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ORIGINAL ARTICLE

Epidemiology of lumbar osteoporosis and osteoarthritis and their causal relationship—is osteoarthritis a predictor for osteoporosis or vice versa?: The Miyama study

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Abstract
Summary In a 10-year follow-up of a population-based cohort of Japanese subjects, incidences of and causal relationships between osteoporosis (OP) and osteoarthritis (OA) at the lumbar spine were clarified. OP might reduce the risk of subsequent OA at the spine in women, but not in men.
Introduction The aim of this study is to clarify the contribution of osteoarthritis (OA) to osteoporosis (OP) and vice versa.
Methods A population-based, epidemiological study was conducted in a Japanese rural community. From 1,543 participants aged 40–79 years, 200 men and 200 women were selected and followed up for 10 years. Bone mineral density measurements were repeated after 3, 7, and 10 years, and X-rays were repeated after 10 years.
Results The incidence of lumbar OP per 10,000 person-years for persons in their 40s, 50s, 60s, and 70s was 0, 0, 109.5, and 151.1 for men and 124.2, 384.0, 227.3, and 239.5 for women, respectively. The cumulative incidence of lumbar OA over 10 years aged 40–79 years was 25.8% in men and 45.2% in women. Cox's proportional hazards model showed no significant relationship between the presence of lumbar OA at the baseline and incidence of lumbar and femoral neck OP in both genders. A significant relationship was demonstrated between the presence of lumbar OP, not femoral neck OP, at the baseline and cumulative incidence of lumbar OA in women (odds ratio, 0.20; 95% confidence interval, 0.05–0.80; P=0.02).
Conclusion OP in women appears to reduce the future incidence of OA at the lumbar spine.

Keywords Causal relationship · Disc space narrowing · Incidence · Population-based cohort · Prevalence · Risk factors

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Introduction

As the proportion of aging population rapidly increases, the strategy for disease prevention is changing from simply extending life expectancy to extending healthy life expectancy in Japan. Thus, there is an urgent need for the development of methods for preventing musculoskeletal disorders that impair activities of daily life (ADL) and quality of life (QOL) in the elderly. Osteoporosis (OP) and osteoarthritis (OA) are two major bone and joint health problems among the elderly that cause impairment of ADL and QOL, leading to increased morbidity and mortality. The estimated number of patients with OP in Japan is about 11 million [1], and the prevalence of this disease is the highest among bone metabolic diseases. Hip fracture is the most severe complication of OP, and is ranked third among diseases responsible for bedridden status, according to the National Livelihood Survey of the Ministry of Health, Labour and Welfare in Japan [2]. OP also increases mortality rate [3, 4]. The number of patients with OA has rapidly increased, and OA is now ranked second among the causes of disabilities requiring support for ADL in Japan [2].

Some studies have reported an inverse relationship between OP and OA [5–7]. A higher bone mineral density (BMD) in lumbar OA is well documented [8–11]. A decrease in the amount of bone in OP and the formation of bone spurs and increased amounts of bone in OA are evident from BMD measurements; radiography also reveals the opposing features of these two diseases. According to epidemiological studies, risk factors for the two diseases are in opposition. For example, low body weight is a risk factor for OP [12, 13], whereas high body weight represents a risk factor for OA [14, 15].

In contrast to previous opinions, however, recent studies have indicated the association of osteoporotic fractures with lumbar OA. Thus, narrowing of the intervertebral disc space was suggested to increase the risk of osteoporotic vertebral fractures [16, 17]. Although these results imply that lumbar OA should cause osteoporotic fractures, causal relationships between OP itself (not only osteoporotic fractures) and OA at the same site remain obscure. It is uncertain if OA causes OP, OP causes OA, the conditions only coexist, or OP and OA represent concomitant modifications of each other.

To clarify the contribution of OA to OP and vice versa in the general population, a 10-year follow-up study was performed on a cohort established in Miyama village, a rural Japanese community.

Materials and methods

Establishment of baseline cohort

This population-based, epidemiological study was initiated in 1990 in Miyama, a mountain village in Wakayama Prefecture, Japan. As the Miyama cohort has been profiled in detail elsewhere [18, 19], characteristics of the participants are briefly summarized here. A list of all inhabitants born in this village from 1910 to 1949, and therefore aged 40 to 79 years, was compiled from the register of residents as of the end of 1989. A total cohort of 1,543 inhabitants (716 men, 827 women) was identified, and all members of the cohort completed a self-administered, 125-item questionnaire addressing topics such as dietary habits, smoking habits, alcohol consumption, and physical exercise.

A baseline BMD cohort was recruited from the total cohort, consisting of 400 participants divided into four groups each of 50 men and 50 women and stratified into age decades by year of birth (1910–1919, 1920–1929, 1930–1939, and 1940–1949). An interviewer administered a second questionnaire to these 400 participants, covering items of past medical history including questions related to osteoporotic fractures and falls, family history, calcium intake, dietary habits, physical exercise, occupational activities, sun exposure, and, for women, additional questions about reproductive variables. In addition to the baseline questionnaire survey, physical measurements were performed for participants including height (centimeter), body weight (kilogram), arm span (centimeter), bilateral grip strengths (kilogram) and circumstances of both wrists (centimeter), and body mass index (kilogram per square meter). These questionnaire surveys and measurements were repeated on the same 400 participants after 3, 7, and 10 years (1993, 1997, and 2000, respectively).

BMD measurements

The baseline BMD was measured in 1990 by dual energy X-ray absorptiometry (DXA; Lunar DPX, GE Medical Systems, Madison WI, USA), which provided anteroposterior images of lumbar vertebrae (L2–4) and the proximal femur (femoral neck, Ward's triangle, trochanter). These measurements were repeated on the same participants after 3, 7, and 10 years.

To control the precision of DXA, the equipment was checked at every examination in 1990, 1993, 1997, and 2000 using the same phantom. The BMD of the phantom was regulated to 1.270 ± 0.025 g/cm^2 (2%) during all examinations. In addition, the same physician (N.Y.) examined all participants in order to control observer variability. Intra-observer variability of DXA using the Lunar DPX in vitro and in vivo had been measured by the same physician for another study [20], and the coefficient of variance (CV) for L2–4 in vitro was 0.35%. The CV for L2–4, the proximal femur, Ward's triangle, and the trochanter examined in vivo in five male volunteers was 0.61–0.90%, 1.02–2.57%, 1.97–5.45%, and 1.77–4.17%, respectively.

OP was defined based on World Health Organization (WHO) criteria, in which OP was diagnosed mainly by that T-scores of BMD were lower than peak bone mass −2.5 standard deviations (SD) [21]. Mean L2–4 BMD for young adult men and women measured by Lunar DXA in Japan is 1.192 g/cm^2 while the SD is 0.146 g/cm^2 [22]. The present study therefore defined OP at the lumbar spine as L2–4

BMD <0.827 g/cm^2. Mean femoral neck BMD for young adult women measured by Lunar DXA in Japan is reportedly 0.914 g/cm^2 and the SD is 0.119 g/cm^2 [22]. OP at the femoral neck in women was defined as femoral neck BMD <0.617 g/cm^2. We could not define OP at the femoral neck in men because there was no reported mean femoral neck BMD for young adult men measured by Lunar DXA in Japan.

Radiography

The spine of each participant was examined by radiography in 1990. Diagnoses were based on anteroposterior and lateral images of thoracolumbar vertebrae Th5–L5 (initial X-ray survey). Radiography was repeated for individuals who provided consent after 10 years. Lateral images of thoracolumbar vertebrae Th5–L5 were again used for diagnosis (second X-ray survey).

Anteroposterior and lateral radiographs were scored for OA of the lumbar spine in L1–L5 using the Kellgren–Laurence (KL) grade as follows: KL0, normal; KL1, slight osteophytes; KL2, definite osteophytes; KL3, disc space narrowing with large osteophytes; KL4, bone sclerosis, disc space narrowing, and large osteophytes [23]. In the present study, we defined the lumbar spine with disc space narrowing with and without osteophytes as KL3. KL grade was determined at intervertebral spaces from L1/2 to L5/S1, and the highest score among all intervertebral spaces was then identified as the KL grade for that individual. KL scores of all radiographs were determined by a well-experienced orthopedist (S.M.).

Lateral radiographs of the spine were also utilized for the diagnosis of morphometric vertebral fracture (VFx) between Th5 and L5 using the criteria defined by the Japan Bone and Mineral Society as follows: wedged VFx, anterior height/posterior height ≤0.75; biconcave VFx, central height/anterior height or posterior height ≤0.80; compound VFx, anterior/anterior, central/central, and posterior/posterior height of sequential lower or upper vertebra ≤0.80 [24]. Diagnosis of VFx on all radiographs was performed by the same orthopedist (H.K.).

Detection of incidence of OP and OA

Incidence of OP over 10 years was calculated utilizing the results of BMD measurements at the baseline and follow-up studies after 3, 7, and 10 years. It was obtained by the following formula: the total number of incident cases with new OP divided by totaling the person-years of 'population at risk' at baseline. Population at risk refers to a group of participants having the potential of developing OP. Therefore, individuals with OP at the lumbar spine and femoral neck in the initial survey (lumbar spine, 13 men, 63 women; femoral neck, 46 women) were excluded from the numerators and denominators. To calculate the person-years, information on the drop-out (death or movement from the town) of participants was collected every year.

The cumulative incidence of OA over 10 years was calculated utilizing the diagnosis results. Cumulative incidence is simply defined as the ratio of incident cases to the population at risk at the beginning of the observation period. In the present study, we defined incident OA at the lumbar spine as KL grade ≥3 over 10 years in an individual whose KL grade ≤2 at the baseline.

The cumulative incidence of lumbar OA was determined by the following formula: individuals who developed new lumbar OA over 10 years/population at risk at the baseline. Individuals with existing lumbar OA with KL grade ≥3 at the baseline (69 men, 70 women) were excluded from both numerators and denominators.

Statistical analysis

All statistical analyses were performed using STATA statistical software (STATA Corp., College Station, TX, USA). Differences were tested for significance using ANOVA for comparison among multiple groups and using Scheffe's LSD test for pairs of groups. Significant items were selected, and multiple regression analysis was performed with adjustment of suitable variables.

To clarify the causal relationship of lumbar OA with OP, we applied Cox's proportional hazards model and calculated hazard ratio, in which the incidence of OP was used as an objective factor and lumbar OA at the baseline (1, yes vs. 0, no) was used as an explanatory factor. Next, to clarify the causal relationship of lumbar OA with osteoporotic fractures, we used logistic regression analysis using the cumulative incidence of morphometric VFx over 10 years (1, yes vs. 0, no) as an objective factor and lumbar OA at the baseline (1, yes vs. 0, no) as an explanatory factor, and obtained odds ratio (OR).

Furthermore, logistic regression analysis was used to assess causal relationships of: (a) OP at the lumbar spine and femoral neck with OA; (b) BMD at the lumbar spine L2–4 and femoral neck with OA; and (c) VFx with OA. In the analysis of OP and OA, we calculated the OR using the cumulative incidence of lumbar OA over 10 years (1, yes vs. 0, no) as an objective factor and OP at the baseline (1, yes vs. 0, no) as an explanatory factor. In the analysis of L2–4 and femoral neck BMD and OA, we calculated the OR using the cumulative incidence of lumbar OA over 10 years (1, yes vs. 0, no) as an objective factor and crude BMD values of the L2–4 and femoral neck at the baseline (vs. +1 SD) as an explanatory factor. Finally, in the analysis of VFx and OA, we obtained the OR using the cumulative incidence of lumbar OA over 10 years (1, yes vs. 0, no) as an objective factor and the presence of VFx at the baseline (1, yes vs. 0, no) as an explanatory factor.

All data were analyzed in each gender group after adjustment for age and weight at the baseline.

Results

Eligible participants

A baseline BMD cohort comprising 400 participants was selected from the total cohort of 1,543 inhabitants. Characteristics of this baseline BMD cohort including anthropometric factors and BMD are shown in Table 1. Height, weight, and the body mass index (BMI; weight (kg)/(height (m))^2) for persons in their 70s were smaller than those for persons in their 40s and 50s for both men and women. BMD at the lumbar spine was significantly lower in men in their 60s and 70s than in their 40s. BMD at the lumbar spine in women tended to be lower with an increase in age and was significantly lower for women in their 50s, 60s, and 70s than in their 40s.

Of the 400 participants in the initial BMD examination, 390 provided written informed consent to participate in the initial X-ray survey (194 men, 196 women; 97.5%). Figure 1 shows the distribution of KL grades at the baseline for participants according to gender. The prevalence of KL grade ≥2 was 81.3% in men and 62.2% in women, and that of KL grade ≥3 was 35.8% in men and 35.7% in women.

Radiographic surveys after 10 years were performed for 299 (137 men, 162 women; 74.8%) of the 400 inhabitants. Data from 101 participants (63 men, 38 women) were unavailable due to the following reasons: 55 participants died (37 men, 18 women); 16 moved (eight men, eight women); 13 were ill (four men, nine women); eight were busy (eight men); five declined to participate any further (five men); and four were absent from the area during the follow-up study (one man, three women).

A comparison of physical characteristics between completers and non-completers of the study has been described elsewhere [25] and is briefly summarized here. The height, weight, and BMI classified in terms of age group and gender were identical between completers and non-completers. In addition, the mean age of female completers in their 70s was significantly lower than that of female non-completers (mean (SD) of completers vs. mean (SD) of non-completers, 71.7 (1.8) years vs. 75.1 (2.8) years; $P<0.001$).

Prevalence of lumbar OP and OA and changes over 10 years

Table 2 shows the prevalence of lumbar OP and OA at the time of baseline measurements. Prevalence of lumbar OP in 1990 (baseline) and 2000 (over 10 years) were both significantly higher in women than men ($P<0.001$), while no significant difference was seen in the prevalence of lumbar OA in 1990 and 2000 between men and women. Prevalence of lumbar OP gradually increased with age in both men and women ($P<0.01$). However, age was not associated with the prevalence of lumbar OA in either men or women except female prevalence of lumbar OA in 2000 ($P<0.01$).

We then examined the prevalence of lumbar OP in the same age group of men and women in 2000, which was compared with that in 1990. Prevalence of lumbar OP in 1990 in the age group of 50–79 years was 8.7% in men

Table 1 Characteristics of the participants at the baseline measurement

Birth cohort	Age strata	N	Age (years)	Height (cm)	Weight (kg)	BMI (kg/m^2)	BMD (g/cm^2)
Men							
Total	40–79	200	58.9 (3.1)	160.9 (6.9)	57.6 (9.4)	22.1 (2.7)	1.11 (0.21)
1940–1949	40–49	50	44.2 (3.1)	165.6 (6.8)	63.6 (9.3)	23.1 (2.5)	1.19 (0.17)
1930–1939	50–59	50	54.1 (2.7)[a]	161.4 (5.7)[a]	59.5 (8.4)	22.8 (2.5)	1.15 (0.19)
1920–1929	60–69	50	63.4 (2.7)[a,b]	159.9 (5.5)[a]	56.1 (7.6)[a]	21.9 (2.4)	1.03 (0.18)[a,b]
1910–1919	70–79	50	73.9 (3.0)[a,b,c]	156.9 (6.8)[a,b]	51.0 (7.6)[a,b,c]	20.7 (2.7)[a,b]	1.06 (0.25)[a]
Women							
Total	40–79	200	59.3 (11.0)	148.3 (6.0)	48.8 (8.3)	22.1 (2.9)	0.95 (0.23)
1940–1949	40–49	50	44.7 (3.0)	152.4 (4.7)	53.2 (8.4)	22.8 (2.8)	1.18 (0.16)
1930–1939	50–59	50	54.8 (2.5)[a]	149.8 (5.3)	50.6 (7.4)	22.5 (2.7)	0.99 (0.18)[a]
1920–1929	60–69	50	64.3 (2.7)[a,b]	147.2 (5.0)[a]	47.1 (7.2)[a]	21.7 (3.1)	0.84 (0.19)[a,b]
1910–1919	70–79	50	73.3 (2.9)[a,b,c]	143.9 (5.7)[a,b,c]	44.5 (7.5)[a,b]	21.4 (2.9)[a,b]	0.78 (0.17)[a,b]

Data are means±SD

BMI body mass index, *BMD* bone mineral density

[a] Significantly different from values of the birth cohort group born in 1940–1949

[b] Significantly different from values of the birth cohort group born in 1930–1939

[c] Significantly different from values of the birth cohort group born in 1920–1929

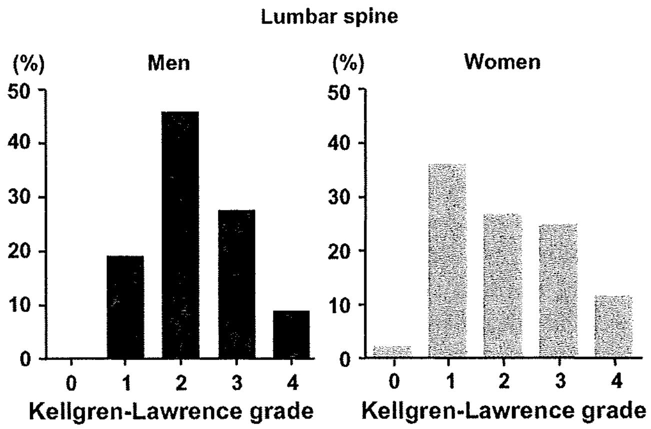

Fig. 1 Distribution of Kellgren–Lawrence grades at the lumbar spine by gender at the baseline in the Miyama population

and 42.0% in women and that in 2000 was 7.8% in men and 37.0% in women. Prevalence of lumbar OP in 2000 in the age group of 50–79 years tended to decrease compared with that in 1990 in both men and women, but no significant differences were identified (men P=0.81, women P=0.39).

Similarly, the prevalence of lumbar OA between the same age group of men and women in 2000 was compared with that in 1990. Prevalence in the age group of 50–79 years was 34.0% in men and 38.5% in women in 1990 and that in the same age group was 51.0% in men and 48.9% in women in 2000. Prevalence of lumbar OA in 2000 in the age group of 50–79 years increased in men and women compared with that in 1990, with significant differences in men (men P<0.01, women P=0.08).

Incidence of OP and cumulative incidence of OA at the lumbar spine

Figure 2 shows the incidence of lumbar OP in male and female participants of the cohort over 10 years. Incidence in men and women aged 40–79 years was 55.6 and 231.7 per 10,000 person-years, respectively. This means the annual incidence of lumbar OP among women is more than four times that of men.

The incidence of lumbar OP in men in their 40s, 50s, 60s, and 70s was 0, 0, 109.5, and 151.1 per 10,000 person-years, respectively, with the highest peak in the oldest group. In contrast, the incidence of lumbar OP in women in their 40s, 50s, 60s, and 70s was 124.2, 384.0, 227.3, and 239.5 per 10,000 person-years, respectively, with the highest peak for women in their 50s, the peri- and early postmenopausal periods, and another mild peak in the oldest group (Fig. 2). Incidence of OP at the femoral neck in women in their 40s, 50s, 60s, and 70s was 80.5, 221.9, 205.8, and 338.2 per 10,000 person-years, respectively, with the highest peak in the oldest age group and the second peak in their 50s.

The cumulative incidence of lumbar OA over 10 years aged 40–79 years was 25.8% in men and 45.2% in women. That for persons in their 40s, 50s, 60s, and 70s was 18.5%, 20.0%, 27.6%, and 37.9% for men and 37.1%, 53.6%, 48.4%, and 43.8% for women, respectively (Fig. 3). The cumulative incidence of lumbar OA tended to increase with age in men but not in women. The peak of the cumulative incidence of lumbar OA as well as that of lumbar OP in women was shown in the perimenopausal stratum. The cumulative incidence of lumbar OA was significantly higher in women than in men (P<0.05).

Table 2 Change of prevalence of osteoporosis and osteoarthritis at the lumbar spine over 10 years

Birth cohort	Baseline study					Follow-up study over 10 years			
	Age strata (years)	Number of participants (BMD)	Number of participants (X-ray)	Prevalence (%)		Age strata (years)	Number of participants	Prevalence (%)	
				Osteoporosis	Osteoarthritis[a]			Osteoporosis	Osteoarthritis[a]
Men									
Total	40–79	200	194	6.5	35.8	50–89	137	11.7	55.4
1940–1949	40–49	50	47	0.0	41.3	50–59	36	0.0	51.4
1930–1939	50–59	50	48	0.0	23.9	60–69	41	0.0	43.3
1920–1929	60–69	50	50	12.0	39.6	70–79	38	23.7	57.6
1910–1919	70–79	50	49	14.0	38.3	80–89	22	31.8	68.8
Women									
Total	40–79	200	196	31.5	35.7	50–89	162	42.6	54.1
1940–1949	40–49	50	48	0.0	27.1	50–59	49	12.2	35.4
1930–1939	50–59	50	49	18.0	42.9	60–69	46	45.7	50.0
1920–1929	60–69	50	50	48.0	38.0	70–79	40	57.5	64.1
1910–1919	70–79	50	49	60.0	34.7	80–89	27	70.4	83.3

[a] Osteoarthritis at the lumbar spine was defined as the KL grade ≥3

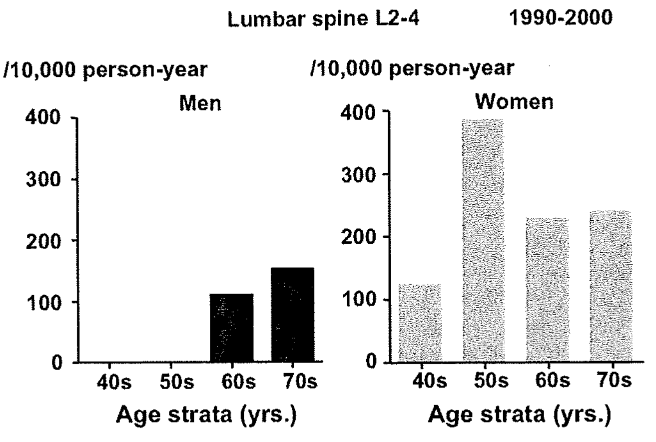

Fig. 2 Incidence of osteoporosis at the lumbar spine over 10 years by age group and gender

Causal relationship between OP and OA

The causal relationships between lumbar OA and OP, BMD, and VFx are summarized in Table 3.

First, the contribution of OA to OP was assessed. Cox's proportional hazard model showed no significant relationship between the presence of lumbar OA at the baseline and incidence of lumbar and femoral neck OP (lumbar OP, men P=0.71, women P=0.79; femoral neck OP, women P=0.52). Then, the association between lumbar OA and the cumulative incidence of VFx was determined by logistic regression analysis. As reported elsewhere, the cumulative incidence of VFx including subjects with previous VFx in their 40s, 50s, 60s, and 70s was 2.1%, 8.3%, 10.0%, and 12.2% for men and 2.1%, 6.1%, 18.0%, and 22.0% for women, respectively [26]. There was no significant relationship between the presence of lumbar OA at the baseline and incidence of VFx in men and women (men P=0.21, women P=0.64).

Secondly, the contribution of OP to OA was examined (Table 3). A significant relationship existed between the presence of lumbar OP at the baseline and cumulative incidence of lumbar OA in women (P<0.05) but not in men (P=0.07). Similarly, there was significant association between lumbar BMD at the baseline and the cumulative incidence of lumbar OA in women (vs. +1 SD, P<0.05) but not in men (P=0.25). No significant association was identified between femoral neck OP and BMD at the baseline and cumulative incidence of lumbar OA in men and women (OP at femoral neck, women P=0.32; BMD at femoral neck, vs. +1 SD, men P=0.23, women P=0.77). These results indicate that the presence of lumbar OP at the baseline would prevent the occurrence of lumbar OA, and conversely, high lumbar BMD would accelerate the progression of lumbar OA in women.

Finally, the association between the presence of VFx at the baseline and cumulative incidence of lumbar OA was assessed. As shown elsewhere, the prevalence of VFx in the present cohort among men in their 40s, 50s, 60s, and 70s was 4.3%, 14.6%, 22.0%, and 24.5% and that among women was 2.1%, 10.2%, 14.0%, and 44.9%, respectively [27]. Logistic regression analysis showed that there was no significant relationship between the presence of previous VFx and the incidence of lumbar OA in men and women (men P=0.72, women P=0.91; Table 3).

Discussion

The present study is a 10-year follow-up study of a population-based cohort of Japanese middle-aged people and elderly who were assessed for lumbar OP and OA. We clarified the prevalence of lumbar OP and OA and its trend of changes as well as the incidence of lumbar OP and cumulative incidence of lumbar OA. As for causal relationship, the presence of lumbar OA did not increase the risk of lumbar OP in both genders. However, the presence of lumbar OP significantly reduced the risk of lumbar OA, and high lumbar BMD values would accelerate the occurrence of lumbar OA over 10 years in women, while the presence of OP and BMD at the femoral neck did not influence the occurrence of lumbar OA.

The prevalence of lumbar OP in both 1990 and 2000 was significantly higher in women than in men (P<0.001) and gradually increased with age. Regarding the trend of changes in the prevalence of lumbar OP between 1990 and 2000 in same-age groups, no significant difference was shown in both men and women. We previously reported that both men and women in later birth cohorts showed higher BMDs in their middle age in this cohort [25]. However, we failed to clarify any significant decrease in the prevalence of lumbar OP in same-age groups of younger birth cohorts in the present study, although the prevalence

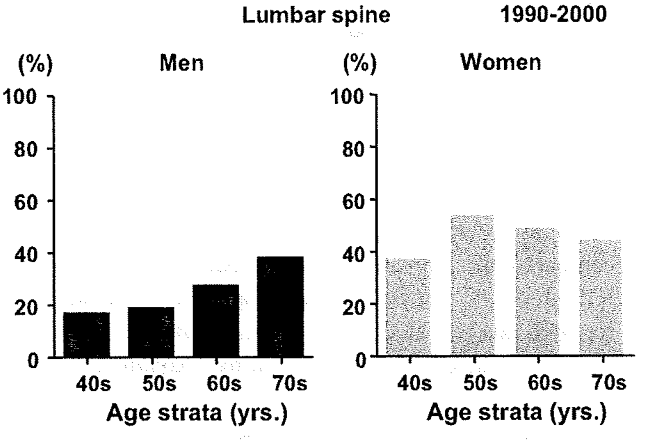

Fig. 3 Cumulative incidence of osteoarthritis at the lumbar spine over 10 years by age group and gender

Table 3 Causal relationship between osteoporosis (OP) and osteoarthritis (OA)

Baseline	Outcome	Reference	Gender	Risk ratio	95% CI	*P* value
Contribution of OA to OP						
OA at lumbar spine	Incidence of OP at lumbar spine	Yes/No	Men	HR 0.76	0.19–3.15	0.71
			Women	HR 0.90	0.40–1.99	0.79
OA at lumbar spine	Incidence of OP at femoral neck	Yes/No	Women	HR 0.74	0.30–1.84	0.52
OA at lumbar spine	Cumulative incidence of VFx	Yes/No	Men	OR 0.41	0.10–1.64	0.21
			Women	OR 1.27	0.46–3.47	0.64
Contribution of OP to OA						
OP at lumbar spine	Cumulative Incidence of OA at lumbar spine	Yes/No	Men	OR 8.68	0.82–92.3	0.07
			Women	OR 0.20	0.05–0.80	0.02
OP at femoral neck	Cumulative Incidence of OA at lumbar spine	Yes/No	Women	OR 0.52	0.14–1.89	0.32
BMD at lumbar spine	Cumulative incidence of OA at lumbar spine	+1 SD	Men	OR 0.80	0.54–1.17	0.25
			Women	OR 1.87	1.16–2.99	0.01
BMD at femoral neck	Cumulative incidence of OA at lumbar spine	+1 SD	Men	OR 0.80	0.56–1.15	0.23
			Women	OR 0.92	0.53–1.60	0.77
VFx	Cumulative incidence of OA at lumbar spine	Yes/No	Men	OR 0.79	0.21–2.95	0.72
			Women	OR 0.91	0.19–4.36	0.91

All analyses were adjusted for age and weight at the baseline

OA at lumbar spine was defined as the KL grade ≥3

BMD bone mineral density, *VFx* vertebral fracture, *SD* standard deviation, *HR* hazard ratio, *OR* odds ratio, *CI* confidence interval

of lumbar OP in 2000 tended to be lower than that in 1990 for all identical age groups in women. This might be explained by the effect of the time gap between the decrease in BMD and occurrence of lumbar OP. Although higher BMD was observed in the middle-aged group, this might not influence epidemiological indices of lumbar OP such as prevalence within only a 10-year span. As participants become old enough to be expected to have lumbar OP, its prevalence is expected to decrease.

Contrary to lumbar OP, the prevalence of lumbar OA was not significantly different between men and women in 1990 and 2000, and age was not associated with the prevalence of lumbar OA except for women in 2000 ($P<0.01$). Regarding the trend of changes in the prevalence of lumbar OA between 1990 and 2000 in same-age groups, the prevalence of lumbar OA in 2000 was higher than that in 1990 in both men and women, with significance in men (men $P<0.01$, women $P=0.08$). Concerning the association between age and lumbar OA, Lawrence found that the radiological prevalence of disc degeneration in the lumbar spine in the age group of 35–45 years increased with age [28]. O'Neill et al. reported that the frequency of vertebral osteophytes increased with age [29]. We previously compared the prevalence of lumbar OA determined by KL grade ≥3 in British and Japanese populations and reported that prevalence was higher in Britain than in Japan [15]. The difference may be partly explained by ethnic variation.

To the best of our knowledge, the present study represents the first report on the incidence of lumbar OP in Japan. If the incidence obtained in this study is generalized to the current Japanese population in the age group of 40–79 years, 970,000 new cases of lumbar OP (160,000 men, 810,000 women) are estimated to occur annually. When classified by age, the incidence of lumbar OP in women was the highest in their 50s, followed by those in their 70s. We previously reported that the rate of change in lumbar spine BMD in women in the present population was the highest in their 50s [12, 25] and is related to the decrease in female hormones [30]. The present finding that the incidence of lumbar OP was the highest among women in their 50s suggests that the incidence of lumbar OP is closely related to the menstrual status, particularly menopause, and rate of change in lumbar spine BMD. Since more than 2.2% of women are estimated to develop lumbar OP annually in their 60s and 70s (ages at which the effects of menopause are thought to be attenuated), measures for preventing lumbar OP among the elderly as well as women during perimenopause are urgently required. The annual incidence of lumbar OP among men in their 60s and 70s was more than 1.0%. Although this incidence is lower than that among women, it is estimated that 160,000 male cases occur annually as previously mentioned, which nevertheless should not be ignored. Predictors for finding early and/or potential lumbar OP in both women and elderly men need to be established immediately.

In addition, we determined the cumulative incidence of lumbar OA with disc space narrowing for the first time in Japan. The 10-year cumulative incidence of lumbar OA with KL grade ≥3 tended to increase with age in men, but not in women, and it was higher in women than in men. Few reports have described the incidence of lumbar OA in population-based cohorts. Hassett et al. showed that the progression rates for anterior osteophytes and disc space narrowing were 4% and 3% per year, respectively, among female participants in the Chingford study [31], which was approximately similar to the results of the present study. However, since epidemiological indices such as prevalence and incidence are highly dependent on the definition of OA, we cannot compare our results directly with those of other studies. For example, we defined lumbar OA as KL grade ≥3, which shows disc space narrowing with or without osteophytes, while the Chingford study determined lumbar OA based on the grading system of osteophytes and disc space narrowing reported by Lane et al. [32]. Since few reports have investigated the incidence of lumbar OA in the general population, further studies are needed to verify ethnic and geographical differences in the incidence of lumbar OA. When classified by age, the cumulative incidence of lumbar OA and OP was highest in women in their 50s during the early postmenopausal period. Therefore, it might be suggested that endogenous sex steroids play a role in the occurrence or progression of lumbar OA in women.

In some population-based prospective studies, OA of extremities was reported to increase the risk of osteoporotic fractures. In the Rotterdam study, knee OA increased the risk of vertebral and non-vertebral fractures [33]. Arden et al. reported that patients with knee OA and knee pain have an increased risk of hip and other non-vertebral fractures, which was not explained by the increased risk of falls [34]. Intervertebral disc space narrowing was found to increase the risk of VFx in the OFELY study [16, 17]. These findings suggest that OA is involved in the onset of fractures resulting from OP. Conversely, Roux et al. reported that intervertebral disc space narrowing and osteophytes decreased the prevalence of VFx in postmenopausal women with OP [35]. In the present study, there was no significant association between the presence of lumbar OA and future occurrence of lumbar OP and VFx. Lumbar OP is diagnosed by lumbar BMD (the value of which is easily affected by osteophytes and sclerosis of vertebrae and facets and the calcification of abdominal aorta [36]), which can artifactually increase BMD. Therefore, lumbar BMD might not be a good surrogate index of OP. As this is the first report about the causal relationship of lumbar OA and OP in the Japanese population, the difference might be partly due to the ethnic variation between Western and Oriental populations. Further studies are necessary to confirm the causal relationship of OA and OP in Japan and other countries.

Regarding the contribution of OP to OA, we elucidated that OP at the lumbar spine reduced the risk for the progression of lumbar OA in women while high BMD at the lumbar spine accelerated this progression. Zhang et al. found that higher BMD at the hip was associated with prevalent and incident knee OA in older women in the Framingham study [37]. They also found that increased BMD over the follow-up period indicated a high risk of incident knee OA [37]. Hart et al. confirmed that, for women that developed incident knee OA, BMD was higher in the Chingford study [38]. Although these studies reported findings on the BMD and OA at extremities, not the spinal OP and OA, our results were almost similar to those of the above-mentioned cohort studies. Further prospective cohort studies with a larger sample size and longer observational periods are required to conclude the causal relationship of OP and OA.

Contrary to lumbar OP, no causal relationship was observed between OP or BMD at the femoral neck and cumulative incidence of lumbar OA. This might be because OP was diagnosed at different sites, which might have diluted the influence of OA occurrence. This hypothesis will be clarified in a study of the association between OP at the femoral neck and hip OA.

The presence of VFx at baseline showed no association with occurrence of lumbar OA. The prevalence of VFx includes various causes, and not all VFx were caused by OP. The geographic area in which the present cohort was established is mountainous, and a significant number of male subjects worked in the forestry industry and had experienced falls from trees or down slopes accidentally. In addition, most participants with previous VFx at the baseline were old and did not complete the 10-year follow-up. This survival bias might have influenced the evaluation of the influences of VFx on occurrence of OA.

The inverse causal relationship between lumbar OP and OA was only observed in women, not in men. These gender differences might be explained partly by differences in the incidence of lumbar OP. The incidence in men in the present study might be insufficient to detect the causal relationship. Alternatively, differences in gender-dependent factors such as endogenous sex steroids could influence the association of OP and OA.

There are several limitations in this study. The primary limitation is that the cohort comprised a relatively small number of participants. We were able to follow male and female residents with confirmed regional representativeness for 10 years with a high participation rate of 74.8%. However, 101 participants were lost in the follow-up study during the 10 years. The main reason for them dropping out of the study was death. The mean age of women completers of the age group 70-79 was significantly younger than that of drop-outs. Therefore, the prevalence of lumbar OP and cumulative incidence of lumbar OA in this age group might be underestimated due to the effects of survival bias. A secondary limitation is related to the definition of lumbar OA. Cumulative incidence as used in the present study was detected by dividing the number of individuals who developed new lumbar OA by the number of participants in the follow-up study. Individuals with previous lumbar OA were excluded from both the numerators and denominators. In this formula, we excluded 69 male and 70 female participants with lumbar OA at the baseline to obtain the incidence of the first lumbar OA, which might reduce the total number of population at risk and cause a decrease in statistical power. Our result regarding lumbar OA incidence in the present study might need to be confirmed in larger population-based cohorts.

With the goal of elucidating the environmental and genetic background of bone and joint diseases represented by OA and OP, we established larger scale cohorts based on the present cohort, called Research on Osteoarthritis/ Osteoporosis Against Disability (ROAD), and have already started the follow-up study [39]. This enlarged population-based cohort study may confirm the consistency of epidemiological trends for OP and OA and clarify the causal relationship between these two major bone and joint diseases.

Conclusion

Based on observations from a population-based cohort over a 10-year period, the estimated incidence of OP at the L2–4 level of the lumbar spine per 10,000 person-years for men in their 40s, 50s, 60s, and 70s was 0, 0, 109.5, and 151.1 and that for women was 124.2, 384.0, 227.3, and 239.5, respectively. The cumulative incidence of lumbar OA over 10 years for men in their 40s, 50s, 60s, and 70s was 18.5%, 20.0%, 27.6%, and 37.9% for men and 37.1%, 53.6%, 48.4%, and 43.8% for women, respectively. Cox's proportional hazards model showed no significant relationship between the presence of lumbar OA at the baseline and future incidence of lumbar and femoral neck OP. A significant relationship existed between the presence of lumbar OP at the baseline and future incidence of lumbar OA in women (odds ratio 0.20, 95% confidence interval 0.05–0.80, $P<0.05$). It may be suggested that the presence of OA does not increase the risk of incident OP in both genders and that the presence of OP reduces the risk of incident OA at the spine in women.

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Conflicts of interest None.

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ORIGINAL ARTICLE

Association of Occupational Activity With Radiographic Knee Osteoarthritis and Lumbar Spondylosis in Elderly Patients of Population-Based Cohorts: A Large-Scale Population-Based Study

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Objective. To investigate the risk of radiographic knee osteoarthritis (OA) and lumbar spondylosis associated with occupational activity in elderly Japanese subjects using the large-scale population-based cohort of the Research on Osteoarthritis Against Disability (ROAD) study.
Methods. From the baseline survey of the ROAD study, 1,471 participants age ≥50 years (531 men and 940 women) living in mountainous and seacoast communities were analyzed. Information collected included a lifetime occupational history and details of specific work place physical activities. Radiographic severity at the knee and lumbar spine was determined by the Kellgren/Lawrence (K/L) grading system.
Results. The prevalence of K/L grade ≥2 knee OA and lumbar spondylosis among agricultural, forestry, and fishery workers was significantly higher than among clerical workers and technical experts in the overall population. For occupational activities, sitting on a chair had a significant inverse association with K/L grade ≥2 knee OA and lumbar spondylosis. Standing, walking, climbing, and heavy lifting were associated with K/L grade ≥2 knee OA, but were not associated with K/L grade ≥2 lumbar spondylosis. Kneeling and squatting were associated with K/L grade ≥3 knee OA.
Conclusion. This cross-sectional study using a population-based cohort suggests that sitting on a chair is a significant protective factor against both radiographic knee OA and lumbar spondylosis in Japanese subjects. An occupational activity that includes heavy lifting appears to have a greater effect on knee OA than on lumbar spondylosis.

INTRODUCTION

Osteoarthritis (OA) and spondylosis, which cause cartilage and disc degeneration and osteophyte formation at joints in the extremities and spine, are major public health issues causing chronic disability in the elderly in developed countries (1–6). Despite the urgent need for strategies to prevent and treat these conditions, epidemiologic data on OA and spondylosis are sparse. Established risk factors for knee OA in whites include older age, female sex, evidence of OA in other joints, obesity, and previous injury or surgery of the knee (7–12). Evidence is accumulating in whites that the disease is more common in people who have performed heavy physical work (13–18), particularly in those whose jobs have involved kneeling or squatting (19–24). However, published work has tended to concentrate on the knee, and few studies have focused on risk

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factors for lumbar spondylosis associated with occupational activity (25–28). In addition, there have been no large-scale population-based epidemiologic studies that have simultaneously evaluated the risk of both knee OA and lumbar spondylosis associated with occupational activity in the same population. Furthermore, most epidemiologic studies of OA and spondylosis associated with occupation are limited in terms of the quality of the information collected about occupational exposure. Occupational histories are not always complete, and exposure has often only been inferred from the subject's job title (13–18). To provide accurate data on the relationship of occupational activities with knee OA and lumbar spondylosis, collected information has to include a lifetime occupational history and details of specific work place physical activities.

With the goal of establishing epidemiologic indexes to evaluate clinical evidence for the development of disease-modifying treatment, we set up a large-scale nationwide OA cohort study called the Research on Osteoarthritis Against Disability (ROAD) study in 2005. In the present study, we used the data of participants living in mountainous and seacoast communities to investigate the association of job title and occupational activity with radiographic knee OA and lumbar spondylosis.

PARTICIPANTS AND METHODS

Participants. The ROAD study is a nationwide prospective study for bone and joint diseases consisting of population-based cohorts established in several communities in Japan. Because the Miyama cohort has been profiled in detail elsewhere (29), the characteristics of the participants are briefly summarized here. To date, we have created a baseline database including clinical and genetic information on 3,040 inhabitants (1,061 men and 1,979 women) ages 23–95 years (mean 70.6 years) who were recruited from listings of resident registrations in 3 communities. All participants provided written informed consent, and the study was conducted with the approval of ethical committees of the University of Tokyo and the Tokyo Metropolitan Institute of Gerontology. Information collected about job title and occupational activity included a lifetime occupational history with details of 7 types of specific work place physical activities, including sitting on a chair, kneeling, squatting, standing, walking, climbing, and heavy lifting. Participants were asked whether they engaged in the following activities: sitting on a chair for ≥2 hours/day, kneeling for ≥1 hour/day, squatting for ≥1 hour/day, standing for ≥2 hours/day, walking ≥3 km/day, climbing up slopes or steps for ≥1 hour/day, and lifting loads weighing ≥10 kg at least once a week. Information on these activities was obtained for the principal job, defined as the job at which the participant had worked the longest. Anthropometric measurements included height, weight, bilateral grip strength, and body mass index (BMI; weight [kg]/height [m^2]). All participants were interviewed regarding knee pain and low back pain by asking them. "In the past 1 month, have you had knee pain on most days lasting?" and "In the past 1 month, have you had low back pain on most days lasting?" Participants who answered yes were defined as having knee pain or low back pain, respectively. From the baseline data of all participants, the present study analyzed 1,471 participants (531 men and 940 women) age ≥50 years living in mountainous and seacoast cohorts.

Radiographic assessment. All participants had a radiographic examination of both knees using anteroposterior and lateral views with weight-bearing and foot map positioning, and an examination of the lumbar spine, including intervertebral levels from L1–L2 to L5–S1 with anteroposterior and lateral views. Knee and lumbar spine radiographs were read without knowledge of participant clinical status by a single well-experienced orthopedist (SM) using the Kellgren/Lawrence (K/L) radiographic atlas, and the severity was determined by K/L grading (30). We defined knee OA and lumbar spondylosis as a K/L grade ≥2 in at least one knee and in one intervertebral level, respectively.

To evaluate the intraobserver variability of K/L grading, 100 randomly selected radiographs of the knee and the lumbar spine were scored by the same observer more than 1 month after the first reading. One hundred other radiographs were also scored by 2 experienced orthopedic surgeons (SM, HO) using the same atlas for interobserver variability. The evaluated intra- and intervariability were confirmed by the kappa analysis to be sufficient for assessment (0.86 and 0.80 for knee OA, 0.84 and 0.76 for lumbar spondylosis, respectively).

Statistical analysis. The differences of age and BMI between men and women were examined by the unpaired t-test. To compare the prevalence of radiographic knee OA and lumbar spondylosis between men and women, we performed a logistic regression analysis after adjustment for age and BMI. The percentage of each occupational activity was compared between men and women by a chi-square test. To determine risk factors for knee OA and lumbar spondylosis with K/L grades ≥2 as well as K/L grades ≥3, logistic regression analyses were used to estimate the odds ratio (OR) and the associated 95% confidence interval (95% CI) for variables such as job title and occupational activities after adjustment for age and BMI compared with K/L = 0 or 1 (for K/L grades ≥2) and K/L = 0, 1, or 2 (for K/L grades ≥3). Furthermore, the overall population was classified into 4 subpopulation groups based on the presence or absence of knee OA and lumbar spondylosis, and a multinomial logistic regression analysis was performed to determine factors associated with knee OA, lumbar spondylosis, and their combination after adjustment for age, sex, and BMI. The subpopulation with neither knee OA nor lumbar spondylosis was used as a reference group. Data analyses were performed using SAS, version 9.0 (SAS Institute, Cary, NC).

RESULTS

Characteristics of the 1,471 participants age ≥50 years in the 2 cohorts of the ROAD study are shown in Table 1. The

Table 1. Characteristics of participants*

	Overall	Men	Women
No. of subjects	1,471	531	940
Age, years	68.4 ± 9.2	69.1 ± 9.1	68.0 ± 9.2†
Height, cm	154.3 ± 9.3	162.3 ± 7.1	149.8 ± 7.2
Weight, kg	55.2 ± 10.5	61.0 ± 10.3	51.8 ± 9.1
BMI, kg/m²	23.1 ± 3.3	23.1 ± 3.1	23.1 ± 3.5
Grip strength, kg	26.7 ± 9.3	34.7 ± 8.4	22.1 ± 6.1
K/L ≥2 knee OA, %	55.6	45.6	61.2‡
K/L ≥3 knee OA, %	23.0	16.8	26.5‡
K/L ≥2 lumbar spondylosis, %	65.3	79.1	57.6‡
K/L ≥3 lumbar spondylosis, %	38.7	38.8	38.7
Current smoker, no. (%)	169 (11.5)	140 (26.4)	29 (3.1)§
Current alcohol drinking, no. (%)	562 (38.2)	343 (64.6)	219 (23.3)§

* Values are the mean ± SD unless otherwise indicated. BMI = body mass index. K/L = Kellgren/Lawrence grading system; OA = osteoarthritis.
† $P < 0.05$ versus men by unpaired *t*-test.
‡ $P < 0.05$ versus men by logistic regression analysis after adjustment for age and BMI.
§ $P < 0.05$ versus men by chi-square test.

prevalence of K/L grade ≥2 and K/L grade ≥3 knee OA was significantly higher in women than in men, whereas that of K/L grade ≥2 lumbar spondylosis was significantly lower in women than in men. The prevalence of K/L grade ≥3 lumbar spondylosis was comparable between sexes.

There was great diversity in the job titles of the study participants (Table 2). Although a substantial proportion includes clerical workers and technical experts, there were many agricultural, forestry, and fishery workers. Among various occupational activities, agricultural, forestry, and fishery workers had the highest rates of kneeling, squatting, standing, walking, climbing, and lifting weights and the lowest rates of sitting on a chair, whereas clerical workers and technical experts had the lowest rates of kneeling, squatting, standing, walking, climbing, and lifting weights and the highest rates of sitting on a chair (Figure 1).

To determine factors associated with K/L grade ≥2 knee OA and lumbar spondylosis, we performed a logistic regression analysis to estimate ORs and 95% CIs (Tables 3 and 4). Analysis of job titles revealed that agricultural, forestry, and fishery workers had a significantly higher risk of knee OA and lumbar spondylosis compared with clerical workers and technical experts in the overall population. We then examined the association of occupational activities with knee OA and lumbar spondylosis (Tables 3 and 4). Sitting on a chair for ≥2 hours/day was a significant protective factor for knee OA and lumbar spondylosis

Table 2. Participants with job title and occupational activity reported as the principal job

	Overall	Men	Women
Job titles, no. (%)			
Clerical workers/technical experts	363 (24.7)	170 (32.0)	193 (20.5)
Agricultural/forestry/fishery workers	318 (21.6)	164 (30.9)	154 (16.4)
Factory/construction workers	153 (10.4)	68 (12.8)	85 (9.0)
Shop assistants/managers	132 (9.0)	25 (4.7)	107 (11.4)
Housekeepers	126 (8.6)	0 (0.0)	126 (13.4)
Teachers	82 (5.6)	42 (7.9)	40 (4.3)
Dressmakers	51 (3.5)	1 (0.2)	50 (5.3)
Clinical workers	41 (2.8)	1 (0.2)	40 (4.3)
Hairdressers	17 (1.2)	6 (1.3)	11 (1.2)
Others (cooks, taxi drivers, etc.)	72 (4.9)	22 (4.1)	50 (5.3)
No answer	116 (7.9)	32 (6.0)	84 (8.9)
Occupational activities, no. (%)			
Sitting on a chair ≥2 hours/day	657 (44.7)	254 (47.8)	403 (42.8)
Kneeling ≥1 hour/day	292 (19.9)	96 (18.1)	196 (20.9)
Squatting ≥1 hour/day	386 (26.2)	131 (24.7)	255 (27.1)
Standing ≥2 hours/day	1,235 (84.0)	456 (85.9)	779 (82.9)
Walking ≥3 km/day	673 (45.8)	268 (50.5)	405 (43.1)
Climbing ≥1 hour/day	346 (23.5)	185 (34.8)	161 (17.1)*
Lifting weights ≥10 kg at least once a week	788 (53.6)	347 (65.3)	441 (46.9)*

* $P < 0.05$ versus men by chi-square test.

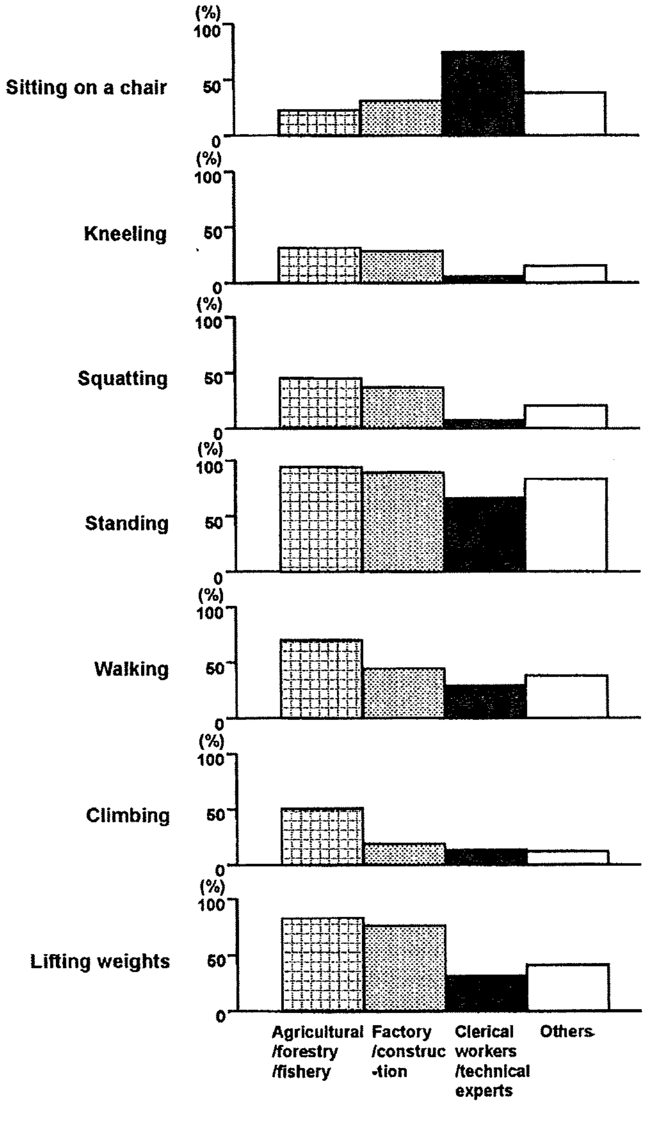

Figure 1. Percentages of participants engaged in each occupational activity: sitting on a chair ≥2 hours/day, kneeling ≥1 hour/day, squatting ≥1 hour/day, standing ≥2 hours/day, walking ≥3 km/day, climbing ≥1 hour/day, or lifting weights ≥10 kg at least once a week among agricultural, forestry, and fishery workers; factory and construction workers; clerical workers and technical experts; and others.

in the overall population and in men. Neither kneeling for ≥1 hour/day nor squatting for ≥1 hour/day was associated with knee OA in the overall population. Standing for ≥2 hours/day, walking ≥3 km/day, climbing for ≥1 hour/day, and lifting weights ≥10 kg at least once a week were significantly associated with knee OA in the overall population and in both sexes (Table 3). A multiple logistic regression analysis after adjustment for age, BMI, sex, and the above 4 occupational activities showed that climbing and lifting weights were significantly associated with knee OA overall (OR 1.65, 95% CI 1.18–2.32 and OR 1.51, 95% CI 1.16–1.95, respectively) and in men (OR 1.75, 95% CI 1.10–2.80 and OR 1.76, 95% CI 1.14–2.73, respectively), suggesting that among the 4 activities that required a standing position, climbing and lifting weights had an independent association with knee OA. In contrast, these occupational activities had no significant association with lumbar spondylosis except for lifting weights in women (Table 4).

We next performed a multinomial logistic regression analysis to determine factors associated with K/L grade ≥2 knee OA, lumbar spondylosis, and their combination after adjustment for age, sex, and BMI. Sitting on a chair was confirmed to be a significant protective factor for the presence of both knee OA and lumbar spondylosis (OR 0.62, 95% CI 0.45–0.86). Although neither kneeling nor squatting was associated with the presence of knee OA or lumbar spondylosis, standing (OR 2.03, 95% CI 1.32–3.12), walking (OR 1.56, 95% CI 1.12–2.17), climbing (OR 2.14, 95% CI 1.38–3.40), and lifting weights (OR 2.05, 95% CI 1.48–2.86) were associated with the presence of both knee OA and lumbar spondylosis. For the subpopulation group with knee OA and without lumbar spondylosis, standing (OR 1.69, 95% CI 1.04–2.79), climbing (OR 2.34, 95% CI 1.39–3.97), and lifting weights (OR 1.92, 95% CI 1.31–2.81) were also significantly associated, although there were no significant associations of the subpopulation group with lumbar spondylosis and without knee OA compared with the subpopulation group without knee OA or lumbar spondylosis.

We further analyzed the association of K/L grade ≥2 knee OA and lumbar spondylosis with job titles and occupational activities according to the presence of knee pain and low back pain at the baseline examination (Supplementary Tables A and B, available in the online version of this article at http://www3.interscience.wiley.com/journal/77005015/home). Although some of the job titles and occupational activities showed higher ORs in the subpopulation with knee pain, the direction of association was similar regardless of the presence of pain, and the results did not differ between the overall population and the subpopulation without knee pain or low back pain.

We next determined factors associated with K/L grade ≥3 knee OA and lumbar spondylosis using logistic regression analysis after adjustment for age and BMI. Analysis of occupational activities revealed that sitting on a chair was a significant protective factor for lumbar spondylosis in men (OR 0.58, 95% CI 0.40–0.84). In the overall population and in women, kneeling (OR 1.40, 95% CI 1.01–1.93 and OR 1.69, 95% CI 1.16–2.47, respectively), squatting (OR 1.34, 95% CI 1.00–1.80 and OR 1.51, 95% CI 1.06–2.15, respectively), and lifting weights (OR 1.60, 95% CI 1.21–3.12 and OR 1.73, 95% CI 1.25–2.43, respectively) were associated with knee OA. A multinomial logistic regression analysis also showed that sitting on a chair was a protective factor for the presence of both K/L grade ≥3 knee OA and lumbar spondylosis, as well as for the presence of lumbar spondylosis and the absence of knee OA in men (OR 0.46, 95% CI 0.23–0.87 and OR 0.63, 95% CI 0.42–0.94, respectively). Lifting weights (OR 1.57, 95% CI 1.10–2.23) was associated with the presence of both knee OA and lumbar spondylosis. For the subpopulation group with knee OA and without lumbar spondylosis, kneeling (OR 1.76, 95% CI 1.13–2.72), squatting (OR 1.85, 95% CI 1.23–2.77), and lifting weights (OR 1.77, 95% CI 1.19–2.65) were significantly associated, although there were no

Table 3. Association of K/L grade ≥2 knee OA with job title and occupational activity*

	Overall, OR (95% CI)	Men, OR (95% CI)	Women, OR (95% CI)
Job titles (vs. clerical workers/technical experts)			
Agricultural/forestry/fishery workers	1.69 (1.19–2.41)	1.58 (0.98–2.56)	1.90 (1.14–3.20)
Factory/construction workers	1.52 (0.99–2.36)	1.33 (0.72–2.47)	1.64 (0.90–3.06)
Other†	1.18 (0.88–1.60)	1.21 (0.73–2.00)	1.20 (0.82–1.76)
Occupational activities			
Sitting on a chair ≥2 hours/day	0.73 (0.57–0.92)	0.63 (0.44–0.92)	0.80 (0.60–1.09)
Kneeling ≥1 hour/day	1.11 (0.83–1.48)	0.79 (0.49–1.26)	1.36 (0.93–1.97)
Squatting ≥1 hour/day	1.23 (0.94–1.61)	0.89 (0.58–1.35)	1.50 (1.06–2.13)
Standing ≥2 hours/day	1.97 (1.43–2.72)	2.31 (1.32–4.17)	1.78 (1.21–2.63)
Walking ≥3 km/day	1.80 (1.42–2.29)	2.17 (1.49–3.16)	1.59 (1.17–2.16)
Climbing ≥1 hour/day	2.24 (1.65–3.04)	2.43 (1.64–3.60)	1.85 (1.19–2.96)
Lifting weights ≥10 kg at least once a week	1.90 (1.50–2.42)	2.26 (1.52–3.40)	1.68 (1.24–2.26)

* ORs were calculated by a logistic regression analysis after adjustment for age, sex, and BMI in the overall population, and for age and BMI in both sexes. K/L = Kellgren/Lawrence grading system; OA = osteoarthritis; OR = odds ratio; 95% CI = 95% confidence interval; BMI = body mass index.
† Includes all participants except for agricultural/forestry/fishery workers, factory/construction workers, and clerical workers/technical experts.

significant associations of the subpopulation group with lumbar spondylosis and without knee OA compared with the subpopulation group without knee OA or lumbar spondylosis.

DISCUSSION

Using baseline data from the ROAD study, the present investigation evaluated the risk of occupational activity for radiographic knee OA and lumbar spondylosis, and revealed that sitting on a chair was a significant protective factor for both radiographic knee OA and lumbar spondylosis in Japanese subjects. For other occupational activities, kneeling, squatting, standing, walking, climbing, and heavy lifting were significantly associated with radiographic knee OA, whereas there was no significant occupational activity for radiographic lumbar spondylosis in the overall population. To our knowledge, this is the first epidemiologic study using a large-scale population-based cohort to determine the risk of occupational activity for both knee OA and lumbar spondylosis simultaneously in the same population. Information on occupational activities was collected by direct inquiry rather than being inferred from the job title.

In the present study, agricultural, forestry, and fishery workers had a significantly higher prevalence of both radiographic knee OA and lumbar spondylosis compared with clerical workers and technical experts in the overall population. These jobs have historically been among the first to be identified in relation to knee OA in whites (31,32), which is also compatible with our data in this Japanese population. As other authors have hypothesized, the combination of intense exposure to heavy labor of varied nature and repeated local stresses, especially at a young age, could contribute to some systemic mechanism in the development of OA (33). This argument would support the implementation of preventive measures as a priority to reduce the intensity of physical labor in this sector, particularly for young male and female farm workers.

For occupational activities, standing, walking, climbing, and heavy lifting were associated with K/L grade ≥2 knee OA in the overall population, whereas kneeling and squat-

Table 4. Association of K/L grade ≥2 lumber spondylosis with job title and occupational activity*

	Overall, OR (95% CI)	Men, OR (95% CI)	Women, OR (95% CI)
Job titles (vs. clerical workers/technical experts)			
Agricultural/forestry/fishery workers	1.46 (1.02–2.11)	1.49 (0.83–2.68)	1.42 (0.89–2.28)
Factory/construction workers	1.05 (0.68–1.55)	1.52 (0.76–3.22)	0.84 (0.49–1.44)
Other†	1.22 (0.91–1.64)	1.53 (0.87–2.76)	1.11 (0.78–1.58)
Occupational activities			
Sitting on a chair ≥2 hours/day	0.78 (0.62–0.99)	0.48 (0.30–0.76)	0.93 (0.71–1.23)
Kneeling ≥1 hour/day	0.96 (0.72–1.28)	0.95 (0.55–1.70)	0.97 (0.70–1.35)
Squatting ≥1 hour/day	1.05 (0.81–1.38)	0.95 (0.58–1.61)	1.09 (0.80–1.48)
Standing ≥2 hours/day	1.11 (0.81–1.50)	1.14 (0.61–2.04)	1.10 (0.77–1.57)
Walking ≥3 km/day	1.00 (0.79–1.26)	0.89 (0.57–1.40)	1.04 (0.79–1.37)
Climbing ≥1 hour/day	1.02 (0.76–1.38)	1.09 (0.68–1.78)	0.98 (0.67–1.44)
Lifting weights ≥10 kg at least once a week	1.15 (0.91–1.45)	1.09 (0.69–1.72)	1.23 (1.01–1.55)

* ORs were calculated by a logistic regression analysis after adjustment for age, sex, and BMI in the overall population, and for age and BMI in both sexes. See Table 3 for definitions.
† Includes all participants except for agricultural/forestry/fishery workers, factory/construction workers, and clerical workers/technical experts.

Table 5. Comparison of characteristics of epidemiologic studies

Author, ref.	Ethnicity/country	Age, years	Total no.	Men:women
Muraki et al, current study	Japan	≥50	1,471	531:940
Yoshimura et al, 34	Japan	≥45	202	0:202
Lau et al, 35	Chinese		1,316	332:984
Anderson and Felson, 19	Blacks and whites/US	55–64	1,250	606:644
Felson et al, 20	Whites/US	≥63	1,376	569:807
Cooper et al, 21	UK	≥55	327	90:237
Coggon et al, 22	UK	≥47	1,036	410:626
Sandmark et al, 23	Sweden	≥55	1,173	589:584
Manninen et al, 24	Finland	≥55	805	195:610

ting were not, which was similar to previous studies in Japan and China (34,35). Comparison of characteristics and ORs for knee OA associated with occupational activity among epidemiologic studies is shown in Tables 5 and 6. The present study showed different results from other previously published studies (Table 6). Because each study defined knee OA and cases somewhat differently (in some studies, a case was defined as a subject with K/L grade ≥3 OA with knee pain, while it was defined as a subject with K/L grade ≥2 or K/L grade ≥3 OA in the present study), our results are not directly comparable with those of other studies. Even so, studies of whites have suggested that occupational activities of kneeling and squatting and job titles that required kneeling and squatting were associated with knee OA (19–24), whereas these activities were not associated with K/L grade ≥2 OA in this study. The discrepancies between white and Japanese subjects may be partly explained by the Japanese traditional lifestyle, which includes sitting on the heels on a mat and using the Japanese-style lavatory, where subjects have to take a deep squatting position. These positions may cause mechanical stress to the knee joint and possibly lead to the acceleration of knee OA. Among elderly Japanese subjects, kneeling and squatting are common postures in daily life, which could obscure the association between knee OA and occupational activities of kneeling and squatting.

The direction of the association of kneeling and squatting with knee OA was also different between sexes in the present study, although these differences were not signif-

Table 6. Comparison of odds ratios for knee osteoarthritis associated with occupational activity among epidemiologic studies*

	Muraki et al (current study)		Yoshimura et al (34), K/L ≥3 with knee pain	Lau et al (35), K/L ≥3	Anderson and Felson (19), K/L ≥2	Felson et al (20)		Cooper et al (21), K/L ≥3 with knee pain	Coggon et al (22), listed for knee surgery	Sandmark et al (23), TKA	Manninen et al (24), TKA
	K/L ≥2	K/L ≥3				K/L ≥2	K/L ≥3				
Sitting on a chair	0.7†	0.8	–					1.2		–	
Men	0.6†	0.8	–					–		0.7	
Women	0.8	0.8	0.4†					–		0.9	
Kneeling	1.1	1.4†	–	–				3.4†	1.8†	–	1.7‡
Men	0.8	0.9	–	1.4				–	1.7†	2.1†	1.7
Women	1.4	1.7†	1.0	0.9				–	2.0†	1.5	1.8†
Squatting	1.2	1.3†	–	–	–	–	–	6.9†	2.3†	–	1.7‡
Men	0.9	1.0	–	1.2	2.5†	2.2†	2.0	–	2.2†	2.9†	1.7
Women	1.5†	1.5†	1.1	1.1	3.5†	0.4	0.7	–	2.8†	1.1	1.8†
Standing	2.0†	1.4	–					0.8		–	0.6†
Men	2.3†	1.1	–					–		1.7†	0.4†
Women	1.8†	1.5	1.2					–		1.6†	0.7
Walking	1.8†	1.1	–	–				0.9	1.9†		1.1
Men	2.2†	0.9	–	2.2†				–	1.7		1.5
Women	1.6†	1.1	0.9	1.4†				–	2.1†		1.1
Climbing	2.2†	1.3	–	–				2.7†	1.5†	–	1.6
Men	2.4†	1.0	–	4.1†				–	2.3†	1.2	2.8
Women	1.9†	1.5	0.9	6.1†				–	0.7	1.4	1.5
Lifting weights	1.9†	1.6†	–	–				1.4	1.7†	–	1.0
Men	2.3†	1.3	–	1.7				–	1.9†	3.0†	0.9
Women	1.7†	1.7†	1.0	1.5†				–	1.5†	1.7†	1.1

* K/L = Kellgren/Lawrence grading system; TKA = total knee arthroplasty.
† $P < 0.05$.
‡ $P < 0.05$. Kneeling or squatting.

icant, except for squatting in women. Because men are known to have greater muscle strength than women of all ages and muscle strength has a protective effect on knee OA (36–38), it might be that the greater muscle strength obscures the harmful effects of kneeling and squatting on knee OA in men, resulting in lower ORs for knee OA than in women.

For K/L grade ≥2 lumbar spondylosis, there were no occupational activities associated with the increased prevalence except for heavy lifting in women. Few studies have focused on risk factors for lumbar spondylosis associated with occupational activity (25–28), and no increased risk of lumbar osteophytes due to physical activities has been reported (25,39,40).

In the present study, the occupational activity of sitting on a chair was inversely associated with both K/L grade ≥2 knee OA and lumbar spondylosis. For knee OA, our previous small-scale study showed that prolonged sitting on a chair at work was associated with a reduced prevalence of knee OA (34) (Table 5). Regarding the relationship between sedentary work and OA, the results of studies investigating the influence of sedentary work on knee OA are controversial (21,22). Although sitting on a chair clearly involves reduced load on many joints compared with other working activities, no other studies have reported a relationship between sedentary activity and knee OA. Sitting on a chair as a physical activity in the work place appears to represent a characteristic protective factor for OA in Japan.

Contrary to K/L grade ≥2 knee OA, occupational activities of kneeling and squatting were significantly associated with K/L grade ≥3 knee OA, whereas those of standing, walking, and climbing were not. Considering the definition of the K/L grade, this may suggest distinct risk factors between osteophytosis and joint space narrowing. In this population-based cohort study, the prevalence of K/L grade ≥2 knee OA was 45.6% in men and 61.2% in women, which was higher than that in whites, whereas that of K/L grade ≥3 was 16.8% and 26.5%, which is comparable with that in whites (41), suggesting that the Japanese lifestyle may be associated with osteophytosis rather than joint space narrowing. Therefore, regarding K/L grade ≥2 knee OA, the Japanese lifestyle could obscure the association between knee OA and occupational activities of kneeling and squatting as mentioned above. Furthermore, the discrepancy between risk factors for K/L grade ≥2 and K/L grade ≥3 knee OA may also be due to differences between the mechanism of osteophytosis and joint space narrowing. There is accumulating evidence that osteophytosis and joint space narrowing have distinct etiologic mechanisms (25,42–47). A previous prospective study using a large-scale OA cohort reported that there was no association between the 2 representative features of knee OA (44). A recent cross-sectional study also showed that osteophytosis was unrelated not only to joint space narrowing on plain radiographs, but also to cartilage loss measured by quantitative magnetic resonance imaging (45). Furthermore, our study on an experimental mouse model for OA has identified a cartilage-specific molecule, carminerin, which regulates osteophytosis without affecting joint cartilage destruction during OA progression (46,47). Further clinical and basic research will disclose the distinct backgrounds of these 2 features of OA.

There are several limitations in the present study. First, this is a cross-sectional study on factors associated with knee OA and lumbar spondylosis, so a causal association with occupational activity could not be determined. However, information collected included a lifetime occupational history and details of specific work place physical activities; therefore, ample evidence on the background of knee OA and lumbar spondylosis could be obtained. Second, information regarding past occupational exposures was obtained by self-report and there is a possibility that both self-selection bias and recall bias may have occurred. People with painful conditions may choose work that allows them to avoid aggravation of their conditions, so the impact of job titles and occupational activities on knee OA and lumbar spondylosis may be underestimated in the present study. Conversely, people with painful knee and lumbar conditions are likely to look for and assign a cause when asked about past work exposures. To determine the impact of working conditions on knee OA and lumbar spondylosis independently of the presence of pain at the examination, we analyzed the association of knee OA and lumbar spondylosis with job titles and occupational activities according to the presence of knee pain and low back pain at the baseline examination. The direction of association was similar regardless of the presence of pain, and the results between the overall population and the subpopulation without knee pain or low back pain were not different, suggesting that pain at the examination may not affect the results of the overall population very much in this study.

In conclusion, the present cross-sectional study using a large-scale population from the ROAD study revealed distinct risk factors of occupational activities for radiographic knee OA and lumbar spondylosis in Japanese subjects. Sitting on a chair was a significant protective factor for both radiographic knee OA and lumbar spondylosis. Other occupational activities of kneeling, squatting, standing, walking, climbing, and heavy lifting were risk factors for radiographic knee OA, but not for radiographic lumbar spondylosis. Further studies, along with longitudinal data in the ROAD study, will elucidate the environmental backgrounds of OA and spondylosis and clarify clinical evidence for the development of disease-modifying treatments.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Muraki had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Analysis and interpretation of data. Muraki, Akune, Oka, Mabuchi, En-yo, Yoshida, Saika, Nakamura, Kawaguchi, Yoshimura.

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Prevalence of radiographic lumbar spondylosis and its association with low back pain in elderly subjects of population-based cohorts: the ROAD study

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ABSTRACT

Objectives: Although lumbar spondylosis is a major cause of low back pain and disability in elderly people, few epidemiological studies have been performed. The prevalence of radiographic lumbar spondylosis was investigated in a large-scale population study and the association with low back pain was examined.

Methods: From a nationwide cohort study (Research on Osteoarthritis Against Disability; ROAD), 2288 participants aged ⩾60 years (818 men and 1470 women) living in urban, mountainous and coastal communities were analysed. The radiographic severity at lumbar intervertebral levels from L1/2 to L5/S was determined by Kellgren/Lawrence (KL) grading.

Results: In the overall population the prevalence of radiographic spondylosis with KL⩾2 and ⩾3 at the severest intervertebral level was 75.8% and 50.4%, respectively, and that of low back pain was 28.8%. Although KL⩾2 spondylosis was more prevalent in men, KL⩾3 spondylosis and low back pain were more prevalent in women. Age and body mass index were risk factors for both KL ⩾2 and KL⩾3 spondylosis. Although KL = 2 spondylosis was not significantly associated with low back pain compared with KL = 0 or 1, KL⩾3 spondylosis was related to the pain only in women.

Conclusions: This cross-sectional study in a large population revealed a high prevalence of radiographic lumbar spondylosis in elderly subjects. Gender seems to be distinctly associated with KL⩾2 and KL⩾3 lumbar spondylosis, and disc space narrowing with or without osteophytosis in women may be a risk factor for low back pain.

Lumbar spondylosis is considered a major public health issue causing chronic disability of elderly people in most developed countries.[1 2] Despite the urgent need for strategies for the prevention and treatment of this condition, epidemiological data on lumbar spondylosis such as its prevalence and association with symptoms are sparse. With the goal of establishing epidemiological indices to evaluate clinical evidence for the development of disease-modifying treatment, we set up a large-scale nationwide cohort study for bone and joint disease called ROAD (Research on Osteoarthritis Against Disability) in 2005. We have to date created a baseline database with detailed clinical and genetic information on three population-based cohorts in urban, mountainous and coastal communities of Japan.

Lumbar spondylosis is characterised by disc degeneration and osteophytosis.[2 3] Although this disorder has been widely studied in a clinical setting, few population-based radiological studies have been attempted.[4–11] The reported prevalence of radiographic lumbar spondylosis differs greatly in these reports from about 40% to 85%. This may be due to limitation of the sample size and variability in age. The present study therefore initially investigated the prevalence and distribution of this disorder according to age, gender and community using cohorts of 2288 participants aged ⩾60 years in the baseline survey of the ROAD study.

The most popular grading system for the radiographic severity of osteoarthritis is the Kellgren/Lawrence (KL) system with classification into five grade scales (0–4) where KL⩾2 is the conventional standard of the diagnosis.[12] For lumbar spondylosis, KL grade 2 is defined as osteophyte formation and grade 3 as disc space narrowing in addition to osteophyte formation,[12] although few epidemiological studies have applied the KL system to evaluate the lumbar spine.[2 4 5] Hence, to assess osteophyte formation alone and disc space narrowing with or without osteophytosis separately, this study examined not only the prevalence of KL⩾2 spondylosis but also that of KL⩾3 spondylosis.

Although low back pain is believed to be the principal clinical symptom of lumbar spondylosis, its association with the radiographic severity remains unclear. The correlation was not as strong as one would expect, and there is often a disconnection between them.[7 8] In previous reports radiographic spondylosis was determined at the severest intervertebral level, but it is possible that other levels with milder spondylotic change might give rise to low back pain. This study therefore assessed the radiographic severity at all intervertebral levels of the lumbar spine by the KL system, and examined the association between radiographic severity and low back pain.

METHODS

Participants

The ROAD study is a nationwide prospective cohort study for bone and joint diseases consisting of population-based cohorts established in several communities in Japan. To date we have created a baseline database which includes clinical and genomic information of 3040 inhabitants (1061 men, 1979 women) in the age range 23–95 years (mean 70.6) in three communities: an urban region in Itabashi, Tokyo; a mountainous region in Hidakagawa, Wakayama; and a coastal region in

Taiji, Wakayama. Participants in the urban region were recruited from those of a cohort study[15] in which the participants were randomly drawn from the register database of Itabashi ward residents, with a response rate in the age group ≥60 years of 75.6%. Participants in the mountainous and coastal regions were recruited from resident registration lists, with response rates in the groups aged ≥60 years of 68.4% and 29.3%, respectively.

Participants completed an interviewer-administered questionnaire of 400 items which included lifestyle information such as smoking habits, alcohol consumption, family history, past history, physical activity, reproductive variables and health-related quality of life. Anthropometric measurements included height, weight, arm span, bilateral grip strength and body mass index (BMI, kg/m^2). Medical information was taken by experienced orthopaedic surgeons (SM and HO) on systemic, local and mental status including information on low back, knee and hip pain, swelling and range of motion of the joints, and patellar and achilles tendon reflex. All participants were interviewed regarding low back pain by asking: "In the past month, have you had pain on most days lasting?", and those who answered yes were defined as having low back pain. Blood and urine samples were collected for biochemical and genetic examinations. Plain radiographs of the lumbar spine, knee and hip were taken for all participants. Participants were confirmed to be comparable to the Japanese general population according to the national nutrition survey by the Ministry of Health, Labour and Welfare (Japan). The height of the men and women in the ROAD study was 162.5 cm and 149.7 cm, respectively, compared with 162.6 cm and 149.9 cm in the Japanese general population. Weight was 61.3 kg and 51.8 kg, respectively, compared with 61.6 kg and 53.8 kg. The percentage of the men and women in the study population with a smoking habit was 26.4% and 3.2%, respectively, compared with 29.4% and 4.0% in the general population. From the baseline data of the overall participants, the present study analysed 2288 subjects (818 men and 1470 women) aged ≥60 years.

Radiographic assessment

Plain radiographs of the lumbar spine were taken in the anteroposterior and lateral positions and the images were downloaded into Digital Imaging and Communication in Medicine (DICOM) format files to assess radiographic spondylosis. Contrast-adjusted images were used to detect osteophytes and intervertebral spaces when the original images were obscure. Osteophytes were analysed at endplates. The severity of lumbar spondylosis was determined according to the KL grading[12] at each intervertebral level from L1/2 to L5/S by a single experienced orthopaedic surgeon (SM) who was blind to the background of the patients. To evaluate the intra-observer variability of the KL grading, 100 randomly selected radiographs of the lumbar spine were scored by the same observer more than 1 month after the first reading. Furthermore, 100 other radiographs were scored by two experienced orthopaedic surgeons (SM and HO) using the same radiographic atlas for inter-observer variability. The intra- and inter-observer variabilities were evaluated by kappa analysis. The variability in KL grading of the lumbar radiographs was found to be sufficient for assessment (0.84 and 0.76, respectively).

Statistical analysis

The non-paired *t* test was used to examine the difference in age and BMI between men and women. To compare the percentage of patients with radiographic spondylosis (KL≥2 or ≥3 at the severest level) and low back pain between men and women, logistic regression analysis was performed after adjustment for age and BMI. The differences in prevalence among the age groups were determined using one-way analysis of covariance and Scheffe's test after adjustment for BMI. The association of the variables such as age, BMI, gender and community with radiographic spondylosis and low back pain was evaluated by multivariate logistic regression analysis. The association of radiographic spondylosis at each intervertebral level with low back pain was determined by logistic regression analysis after adjustment for age and BMI. The association of the number of intervertebral level with KL≥3 with low back pain was determined by multiple regression analysis after adjustment for age and BMI. Data analyses were performed using SAS Version 9.0 (SAS Institute, North Carolina, USA).

RESULTS

Table 1 shows the overall characteristics of the 2288 participants aged ≥60 years in the three cohorts of the ROAD study. Although the men were significantly older than the women in the overall population and in some communities, BMI was comparable between them.

Table 2 shows the prevalence of radiographic lumbar spondylosis and low back pain in the overall population and subgroups classified by gender and age strata. In the overall population the prevalence of radiographic spondylosis with KL≥2 and ≥3 at the severest intervertebral level was 75.8% and 50.4%, respectively, and that of low back pain was 28.8%. The prevalence of osteoporotic fracture at the lumbar spine was 10.7%. Logistic regression analysis after adjustment for age and BMI showed that the prevalence of radiographic spondylosis with KL≥2 was higher in men than in women, while the prevalence of KL≥3 radiographic spondylosis and low back pain was higher in women than in men. When the prevalence was

Table 1 Characteristics of study participants

	Men				Women			
	Overall	Urban	Mountainous	Coastal	Overall	Urban	Mountainous	Coastal
No of subjects	818	397	266	155	1470	742	434	294
Age (years)	74.7 (6.1)	77.3 (4.1)	72.1 (6.2)	72.7 (7.4)	74.0 (6.4)*	76.4 (4.8)*	72.1 (7.1)	70.9 (6.8)*
Height (cm)	161.3 (6.3)	161.2 (5.9)	160.3 (6.6)	163.0 (6.1)	148.6 (6.2)	148.6 (5.8)	146.8 (6.4)	151.2 (5.9)
Weight (kg)	60.1 (9.9)	59.8 (8.3)	59.3 (11.4)	62.2 (10.6)	50.9 (9.0)	50.7 (8.4)	49.8 (9.8)	53.1 (8.8)
BMI (kg/m^2)	23.0 (3.2)	23.0 (2.7)	23.0 (3.8)	23.3 (3.3)	23.0 (3.7)	22.9 (3.4)	23.1 (4.2)	23.2 (3.5)
Current smoker (%)	24.6	25.2	26.3	20.0	3.1*	3.1*	4.4*	1.0*
Current drinker (%)	61.2	60.0	67.0	54.8	20.2*	21.0*	22.1*	15.3*

Data are mean (SD).
*$p < 0.05$ vs men in the corresponding group by the non-paired *t* test.
BMI, body mass index.

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