studies. Life-long knee bending and squatting behaviors, a component of the traditional Japanese lifestyle, may have had a long-term effect on occurrence of knee OA. Since Japanese elderly spent most of their lives using tatami mats and Eastern-style toilets (all of which are within inches of ground level and require squatting), these daily activities of the traditional Japanese lifestyle may have contributed to the development of knee OA even among those with low bone mass (osteoporosis). Prospective studies are required to confirm a causal association between knee bending and knee OA. Furthermore, Half of the women we studied were engaged in farming, and these women may have a high risk of joint injury and of repetitive hand use, which may be risk factors for OA [34,35]. There was no association of higher bone mass with OA at the knee, DIP and PIP joints in the current study. This suggests that environmental factors may have contributed more to the occurrence of OA at knee, DIP and PIP joints in our Japanese sample, and this might have masked an association between bone mass and OA.

Heel bone stiffness index was lower in women with grade 4 at the knee than those with no OA in the current study. Although the explanation is unclear, one possibility is that women with severe knee OA may have less physical (walking) activity, which could lead to lower bone mass than women of comparable age.

The measurements of bone mass at 2 appendicular sites (calcaneus and metacarpal) may offer insights regarding possible differences in associations of cancellous and cortical bone with OA [36]. The calcaneus is of primarily cancellous bone, and the metacarpal of primarily cortical bone. Furthermore, the calcaneus is weight-bearing, and may reflect to some degree the usual level of physical activity, whereas the metacarpal is not a weight-bearing bone. Previous studies tended to find associations between OA (at the hip, knee and hand) and BMD measured at weight-bearing sites [5,9,10,12,23], but not when BMD was measured at the hand [23,28–30]. However, there

Table 9: Age and body mass index adjusted means (SEM) of bone mass (stiffness index[a] and mBMD[b]) by osteoarthritis (OA) grade at the knee, distal interphalangeal (DIP), proximal interphalangeal (PIP), carpometacarpal/metacarpophalangeal (CMC/MCP) joints, ages 60 years over. (n = 405)

OA grades	No.	Stiffness index[a]	P value*	No.	mBMD[b]	P value*
Knee						
0		65.8 (0.8)			2.14 (0.02)	
1–4		66.0 (0.6)	0.82		2.10 (0.02)	0.13
DIP						
0		65.9 (1.4)			2.11 (0.04)	
1–4		65.9 (0.5)	0.97		2.22 (0.01)	0.93
PIP						
0		66.0 (0.6)			2.11 (0.02)	
1–4		65.8 (0.7)	0.87		2.12 (0.02)	0.55
CMC/MCP						
0		65.9 (0.6)			2.12 (0.01)	
1–4		65.9 (0.9)	0.98		2.11 (0.02)	0.63

a: Stiffness index values were missing for 10 women. b: metacarpal bone mineral density. *P value versus women with no OA.

was no apparent relationship between the type of bone measured and the presence of OA in the present study.

Our study has several limitations. Although we attempted to obtain a representative sample of the population, the subjects had to be mobile enough to attend the examination center. Women with the most severe symptoms and disability (especially in the oldest age groups) may have chosen not to participate. The response rate in the Hizen-Oshima Study was approximately 30% of eligible women, so there is a possibility of selection bias. Our mail survey did not yield a high response rate but there was only one mailing to the general community and no attempted follow-up. The subjects in this analysis were all Japanese women; thus, our results may not be generalizable to men, or men and women of different racial groups. These analyses are cross-sectional by design, and causality cannot be inferred from the differences in adjusted bone mass between women with and without knee or hand OA. For example, women with higher bone mass at an earlier point in life may be more likely to develop OA, but subsequent declines in physical activity due to OA symptoms could contribute to accelerated bone loss which would confound the cross-sectional analyses reported here. Considering the exploratory nature of these analyses, and the use of multiple endpoints and predictors, it may be appropriate to adjust the p-values for multiple comparisons. Taking the dozens of comparisons into account, none of the associations would be considered statistically significant.

Conclusions

Our results showed that age and BMI adjusted appendicular bone mass is increased with radiographic changes of OA at CMC/MCP joint, especially with osteophyte status, among Japanese women. Our findings also failed to detect an association of bone mass with OA for knee, DIP or PIP joint in Japanese women, in contrast to other populations. Factors associated with OA may differ by site of joint involvement [18]. However, the cross-sectional nature of our study makes it difficult to make etiologic inferences, and prospective studies are needed to investigate this issue further.

Competing interests

Philip D. Ross is an employee of and holds stock options in Merck & Co., Inc.

Authors' contributions

YY participated in the study design, data analysis and drafting the manuscript. KA participated in the study design, standardization of data collection, data analysis and preparation of the manuscript. SY participated in the study design and reading the X-ray films. PDR participated in the study design, standardization of data collection, data analysis and writing of the manuscript. IY participated in the study design and critical review of the manuscript. KM participated in critical review of the manuscript. TT participated in critical review of the manuscript.

All authors read and approved the final manuscript.

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References

1. Lawrence RC, Helmick CG, Arnett FC, Deyo RA, Felson DT, Giannini EH, Heyse SP, Hirsch R, Hochberg MC, Hunder GG, *et al*: **Estimates of the prevalence of arthritis and selected musculoskeletal disorders in the United States.** *Arthritis Rheum* 1998, **41:**778-799
2. Cummings SR, Kelsey JL, Nevitt MC, O'Dowd KJ: **Epidemiology of osteoporosis and osteoporotic fractures.** *Epidemiol Rev* 1985, **7:**178-208
3. Foss MV, Byers PD: **Bone density, osteoarthrosis of the hip, and fracture of the upper end of the femur.** *Ann Rheum Dis* 1972, **31:**259-264
4. Dequeker J, Goris P, Uytterhoeven R: **Osteoporosis and osteoarthritis (osteoarthrosis). Anthropometric distinctions.** *JAMA* 1983, **249:**1448-1451
5. Hart DJ, Mootoosamy I, Doyle DV, Spector TD: **The relationship between osteoarthritis and osteoporosis in the general population: the Chingford Study.** *Ann Rheum Dis* 1994, **53:**158-162
6. Gevers G, Dequeker J, Martens M, Van Audekercke R, Nyssen-Behets C, Dhem A: **Biomechanical characteristics of iliac crest bone in elderly women according to osteoarthritis grade at the hand joints.** *J Rheumatol* 1989, **16:**660-663
7. Sowers M, Zobel D, Weissfeld L, Hawthorne VM, Carman W: **Progression of osteoarthritis of the hand and metacarpal bone loss. A twenty-year followup of incident cases.** *Arthritis Rheum* 1991, **34:**36-42
8. Hordon LD, Stewart SP, Troughton PR, Wright V, Horsman A, Smith MA: **Primary generalized osteoarthritis and bone mass.** *Br J Rheumatol* 1993, **32:**1059-1061
9. Belmonte-Serrano MA, Bloch DA, Lane NE, Michel BE, Fries JF: **The relationship between spinal and peripheral osteoarthritis and bone density measurements.** *J Rheumatol* 1993, **20:**1005-1013
10. Marcelli C, Favier F, Kotzki PO, Ferrazzi V, Picot MC, Simon L: **The relationship between osteoarthritis of the hands, bone mineral density, and osteoporotic fractures in elderly women.** *Osteoporos Int* 1995, **5:**382-388
11. Nevitt MC, Lane NE, Scott JC, Hochberg MC, Pressman AR, Genant HK, Cummings SR: **Radiographic osteoarthritis of the hip and bone mineral density. The Study of Osteoporotic Fractures Research Group.** *Arthritis Rheum* 1995, **38:**907-916
12. Sowers MF, Hochberg M, Crabbe JP, Muhich A, Crutchfield M, Updike S: **Association of bone mineral density and sex hormone levels with osteoarthritis of the hand and knee in premenopausal women.** *Am J Epidemiol* 1996, **143:**38-47
13. Radin EL: **Mechanical aspects of osteoarthrosis.** *Bull Rheum Dis* 1976, **26:**862-865
14. Radin EL, Rose RM: **Role of subchondral bone in the initiation and progression of cartilage damage.** *Clin Orthop* 1986, **213:**34-40
15. Bauer DC, Browner WS, Cauley JA, Orwoll ES, Scott JC, Black DM, Tao JL, Cummings SR: **Factors associated with appendicular bone mass in older women. The Study of Osteoporotic Fractures Research Group.** *Ann Intern Med* 1993, **118:**657-665
16. Ross PD: **Osteoporosis. Frequency, consequences, and risk factors.** *Arch Intern Med* 1996, **156:**1399-1411
17. Felson DT: **Epidemiology of hip and knee osteoarthritis.** *Epidemiol Rev* 1988, **10:**1-28
18. Silman AJ, Hochberg MC: **Osteoarthritis.** *In: Epidemiology of the rheumatic diseases (Edited by: Silman AJ, Hochberg MC) Oxford, Oxford University Press* 1993, 257-288
19. Hordon LD, Wright V, Smith MA: **Bone mass in osteoarthritis.** *Ann Rheum Dis* 1992, **51:**823-825
20. Knight SM, Ring EF, Bhalla AK: **Bone mineral density and osteoarthritis.** *Ann Rheum Dis* 1992, **51:**1025-1026
21. Lane NE, Nevitt MC: **Osteoarthritis and bone mass.** *J Rheumatol* 1994, **21:**1393-1396
22. Dequeker J, Boonen S, Aerssens J, Westhovens R: **Inverse relationship osteoarthritis-osteoporosis: what is the evidence? What are the consequences?** *Br J Rheumatol* 1996, **35:**813-818
23. Hannan MT, Anderson JJ, Zhang Y, Levy D, Felson DT: **Bone mineral density and knee osteoarthritis in elderly men and women. The Framingham Study.** *Arthritis Rheum* 1993, **36:**1671-1680
24. Naitou K, Kushida K, Takahashi M, Ohishi T, Inoue T: **Bone mineral density and bone turnover in patients with knee osteoarthritis compared with generalized osteoarthritis.** *Calcif Tissue Int* 2000, **66:**325-329
25. Yoshida S, Aoyagi K, Felson DT, Aliabadi P, Shindo H, Takemoto T: **Comparison of the prevalence of radiographic osteoarthritis of the knee and hand between Japan and the United States.** *J Rheumatol* 2002, **29:**1454-1458
26. Kellgren JH, Lawrence JS: **Atlas of standard radiographs. The epidemiology of chronic rheumatism.** *Oxford, Blackwell Scientific Publications* 1963
27. Goker B, Sumner DR, Hurwitz DE, Block JA: **Bone mineral density varies as a function of the rate of joint space narrowing in the hip.** *J Rheumatol* 2000, **27:**735-738
28. Hochberg MC, Lethbridge-Cejku M, Scott WW, Reichle R, Plato CC, Tobin JD: **Upper extremity bone mass and osteoarthritis of the knees: data from the Baltimore Longitudinal Study of Aging.** *J Bone Miner Res* 1995, **10:**432-438
29. Hochberg MC, Lethbridge-Cejku M, Scott WW, Plato CC, Tobin JD: **Appendicular bone mass and osteoarthritis of the hands in women: data from the Baltimore Longitudinal Study of Aging.** *J Rheumatol* 1994, **21:**1532-1536
30. Reid DM, Kennedy NS, Smith MA, Tothill P, Nuki G: **Bone mass in nodal primary generalised osteoarthrosis.** *Ann Rheum Dis* 1984, **43:**240-242
31. Stewart A, Black AJ: **Bone mineral density in osteoarthritis.** *Curr Opin Rheumatol* 2000, **12:**464-467
32. Kivimaki J, Riihimaki H, Hanninen K: **Knee disorders in carpet and floor layers and painters.** *Scand J Work Environ Health* 1992, **18:**310-316
33. Cooper C, McAlindon T, Coggon D, Egger P, Dieppe P: **Occupational activity and osteoarthritis of the knee.** *Ann Rheum Dis* 1994, **53:**90-93
34. Hadler NM, Gillings DB, Imbus HR, Levitin PM, Makuc D, Utsinger PD, Yount WJ, Slusser D, Moskovitz N: **Hand structure and function in an industrial setting.** *Arthritis Rheum* 1978, **21:**210-220
35. Partridge RE, Duthie JJ: **Rheumatism in dockers and civil servants. A comparison of heavy manual and sedentary workers.** *Ann Rheum Dis* 1968, **27:**559-568
36. Dequeker J, Geusens P: **Osteoporosis and arthritis.** *Ann Rheum Dis* 1990, **49:**276-280

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