PROGRESSION OF OSTEOARTHRITIS OF THE HAND AND METACARPAL BONE LOSS

A Twenty-Year Followup of Incident Cases

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We examined the prospective relationship between metacarpal bone mass and osteoarthritis (OA) of the hand, using incidence data from the historical cohort in the Tecumseh Community Health Study (Tecumseh, MI). Women were examined for radiographic evidence of OA and for bone mass twice, 20–23 years apart (1962–1965 and 1985; 683 subjects with an age range of 55–74 in 1985). Two measures of OA were evaluated: the highest score assigned to any of the 32 wrist/hand joints, and the sum of scores for all wrist/hand joints. After adjustment for age, women who were classified as having OA (by either measure of OA) in 1985 were more likely to have more cortical area at baseline, which indicates greater bone mass. Women who developed OA in the 23-year period were more likely to experience a significantly greater widening of the medullary cavity over time, an indicator of increased bone resorption. Women with increasing levels of OA involvement also had an increased likelihood of greater cortical area loss. We conclude that women who later developed OA were more likely to have higher baseline bone mass than women who did not develop OA, but these women also had a greater likelihood of bone loss over time.

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Decreased bone mass and osteoarthritis (OA) are common in elderly woman. It has been estimated that 1 in 4 women of Northern European ancestry has low bone mass (1), and 1 woman in 5 has OA (2). An early study (3) suggested that the 2 conditions rarely coexisted clinically. Other investigations reported a negative relationship between the 2 disease processes in the hip (4,5) and in measures derived from radiographs of the hand (6). In contrast, other studies suggested that the conditions do coexist (7,8).

Radin (9) postulated that the failure of subchondral bone in weight-bearing joints to deform upon impact, with the subsequent development of cartilage damage, was a cause of OA. If this were true, then persons with OA might be expected to have greater antecedent bone mass or less flexible bony architecture.

It has also been suggested that any independence of the 2 conditions might be associated with body size. Healey et al (10) observed that women with OA and greater weight and height, for whom hip replacement was undertaken, had fewer vertebral compression fractures and less femoral osteoporosis, as reflected in the Singh Index, when compared with controls with idiopathic osteoporosis who had undergone a transiliac bone biopsy. Dequeker et al (11) reported that women with OA were more obese and had greater muscle strength than those with osteoporosis, suggesting that these characteristics explained the increased bone mass observed. Price et al (12) observed that bone mass values were similar in female patients with OA and in normal controls, after adjustment for age and weight.

The nature of the relationship between osteoporosis and osteoarthritis may be mediated by the site of involvement or the primary type of bone involved. Nilas and coworkers (13), using photon densitometry, found that women with OA and normal postmenopausal women of comparable age had similar cortical bone density in the forearm. However, the women with OA had significantly greater bone mineral density in the spine than did the controls.

Limitations of clinical studies of the relationship between osteoarthritis and osteoporosis include selection bias in the ascertainment of cases of both osteoporosis and osteoarthritis. The use of cross-sectional data fails to capture the influence of changes in bone mass and arthritis status. Additionally, sample sizes are frequently too small to characterize differences that might exist.

In the present study, we examined changes in bone mass (derived from measures on radiographs taken in 1962–1965 and 1985) in women classified for OA status, after adjusting for age and considering body size. Additionally, the relationship between change in bone mass and change in OA status was assessed. Women eligible for evaluation were those who were radiographically free of disease at baseline (1962–1965 evaluation).

SUBJECTS AND METHODS

Women who participated in the Tecumseh Community Health Study were examined for evidence of osteoarthritis and for bone mass using radiographs taken in 1962–1965 and in 1985. The Tecumseh Community Health Study was a comprehensive, longitudinal, epidemiologic investigation of the entire population of Tecumseh, Michigan and its environs.

Baseline studies were undertaken in 3 rounds, conducted from 1956–1969; participation was >80%. During the second round of examinations, in 1962–1965, radiographs of the hands and wrists were obtained on 96% of the participants aged 20 years or older.

The measurement and scoring of radiographs for evidence of OA have been previously described (14,15). In 1985, participants from the second round of examinations, who were then aged 50–74 years, had repeat radiographs (a single posteroanterior view, average exposure of 0.355 seconds at 100 mA and 46 kVp [14]) of both hands and wrists. These participants represent 79% of the portion of the original cohort who were still residing in the Tecumseh area. This study presents only data for women who had radiographs from both the 1962–1965 study and the 1985 study. The same radiographic technique was employed at both examinations; General Electric machines, a large focal setting, a distance of 40 inches at table top, and film-screen cassettes were used.

Table 1 presents the classification criteria used to score the degree of OA in individual joints. Scoring was done using a 5-point scale (0 = none, 1 = minimal, 2 = mild, 3 = moderate, and 4 = severe), according to the Atlas of Standard Radiographs of Arthritis (16). The degree of OA for each of the 32 joints assessed per individual was scored by 3 physician readers, who scored the 1985 films and rescored the 1962–1965 (baseline) films. Three approaches to the reliability of the OA score were undertaken and have been described previously (14). The maximum score variable was defined as the highest score assigned to any of the 32 joints of the hands and wrists. Subjects with a maximum score of 2–4 were designated as having a radiologically defined diagnosis of osteoarthritis of the hands and wrists. The sum of scores variable was the sum of the scores assigned to all 32 joints. These values ranged from 0 to 55 in these 683 subjects. To facilitate comparison between the 2 measures, the sum of scores variable was categorized into quintiles.

Table 1. Criteria for scoring osteoarthritis (OA) on hand radiographs and the numbers of women classified into each category in 1962–1965 and in 1985*

OA grade	No. in 1962–1965 (n = 716)	No. in 1985 (n = 716)	Definition
0	481	48	Normal
1	202	314	Doubtful narrowing of joint space; possible osteophytes
2	22	221	Definite osteophytes; absent or questionable narrowing of joint space
3	3	69	Moderate osteophytes; marked narrowing of joint space; severe sclerosis; possible deformity
4	8	64	Large osteophytes; marked narrowing of joint space; severe sclerosis; definite deformity

* Radiographs were scored on a 0–4 scale, as defined above (from ref. 16). Only those whose baseline (1962–1965) scores were <2 were further analyzed in our studies.

In 1989, the hand/wrist radiographs were also assessed for physical characteristics associated with bone mass. The mean cortical area of the left and right second metacarpal bones, the measure of bone mass, was generated from measures of the total periosteal and medullary cavity diameters. Bone cortical area was calculated as 0.0785 times the square of the total periosteal diameter minus the square of the medullary cavity diameter (17). As shown in Figure 1, medullary cavity diameter increases with resorptive bone loss, while periosteal diameter increases because of bone formation. The cortical area value generated from these 2 dimensions should reflect the relative balance between bone formation and bone resorption.

The bone mass characteristics of the radiographs were measured to the nearest millimeter by 2 readers, independently, using Helios dial calipers. A computerized editing program was used to identify those data which reflected between-reader discordance of more than 10% in periosteal diameter or 20% in medullary cavity diameter per radiograph. Radiographs for which the values were discrep-

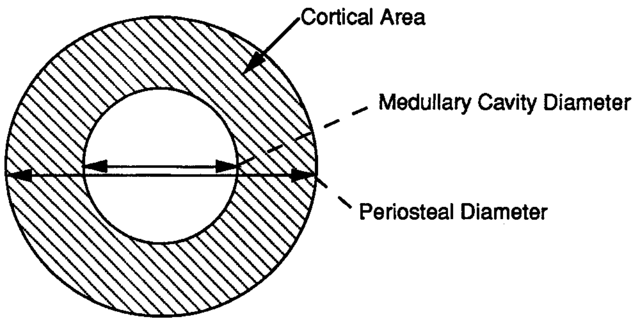

Figure 1. Parameters associated with bone change in aging. The medullary cavity and periosteal diameters typically increase, although not necessarily proportionately, while the cortical area typically decreases with aging.

ant beyond these limits were reread independently and blindly, and the 2 most congruent values were accepted. If concordant values for a particular radiograph could not be achieved within the defined limits, the value for that film was omitted from the analysis. Additionally, radiographs were given a rating to indicate the quality of the film and the relative difficulty in observing the landmarks needed to read the film. Only values with an "acceptable" quality rating were included in the data analyses. After these measures of bone mass met the reproducibility criteria, a mean value, reflecting the contribution of both the right and left hand, was used in the data analyses.

Of the 813 women surveyed in 1962–1965 and in 1985, 716 (88%) had hand radiographs that were scorable for both measures of OA in all 32 joints, were free of evidence of rheumatoid arthritis, and were readable for measures of bone mass in both rounds (see Table 1). Of these 716 women, 683 (95%) had radiographs with an OA maximum score <2, and were therefore categorized as free of OA at baseline. This report includes only information from those 683 women.

To assess the association of change in OA status over time with change in bone mass over time, women were categorized according to the change in their OA scores from 1962–1965 to 1985. One group of women (n = 362) had low scores for OA (0 or 1) both in 1962–1965 and in 1985, and these were classified as "primarily no OA." The other group (n = 321) had low scores for OA in 1962 (0 or 1) and higher scores in 1985 (2, 3, or 4), and these were classified as "becoming OA."

The change in bone mass over time was evaluated using the difference of continuous variables. These variables were the 1985 medullary cavity diameter, total metacarpal periosteal diameter, and cortical area subtracted from their respective 1962 values.

Data about weight (in kg), height (in cm), and triceps skinfold thickness (in mm) were available as a result of physical examinations at baseline (1962–1965) and in 1985. The Quetelet Index was calculated as the weight divided by the square of the height. Preliminary analyses indicated that the Quetelet Index was the variable that was most consistently associated with bone mass and OA at both time periods compared with weight or triceps skinfold thickness. The Quetelet Index (1962) and age were used as variables to adjust for confounding.

Univariate statistics of continuous measures were generated for the entire sample and by degrees of OA in 1985 and by OA change from 1962–1965 to 1985. Values for triceps skinfold thickness were log-transformed because of the skewness of their distribution.

Simple linear regression and multiple regression analyses were used to investigate the relationship between measures of bone mass, bone mass change, age, and Quetelet Index. Analysis of variance was performed to determine if there were differences between the OA classification groups and the continuous physical measures. Tests for trend across OA classification groups were utilized to determine if the differences in the continuous physical measures were increasing or decreasing with increasing OA severity. Multiple regression analyses were also used to control for potentially confounding continuous variables, including age and Quetelet Index, in tests for trend across OA classification groups for bone mass and bone mass change measures (18).

Logistic regression models were formulated to assess whether changes in bone mass measures were substantially related to OA classification after accounting for the confounding variables. The change in log-likelihood, after simultaneously removing the effect of potential confounders, was used to determine the relationship between bone mass and OA classification. The beta coefficients and variability estimates from the logistic regression models were used to calculate the adjusted odds ratio and its 95% confidence interval (CI) (19).

RESULTS

Maximum joint score as a measure of OA. The age and anthropometric characteristics associated with the study subjects, according to the 5-level "maximum joint score" are shown in Table 2. Age was associated positively with the maximum joint score ($P < 0.0001$, test for trend). Prospectively, 1962 measures of body size, including weight, triceps skinfold thickness, and Quetelet Index, were associated positively with the 1985 maximum score ($P < 0.0002$, $P < 0.0034$, and $P < 0.0001$, respectively, by test for trend). Measures of body size, undertaken concurrently with the 1985 OA ascertainment, were less likely to be associated with OA classification. Height (1985) was negatively associated with OA levels ($P < 0.02$, by test for trend), while the Quetelet Index was positively associated with OA levels ($P < 0.04$, by test for trend).

The nature and direction of the relationships between measures of bone mass, age, and the Quetelet Index were determined using regression analyses. The medullary cavity diameter increased with age, while the cortical area declined with age, indicative of the expected bone loss with age (Table 3). The Quetelet Index (1985) was associated with a smaller medullary

Table 2. Age and anthropometric characteristics associated with the maximum joint score in 1985 in 683 women designated radiologically free of osteoarthritis in 1962*

Characteristic	Grade 0 (n = 48)	Grade 1 (n = 314)	Grade 2 (n = 214)	Grade 3 (n = 63)	Grade 4 (n = 44)	P
Age (years)						
1962	33.96	36.45	40.41	41.00	43.02	<0.0001
Weight (kg)						
1962	59.12	63.44	65.48	65.63	67.75	<0.0002
1985	67.65	71.68	72.46	70.07	72.52	0.2082
Height (cm)						
1962	162.48	161.67	161.51	161.34	161.15	0.2159
1985	161.35	160.21	159.88	159.15	158.92	0.0143
Quetelet Index (kg/cm^2)						
1962	22.45	24.29	25.12	25.19	26.11	<0.0001
1985	26.01	27.93	28.33	27.72	28.74	0.0328
Triceps skinfold thickness (mm)						
1962	22	25	26	26	26	<0.0034
1985	24	26	25	23	26	0.7863

* The maximum joint score was the highest score for any of the 32 joints of the hands and wrists (see Table 1 and Subjects and Methods for further details). The *P* values describe the probability that the trend is the result of chance.

cavity, as evidenced by the negative sign in Table 3, the greater periosteal diameter, and the greater cortical area, all of which are measures indicative of greater bone mass.

The relationships between measures of bone mass and 1985 maximum joint score are shown in Table 4. The mean medullary cavity diameter (1962) was significantly smaller, indicative of more bone, in women classified as having a higher 1985 maximum joint score ($P < 0.0022$, by test for trend). There was a greater difference in the medullary cavity width over the 20-year interval in women with the higher score, indicating increased likelihood of greater bone resorption over time in women with OA ($P < 0.0001$, by test for trend). There was no statistically significant difference in mean periosteal diameter (1962 or 1985) according to the level of OA. The mean cortical area (1962) increased across the OA levels ($P < 0.0126$), indicating greater bone mass among women who would be classified as having more OA in 1985. Values for the cortical area difference suggest that women who were classified as having OA had significantly more metacarpal bone mass loss ($P < 0.0001$, by test for trend).

Table 3. Beta coefficients from single regression analyses describing the association between measures of bone mass and age, 1962 Quetelet Index, and 1985 Quetelet Index

Bone mass measure	Model 1 (1962 age)	Model 2 (1962 Quetelet Index)	Model 3 (1985 Quetelet Index)
Medullary width (cm)			
1962	0.0011*	−0.0005	–
1985	0.0062†	0.0035	−0.0137*
Difference	0.5134†	0.3785	−1.0537*
Periosteal width (cm)			
1962	0.0002	0.0098*	–
1985	0.00004	0.0128*	0.0101*
Difference	−0.0134	0.3329*	0.2822*
Cortical area (cm^2)			
1962	−0.0007*	0.0080‡	–
1985	−0.0049†	0.0073	0.0187†
Difference	−0.4141†	−0.0401	1.0450*

* $P < 0.05$.
† $P < 0.001$.
‡ $P < 0.10$.

Relationships between measures of bone mass and 1985 maximum joint score, including adjustment for age as well as the Quetelet Index (1962), were also evaluated. The Quetelet Index (1962) was chosen as a measure of body size to retain an appropriate temporal relationship. Relationships were consistent whether values were unadjusted or adjusted for Quetelet Index.

The odds of having a 1985 maximum joint score >2 was 1.3 (95% CI 1.2–1.4) if the difference in medullary cavity diameter was in the 90th percentile, indicative of greater bone resorption, compared with the 10th percentile of difference. This was observed following adjustment for age and body size. Similarly, the odds of having a 1985 maximum joint score >2 was 1.6 (95% CI 1.5–1.63) if the difference in cortical area was in the 90th percentile, indicative of greater metacarpal bone loss, compared with the 10th percentile of difference.

Sum of joint scores as a measure of OA. The age and body size characteristics of the study subjects,

Table 4. Bone mass characteristics associated with the 1985 maximum joint score, adjusted for age (1962), among 683 women designated radiologically free of osteoarthritis in 1962*

Characteristic	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	*P*
Medullary width (cm)						
1962	0.307	0.283	0.288	0.273	0.251	<0.0022
1985	0.371	0.359	0.359	0.363	0.365	0.8285
Difference	0.06	0.08	0.07	0.09	0.11	<0.0001
Periosteal width (cm)						
1962	0.802	0.802	0.796	0.787	0.786	0.0806
1985	0.812	0.812	0.806	0.796	0.796	0.0896
Difference	0.012	0.010	0.010	0.009	0.010	–
Cortical area (cm^2)						
1962	0.389	0.408	0.399	0.404	0.420	<0.0126
1985	0.346	0.356	0.350	0.340	0.339	0.1726
Difference	−0.043	−0.051	−0.049	−0.063	−0.081	<0.0001

* The maximum joint score was the highest score for any of the 32 joints of the hands and wrists (see Table 1 and Subjects and Methods for further details. The *P* values describe the probability that the trend is the result of chance.

according to quintile categorization of the sum of all joint scores are shown in Table 5. Women in the higher quintile of the sum of joint scores had greater bone mass, as described by 1962 cortical area and 1962 medullary cavity (see Table 6). In addition, women in the higher quintiles of the sum of joint scores were significantly more likely to have greater bone loss, as shown by a greater cortical area difference ($P < 0.0137$) and an increased difference in medullary width ($P < 0.0186$). Similar findings were noted when the relationships were adjusted for both age and Quetelet Index measured in 1962.

DISCUSSION

This study is, to our knowledge, the first report of a prospective examination of the relationship of bone dimensions and osteoarthritis of the hand. These observations concur with those of Price et al (12), in that our measure of bone mass, the metacarpal cortical area (1985), was similar in women with OA and in those without OA when the mean cortical area was adjusted for age and Quetelet Index, using a cross-sectional perspective. However, longitudinal observation disclosed that women who were designated as

Table 5. Age and physical characteristics associated with the 1985 sum of scores quintiles in women designated radiologically free of osteoarthritis in 1962*

Characteristic	Quintile 1 (0–1)	Quintile 2 (2–4)	Quintile 3 (5–8)	Quintile 4 (9–15)	Quintile 5 (16–55)	*P*
Age (years)						
1962	34.30	35.60	37.95	40.03	42.71	0.0001
Weight (kg)						
1962	62.31	62.66	63.41	65.46	67.27	0.0004
1985	71.25	70.99	70.66	73.53	72.08	0.3438
Height (cm)						
1962	162.34	161.61	161.15	161.88	161.32	0.2809
1985	161.25	160.24	159.58	160.20	159.16	0.0102
Quetelet Index (kg/cm^2)						
1962	23.68	24.01	24.40	25.02	25.88	0.0001
1985	27.42	27.66	27.71	28.65	28.49	0.0634
Triceps skinfold thickness (mm)						
1962	24	24	25	26	27	0.0108
1985	26	25	25	26	24	0.0883

* The sum of scores variable was the sum of the scores for all 32 joints of the hands and wrists (see Table 1 and Subjects and Methods for details). Numbers in parentheses are actual score cut points. The *P* values describe the probability that the trend is the result of chance.

Table 6. Mean bone mass measures associated with the 1985 sum of scores quintiles, adjusted for age, in women designated radiologically free of osteoarthritis in 1962*

Characteristic	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	*P*
Medullary width (cm)						
1962	0.31	0.28	0.28	0.28	0.27	0.0756
1985	0.37	0.36	0.36	0.36	0.36	0.8712
Difference	0.06	0.08	0.08	0.08	0.09	<0.0186
Periosteal width (cm)						
1962	0.80	0.80	0.80	0.80	0.79	0.5908
1985	0.81	0.81	0.81	0.81	0.80	0.4743
Difference	0.01	0.01	0.01	0.01	0.01	0.8169
Cortical area (cm^2)						
1962	0.39	0.41	0.41	0.41	0.41	0.0298
1985	0.35	0.36	0.35	0.35	0.34	0.2628
Difference	−0.04	−0.05	−0.06	−0.06	−0.07	<0.0137

* The sum of scores variable was the sum of the scores for all 32 joints of the hands and wrists (see Table 1 and Subjects and Methods for details). The *P* values describe the probability that the trend is the result of chance.

having OA of the hand in 1985 (by either the maximum joint score or quintiles of the sum of joints score) had a greater mean metacarpal bone mass 2 decades earlier. Furthermore, women with OA appeared to have lost more metacarpal bone mass over the 2 decades than women who did not have OA.

The observation of greater bone mass 20–23 years prior to classification as having OA may support one of Radin's contentions (9), that OA may arise, at least in part, because the more mineralized bone fails to deform on impact, damaging the cartilage. Of course, this hypothesis was related to weight-bearing joints, and OA of the hand may be a limited surrogate in which the hypothesis can be tested. Furthermore, these data do not resolve the issue of whether greater bone mass in mid-life is causally related to OA in the elderly. Potentially, an undescribed metabolic environment, such as obesity, led to increased bone mass, which, in turn, resulted in joint deterioration. The metabolic environment is only crudely approximated by the body weight value.

A number of events might promote greater loss of bone mass among women once OA is established. Women with increasing joint involvement may become less active, resulting in bone demineralization associated with disuse. Women with OA may also be using over-the-counter or prescription medications to treat pain; such preparations may have an impact on bone mass. Finally, underlying metabolic activity may negatively influence both cartilage and bone mass simultaneously. For example, recent studies of interleukin-1, a cytokine, suggest an effect on collagen metabolism in cartilage explant cultures by limiting the formation of type II collagen in the chondrocyte (20,21). Studies of interleukin-1 therapy suggest that high doses or prolonged therapy can inhibit collagen synthesis (22). Studies in bone mass tissue culture systems also suggest the potential for an uncoupling of the bone resorption–formation process in association with interleukin-1 (23).

Clinically, this study suggests that women with OA should not be considered free of risk for bone mass loss. This loss could be associated with increased risk of fracture, particularly in those women who do not have increased body size as a protective factor.

The study has several limitations. Variations in film exposure/development and the shortcomings of using a scalar system for various opacities of radiographs (24) are overcome with the use of medullary and cortical diameters of the metacarpal midpoints. These measurements reflect distance between landmarks, rather than film opacity, as a measure of bone mass. Thus, our data reflect area measurements as an index of bone mass, rather than a direct estimate of bone density. Nevertheless, great skill and concentration is necessary for the radiograph reader to consistently locate edges that are poorly demarcated. Additionally, constant monitoring of reader "drift," data consistency, and film quality is necessary to generate accurate data.

While using radiographs to estimate bone mass would be considered technologically inappropriate considering the availability of dual-photon and dual–x-ray bone densitometry techniques, it is the only method available to characterize the longitudinal relationship between bone mass and osteoarthritis. This is particularly relevant in describing general populations and trying to minimize selection biases associated with clinical samples.

The data are limited to 2 points in a time period which encompasses the menopause. Additional data points might allow us to determine whether interim events are associated with substantial bone loss in woman with various degrees of OA.

The measures of both bone mass and OA are based on hand radiographs. The literature suggests that the relationship between osteoarthritis and osteoporosis may be modified by disease site or type of bone involved. The characteristics observed in the hand may be different from those in the hip, spine, or knee.

This research suggests a variety of issues to explore relative to bone mass and OA. For example, future studies might investigate whether those hormonal characteristics associated with bone mass maintenance, such as perimenopausal estrogen use or early ovarian failure, are different in women who have OA. Certainly, clinical studies of medications for the treatment of osteoarthritis should include bone mass evaluation using sensitive technology such as dual-x-ray densitometry. Finally, studies of the underlying metabolic processes associated with arthritic inflammation should also consider evaluation for impact on bone.

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