activities of daily life (ADL) and quality of life (QOL), leading to increased morbidity and mortality. The number of patients with OA increases with the age of the population. According to the recent National Livelihood Survey of the Ministry of Health, Labour and Welfare in Japan, OA is ranked fourth, and falls and osteoporotic fractures are ranked fifth, among the diseases causing disabilities that subsequently require support for activities related to daily living [1]. The authors of the present study as well as other authors have reported increased mortality following osteoporotic fractures at the hip and other sites [2, 3].

Because of the increasing proportion of the aging population in Japan, there is an urgent need for a comprehensive and evidence-based prevention strategy for musculoskeletal diseases, including OA and OP. However, few prospective longitudinal studies have been undertaken, and little information is available regarding the prevalence and incidence of OA and lumbar spondylosis (LS), as well as pain and disability, in the Japanese population [4–7]. Only the estimated number of patients with knee osteoarthritis (KOA) and LS is not known.

More population-based prospective studies have been performed for OP than for OA [8–12]. Japanese guidelines for the prevention and treatment of OP, on the basis of evidence obtained from studies conducted with Japanese subjects, were published in 2006 [13]; however, many epidemiological indices of OP still remain to be clarified. For instance, there is insufficient evidence regarding the risks relating to the incidence of OP, osteoporotic vertebral fractures, and bone loss. Further, data on the number of patients with OP were last reported in 1999 [14], thus necessitating an analysis based on the current prevalence of OP. It is difficult to design rational clinical and public health approaches for the diagnosis, evaluation, and prevention of OA and OP without such epidemiological data.

The research on osteoarthritis/osteoporosis against disability (ROAD) study is a prospective cohort study that aims to elucidate the environmental and genetic background for bone and joint diseases, especially OA and OP; it is designed to examine the extent to which risk factors for these diseases are related to clinical features, laboratory and radiographic findings, bone mass and bone geometry, lifestyle, nutritional factors, anthropometric and neuromuscular measures, and fall propensity, as well as to determine how these diseases affect ADL and QOL in Japanese men and women.

Here, the prevalence of KOA, LS, and OP is clarified, and the number of patients with these diseases in Japan is estimated by analyzing the baseline data of the ROAD study.

Participants and methods

Study population

A complete baseline database was established that included the clinical and genomic information of 3,040 inhabitants (1,061 men and 1,979 women) with a mean age of 70.3 [standard deviation (SD), 11.0] years, 71.0 (SD, 10.7) years in men and 69.9 (SD, 11.2) years in women. These subjects were recruited from listings of resident registrations in three communities with different characteristics: an urban region in Itabashi, Tokyo; a mountainous region in Hidakagawa, Wakayama; and a coastal region in Taiji, Wakayama (Fig. 1).

Itabashi Ward, an urban community located in the eastern Tokyo (area, 32 km^2) has a population of 529,400, and the proportion of aged people in this region, defined as the number of residents who were 65 years old or older ($\geq$65) divided by the total population, is 19.1%. The percentage of the population having jobs in primary industries (agriculture, forestry, fishing, or mining), secondary industries (manufacturing and construction), and in tertiary industries (service industries) is 0.1, 25, and 75%, respectively [15]. Hidakagawa Town, a rural mountainous community located in the center of Wakayama (area, 330 km^2), has a population of 11,300 and 30.5% of the inhabitants are $\geq$65 years old. The percentages of workers with jobs in the primary, secondary, and tertiary industries are 29, 24 and 47%, respectively [15]. Taiji Town, a rural coastal community located south of Wakayama (area, 6 km^2), has a population of 3,500, with 34.9% of inhabitants $\geq$65 years old; the percentages of workers with jobs in primary, secondary, and tertiary industries are 13, 18, and 69%, respectively [15].

Residents of these three urban, mountainous, and coastal regions were recruited from the resident-registration lists of the relevant regions. Participants in the urban region, aged $\geq$60 years, were recruited from among those of a randomly selected cohort study from the previously established Itabashi Ward resident registration database [16]. The

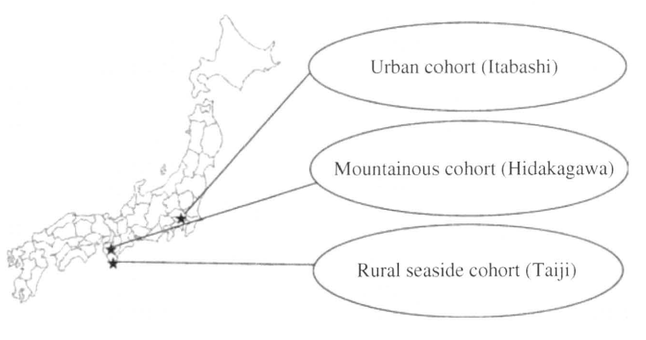

Fig. 1 Location of the three cohorts with different characteristics in Japan

response rate was 75.6%. Participants in the mountainous and coastal regions, aged ≥40 years, were recruited from listings of resident registration. However, those inhabitants aged <60 years in the urban area and <40 years in the mountainous and coastal areas who were interested in participating in the study were invited to be examined.

In addition to residence in the communities as outlined above, the inclusion criteria were as follows: the patient had to (1) be able to walk to the clinic at which the survey was performed, (2) provide self-reported data, and (3) understand and sign an informed consent form. No other exclusion criteria were used.

Participants were enrolled and the initial baseline examinations were completed over a 1.5-year period from October 2005 through March 2007. All participants provided written informed consent. The study was conducted with the approval of the ethics committees of the University of Tokyo (nos. 1264 and 1326) and the Tokyo Metropolitan Institute of Gerontology (no. 5). Careful consideration was given to ensure a safe experience for participants during their examinations and any other study procedures.

Radiographic assessment

Plain radiographs of the lumbar spine in the anteroposterior and lateral views and bilateral knees in the anteroposterior view with weight-bearing and foot map positioning were obtained. The severity of radiographic OA was determined according to Kellgren–Lawrence (KL) grading as follows [17]: KL0, normal; KL1, slight osteophytes; KL2, definite osteophytes; KL3, joint or intervertebral space narrowing with large osteophytes; KL4, bone sclerosis, joint or intervertebral space narrowing, and large osteophytes. In the ROAD study, participants were classified into KL3 if they had joint or intervertebral space narrowing without large osteophytes. Radiographs at each site, i.e., the knees, hips, and vertebrae, were examined by a single, experienced orthopaedic surgeon (S.M.), who was masked regarding participants' clinical status. If at least one knee joint was graded as KL2 or higher, the participant was diagnosed with radiographic KOA. Similarly, if at least one intervertebral level of the lumbar spine was graded as KL2 or higher, the participant was diagnosed with radiographic LS.

Bone mineral density measurement

In the mountainous and coastal areas, bone mineral density (BMD) was measured at the lumbar spine (L2–L4) and the proximal femur using dual-energy X-ray absorptiometry (DXA) (Hologic Discovery; Hologic, Waltham, MA, USA) at baseline.

To control quality, the same DXA equipment was used and the same spine phantom was scanned daily to monitor the machine's performance in study populations at different regions. The BMD of the phantom was adjusted to 1.032 ± 0.016 g/cm^2 ($\pm 1.5\%$) during all examinations. In addition, the same physician (N.Y.) examined all participants to prevent observer variability. Intraobserver variability using the Lunar DPX in vitro and in vivo had been measured by the same physician (N.Y.) for another study [18]. Coefficient of variance (CV) for L2–L4 in vitro was 0.35%, and CVs for L2–L4, the proximal femur, Ward's triangle, and the trochanter examined in vivo in five male volunteers were 0.61–0.90, 1.02–2.57, 1.97–5.45, and 1.77–4.17%, respectively.

OP was defined as a BMD of less than 70% of peak bone mass according to the criteria of the Japanese Society for Bone and Mineral Research [19]. OP was defined by BMD < 0.708 g/cm^2 at the lumbar spine in the case of both men and women, and by BMD < 0.604 g/cm^2 at the femoral neck for men and <0.551 g/cm^2 for women, respectively.

Statistical analysis

All statistical analyses were performed using STATA statistical software (STATA, College Station, TX, USA). Differences in proportion were compared by the chi-square test. Differences of continuous values were tested for significance using analysis of variance (ANOVA) for comparisons among multiple groups and Scheffe's least significant difference (LSD) test for pairs of groups. Significant items were selected, and multiple regression and logistic regression analyses were performed by adjusting suitable variables.

Results

Table 1 shows selected characteristics of the participants in the three regions including age, height, weight, body mass index (BMI), and BMD. The percentage of participants >60 years of age was 99.8, 84.3, and 54.7% in the urban, mountainous, and seacoast regions, respectively. Two-thirds of the 3,040 participants were women, and the mean age of female participants was 1 year less than that of the male participants.

Regarding the gender differences in the anthropometric measurements, height and weight were significantly lower in women than in men, but no significant difference in BMI was noted between the genders. All values of BMD at L2–L4, femoral neck, and total hip were significantly higher in men than in women ($P < 0.001$).

Table 1 Age–sex distribution and mean values (standard deviation) of selected characteristics of the participants

Age strata (years)	Men				Women			
	Total	Urban	Mountainous	Seacoast	Total	Urban	Mountainous	Seacoast
-39	14	0	2	12	31	0	7	24
40–49	44	0	7	37	105	0	17	88
50–59	107	0	36	71	211	2	67	142
60–69	168	11	93	64	385	60	183	142
70–79	535	315	150	70	913	594	196	123
80–	193	139	31	23	334	229	75	30
Total	1,061	465	319	277	1,979	885	545	549
Age (years)	71.0 (10.7)	77.2 (4.3)	69.5 (9.1)	62.6 (13.2)	69.9 (11.2)	76.3 (5.0)	68.6 (10.4)	60.8 (12.5)
Height (cm)	162.5 (6.7)	161.3 (5.9)	161.4 (6.9)	165.8 (6.8)	149.8 (6.5)	148.5 (5.6)	148.2 (6.7)	153.2 (6.2)
Weight (kg)	61.3 (10.0)	60.0 (8.5)	60.0 (10.2)	64.8 (11.0)	51.5 (8,6)	50.8 (8.3)	50.5 (8.6)	53.5 (8.8)
BMI (kg/m^2)	23.1 (3.0)	23.0 (2.8)	23.0 (3.0)	23.5 (3.4)	22.9 (3.5)	23.0 (3.4)	23.0 (3.4)	22.8 (3.6)
BMD (g/cm^2)								
L2–L4	1.05 (0.20)	–	1.04 (0.20)	1.06 (0.21)	0.87 (0.18)	–	0.83 (0.18)	0.91 (0.18)
Femoral neck	0.74 (0.13)	–	0.73 (0.13)	0.76 (0.13)	0.63 (0.12)	–	0.60 (0.12)	0.66 (0.13)
Total hip	0.88 (0.14)	–	0.87 (0.14)	0.90 (0.14)	0.74 (0.14)	–	0.72 (0.13)	0.76 (0.14)

BMI body mass index, *BMD* bone mineral density

Table 2 shows the age-sex distribution for prevalence of radiographic KOA and LS determined by a KL grade ≥2, classified by region. In the overall population, prevalence of radiographic KOA and LS was 54.6% (42.0% in men and 61.5% in women) and 70.2% (80.6% in men and 64.6% in women), respectively, indicating that the prevalence of LS was higher than that of KOA in the overall population, as well as in the respective genders. When the prevalence was compared among the age strata, radiographic KOA and LS tended to be higher with age in both genders (Table 2). Prevalence of radiographic KOA was 0% in men and 3.2% in women in the <40-year age group and 42.6% in men and 62.4% in women in the ≥40-year age group, and the differences were significant ($P < 0.001$). According to gender, the prevalence was significantly higher in women than in men in the overall population ($P < 0.001$). OA in both knees was observed in 43.1% (31.5% in men and 49.4% in women) of all participants. The overall prevalence of radiographic LS across all ages was 80.6% in men and 64.6% in women, which was considerably higher than that of KOA. In contrast to radiographic KOA, the prevalence of this condition was significantly higher in men than in women ($P < 0.001$). Similar to KOA, the prevalence of LS was lower in the <40-year age group than in the ≥40-year age group, with significant differences in both genders ($P < 0.001$). Among all the participants, 42.3% (37.1% in men and 45.1% in women) had both KOA and LS.

The prevalence of KOA and LS classified by region is also shown in Table 2. Regarding the regional differences, the prevalence of KOA was the highest in the mountainous area, followed by the urban area and the seacoast area in both men and women. By contrast, the prevalence of LS was the highest in the urban area, followed by the mountainous area and the seacoast area.

Logistic regression analysis was performed to determine the effect of region, gender, age, and body build on the prevalence of OA in participants ≥60 years of age, using the presence of KOA as an objective variable, and region (seacoast: 0, mountainous: 1), gender (men: 0, women: 1), age, and BMI as explanatory factors. The analysis revealed that the risk for KOA was significantly higher in the mountainous area [odds ratio (OR), 2.7; 95% confidence interval (CI), 2.1–3.6, $P < 0.001$], in women (OR, 3.4; 95% CI, 2.79–4.06; $P < 0.001$), in advanced age (+1 year: OR, 1.09; 95% CI, 1.07–1.11, $P < 0.001$), and in larger body build (+1 BMI: OR, 1.16; 95% CI, 1.13–1.20; $P < 0.001$). By contrast, the risk of LS was reduced in the mountainous area (OR, 0.63; 95% CI, 0.48–0.83; $P < 0.01$) and in women (OR, 0.47; 95% CI, 0.38–0.58; $P < 0.001$). Advanced age and higher BMI were associated with the presence of LS as well as KOA (+1 year: OR, 1.08; 95% CI, 1.06–1.10; $P < 0.001$; +1 BMI: OR, 1.09; 95% CI, 1.05–1.12; $P < 0.001$, respectively).

Table 3 shows the mean values of BMD among residents of mountainous and coastal regions in the ROAD study. Although the mean BMD values of the lumbar spine were no different between men and women in the age group of <40 years, those of the femoral neck and proximal total hip in the same age group were significantly

Table 2 Prevalence (%) of knee osteoarthritis and lumbar spondylosis classified by age, gender, and region

Age strata (years)	Knee osteoarthritis				Lumbar spondylosis			
	Total	Urban	Mountainous	Seacoast	Total	Urban	Mountainous	Seacoast
Men								
-39	0.0	–	0.0	0.0	14.3	–	0.0	16.7
40–49	9.1	–	42.9	2.7	45.5	–	28.6	48.7
50–59	24.3	–	55.6	8.5	72.9	–	75.0	71.8
60–69	35.2	37.5	44.1	21.9	74.6	75.0	69.9	81.3
70–79	48.2	41.3	63.5	45.7	85.3	83.8	85.3	91.4
80–	51.6	45.6	74.2	56.5	90.1	89.9	90.3	91.3
Total	42.0	42.5	57.1	23.8	80.6	85.5	78.4	75.1
Women								
-39	3.2	–	0.0	4.2	9.7	–	0.0	12.5
40–49	11.4	–	29.4	8.0	28.6	–	29.4	28.4
50–59	30.3	50.0	46.3	22.5	41.7	100.0	29.9	46.5
60–69	57.1	49.1	68.3	45.8	55.4	64.3	50.3	58.5
70–79	71.9	69.3	83.2	66.1	75.1	76.1	70.4	32.0
80–	80.7	77.3	91.9	76.9	78.2	79.6	69.3	90.0
Total	61.5***	70.0***	72.1***	37.8***	64.6***	76.3***	56.3***	54.6***

*** Significantly different ($P < 0.001$) from prevalence in men of the same region

higher in men than in women ($P < 0.001$). When the BMD values were compared among age strata, the prevalence of OP tended to be higher with age in both genders; however, the tendency was much greater in women than in men. Multiple regression analysis was performed to determine the effect of region, gender, age, and body build on BMD in the overall population of the mountainous and seacoast areas, using each value of BMD at lumbar spine, femoral neck, and total hip as an objective variable, and region (seacoast: 0, mountainous: 1), gender (men: 0, women: 1), age, and BMI as explanatory factors. The analysis revealed there was no regional difference in the BMD values at L2–L4, femoral neck, and total hip, whereas there were significant differences in gender (beta at L2–L4, femoral neck, and total hip, −0.41, −0.41, and −0.47, respectively, all $P < 0.001$), age (beta at L2–L4, femoral neck, and total hip, −0.28, −0.43, and −0.42, respectively, all $P < 0.001$), and BMI (beta at L2–L4, femoral neck, and total hip, 0.29, 0.33, and 0.37, respectively, all $P < 0.001$).

Table 4 reveals the prevalence of OP at the lumbar spine, the femoral neck, and the total hip among residents of mountainous and coastal regions in the ROAD study. The prevalence of OP in women was six, two, and threefold higher, respectively, than in men, with a significant difference ($P < 0.001$). Although the prevalence of OP at the lumbar spine was higher for persons in the seacoast area than in the mountainous area, the prevalence at the femoral neck and total hip were higher in the mountainous area than in the seacoast area. In women, the prevalence of OP at the lumbar spine, femoral neck, and total hip were all higher in the mountainous area than in the seacoast area.

Logistic regression analysis was performed to determine the effect of region, gender, age, and body build on the prevalence of OP, using the presence of OP at L2–L4 as an objective variable, and region (seacoast: 0, mountainous: 1), gender (men: 0, women: 1), age, and BMI as explanatory factors. The analysis revealed that the risk for OP at L2–L4 was significantly higher in women (OR, 10.2; 95% CI, 6.07–17.1; $P < 0.001$), in advanced age (+1 year: OR, 1.10; 95% CI, 1.08–1.12; $P < 0.001$), whereas it was significantly lower in larger body build (+1 BMI: OR, 0.74; 95% CI, 0.69–0.79; $P < 0.001$). There was no significant difference in the prevalence of OP at L2–L4 between the mountainous and seacoast area. A similar tendency was shown in the prevalence of OP at the femoral neck and total hip (femoral neck: women versus men, OR, 3.82; 95% CI, 2.77–5.27; $P < 0.001$; +1 year: OR, 1.11; 95% CI, 1.09–1.13; $P < 0.001$; +1 BMI: OR, 0.75; 95% CI, 0.72–0.79; $P < 0.001$; total hip: women versus men, OR, 4.39; 95% CI, 2.88–6.70; $P < 0.001$; +1 year: OR, 1.11; 95% CI, 1.09–1.14; $P < 0.001$; +1 BMI: OR, 0.70; 95% CI, 0.65–0.75; $P < 0.001$).

Discussion

Little epidemiological information is available for musculoskeletal diseases such as OA and OP in Japan. The

Table 3 Mean values (standard deviation) of bone mineral density of participants classified by age, gender, and region

Age strata (years)	L2–L4 (g/cm^2)			Femoral neck (g/cm^2)			Total hip (g/cm^2)		
	Total	Mountainous	Seacoast	Total	Mountainous	Seacoast	Total	Mountainous	Seacoast
Men									
–39	1.05 (0.13)	0.97 (0.03)	1.06 (0.13)	0.83 (0.13)	0.72 (0.02)	0.84 (0.14)	0.96 (0.15)	0.87 (0.12)	0.98 (0.15)
40–49	1.06 (0.15)	1.08 (0.15)	1.06 (0.15)	0.82 (0.13)	0.77 (0.09)	0.83 (0.14)	0.96 (0.14)	0.94 (0.08)	0.96 (0.15)
50–59	1.05 (0.20)	1.03 (0.20)	1.06 (0.19)	0.80 (0.15)	0.81 (0.17)	0.79 (0.14)	0.93 (0.15)	0.93 (0.17)	0.93 (0.14)
60–69	1.04 (0.17)	1.05 (0.16)	1.03 (0.18)	0.75 (0.10)	0.76 (0.10)	0.75 (0.12)b	0.90 (0.12)	0.90 (0.11)	0.89 (0.14)
70–79	1.05 (0.23)	1.03 (0.22)	1.08 (0.25)	0.71 (0.12)abcd	0.70 (0.13)cd	0.73 (0.12)b	0.85 (0.14)bc	0.85 (0.14)	0.86 (0.12)b
80–	1.04 (0.26)	1.05 (0.25)	1.01 (0.30)	0.68 (0.12)abcd	0.69 (0.13)c	0.68 (0.12)abcd	0.80 (0.15)abcd	0.81 (0.13)c	0.78 (0.16)abc
Total	1.05 (0.20)	1.04 (0.20)	1.06 (0.21)	0.74 (0.13)	0.73 (0.13)	0.76 (0.13)	0.88 (0.14)	0.87 (0.14)	0.90 (0.14)
Women									
–39	1.08 (0.12)	1.11 (0.15)	1.07 (0.12)	0.78 (0.13)	0.76 (0.16)	0.78 (0.12)	0.86 (0.13)*	0.86 (0.13)	0.86 (0.13)*
40–49	1.04 (0.13)	1.06 (0.10)	1.04 (0.14)	0.74 (0.12)***	0.75 (0.09)	0.74 (0.12)***	0.85 (0.13)***	0.86 (0.10)	0.84 (0.13)***
50–59	0.94 (0.16)ab***	0.94 (0.16)**	0.94 (0.16)ab***	0.71 (0.11)a***	0.70 (0.10)***	0.71 (0.12)***	0.81 (0.12)***	0.83 (0.12)***	0.80 (0.12)***
60–69	0.85 (0.15)abc***	0.85 (0.15)abc***	0.86 (0.16)abc***	0.63 (0.09)abc***	0.62 (0.10)abc***	0.63 (0.09)abc***	0.75 (0.11)abc***	0.75 (0.11)bc***	0.74 (0.11)abc***
70–79	0.80 (0.17)abcd***	0.79 (0.17)abcd***	0.82 (0.17)abc***	0.57 (0.10)abcd***	0.56 (0.10)abcd***	0.59 (0.10)abcd***	0.68 (0.11)abcd***	0.67 (0.11)abcd***	0.69 (0.11)abcd***
80–	0.76 (0.16)abcd***	0.84 (0.16)abcd***	0.78 (0.16)abc***	0.52 (0.08)abcde***	0.52 (0.08)abcd***	0.52 (0.09)abcd***	0.60 (0.10)abcde***	0.61 (0.10)abcde***	0.59 (0.10)abcde***
Total	0.87 (0.18)***	0.83 (0.18)***	0.91 (0.18)***	0.63 (0.12)***	0.60 (0.11)***	0.66 (0.13)***	0.74 (0.13)***	0.72 (0.13)***	0.76 (0.14)***

[a] Significantly different ($P < 0.05$) from values of the age group in their thirties

[b] Significantly different ($P < 0.05$) from values of the age group in their forties

[c] Significantly different ($P < 0.05$) from values of the age group in their fifties

[d] Significantly different ($P < 0.05$) from values of the age group in their sixties

[e] Significantly different ($P < 0.05$) from values of the age group in their seventies

*, **, *** Significantly different (* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$) from values in men of the same age-strata and the same region

Table 4 Prevalence (%) of osteoporosis according to the JSBMR criteria, classified by age, gender, and region

Age strata (years)	L2–L4			Femoral neck			Total hip		
	Total	Mountainous	Seacoast	Total	Mountainous	Seacoast	Total	Mountainous	Seacoast
Men									
–39	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
40–49	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
50–59	2.8	5.6	1.4	6.5	8.3	5.6	2.8	2.8	2.8
60–69	2.6	0.0	6.3	7.0	4.3	10.9	3.2	1.1	6.3
70–79	3.6	3.3	4.3	22.3	23.3	20.0	8.2	10.0	4.3
80–	7.4	6.5	8.7	13.0	16.1	8.7	18.5	16.1	21.7
Total	3.4	2.8	3.6	12.4	14.7	9.8	6.1	6.9	5.1
Women									
–39	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
40–49	1.9	0.0	2.3	2.9	0.0	3.4	3.8	0.0	4.6
50–59	5.3	3.0	6.3	4.8	1.5	6.4	3.9	1.5	5.0
60–69	13.5	15.3	11.4	22.2	23.0	21.3	10.8	10.9	10.6
70–79	29.8	31.8	26.0	42.9	44.6	40.2	25.9	25.6	26.2
80–	43.8	47.3	36.7	65.1	64.4	66.7	46.6	43.8	53.3
Total	19.2***	23.4***	12.8***	26.5***	32.7***	20.3***	16.3***	19.0***	13.6***

JSBMR Japanese Society for Bone and Mineral Research

*** Significantly different ($P < 0.001$) from prevalence in men of the same region

ROAD study is the first large observational study that was conducted in the Japanese population, and it was designed to supply essential information mainly regarding OA and OP. Among the large-scale population-based epidemiological studies aimed at preventing OA, the present ROAD study, which includes 3,040 participants, ranks at the same level as the Framingham study with 1,805 participants [20] and the Chingford study with 1,353 participants [21].

The present study clarified the age-sex distribution of the prevalence of KOA and LS as radiographically diagnosed in Japanese populations. If the results obtained from the ROAD study were applicable to the total age-sex distribution derived from the Japanese census in 2005 [15], it would be assumed that 25,300,000 people (8,600,000 men and 16,700,000 women) aged 40 years and older would be affected by radiographic KOA and 37,900,000 people (18,900,000 men and 19,000,000 women) aged 40 years and older would be affected by radiographic LS. This estimation would include asymptomatic OA. However, because one-quarter of men with radiographic OA and one-third of women with radiographic OA were reported to have pain, which is considered symptomatic OA [22, 23], it was determined that approximately 7,800,000 people (2,200,000 men and 5,600,000 women) aged 40 years and older would be affected by symptomatic KOA. Further, 11,000,000 people (4,700,000 men and 6,300,000 women) would be affected by symptomatic LS, based on the same assumption of the proportions of symptomatic and asymptomatic OA.

In this study, the Japanese criteria were used to clarify the prevalence of OP at the lumbar spine and hip. If the results obtained from the ROAD study were again applied to the entire Japanese age–sex distribution, 6,400,000 people (800,000 men and 5,600,000 women) aged 40 years and older would be affected by OP at the lumbar spine, and 10,700,000 people (2,600,000 men and 8,100,000 women) and 6,600,000 people (1,300,000 men and 5,300,000 women) would be affected by OP at the femoral and total hip, respectively. Because there are huge estimated numbers of patients with KOA, LS, and OP in Japan, these bone and joint diseases may be called national diseases. The Japanese Orthopaedic Association has proposed that the term "locomotive syndrome" be adopted to designate the condition evident in the high-risk group with musculoskeletal disorders who are highly likely to need nursing care [24]. The present study estimated that a total of 47,000,000 people (21,000,000 men and 26,000,000 women) aged 40 years and older would be affected by either OA or OP and are candidates for developing locomotive syndrome. Considering that the population of Japan is aging very rapidly and that more than 20% of the population is aged 65 years and over, there is an urgent need to develop preventive strategies for addressing these diseases that cause disability in the elderly.

In addition, the various associated factors for KOA and LS were identified in this research. The prevalence of KOA was higher in women than in men, whereas that of LS was higher in men than in women. Further, the prevalence of

KOA was higher in the mountainous area than in the seacoast area, whereas the prevalence of LS was higher in the seacoast area than in the mountainous area. The difference in the presence of KOA and LS based on gender difference may in part relate to the etiological differences of these two diseases, including genetic factors; the differences based on regional differences could be affected by environmental factors. Further investigation of the ROAD study will elucidate the genetic and environmental background underlying these diseases, although these could not be determined by the present study. Regarding OP, a high prevalence of OP among the ROAD study participants was confirmed; female sex and advanced age were associated with the presence of OP; and it was confirmed that BMI was associated with BMD at any site. The ROAD study participants will be followed up for at least 10 years to clarify the relationships between musculoskeletal diseases and risk factors for the early prevention of the disabilities caused by them.

There are several limitations in the present study. First, although the ROAD study includes a large number of participants (>3,000), these participants do not truly represent the general population as they have been recruited from only three areas. To confirm whether the participants of the ROAD study are representative of the Japanese population, we compared anthropometric measurements and frequency of smoking and alcohol drinking between the participants and the general Japanese population. The values for the general population were obtained from the report on the 2005 National Health and Nutrition Survey conducted by the Ministry of Health, Labour and Welfare, Japan [25]. The mean BMI (standard deviation in parentheses) of men in the age groups of 40, 50, 60, 70–74, 75–79, and 80 years or older as reported in the National Health and Nutrition Survey was 23.99 (3.27), 23.74 (3.07), 23.75 (2.94), 23.68 (3.18), 23.31 (3.04), and 22.27 (2.64), respectively, and that of women was 22.44 (3.49), 23.06 (3.37), 23.54 (3.66), 23.16 (3.42), 23.42 (3.53), and 22.50 (3.97), respectively. In the ROAD study, the mean BMI for men in identical age strata was 24.50 (4.36), 23.58 (2.90), 23.78 (3.16), 23.08 (2.82), 22.81 (2.86), and 22.62 (2.90), and for women it was 21.92 (4.08), 23.04 (3.29), 23.31 (3.21), 23.44 (3.46), 22.96 (3.66), and 22.21 (3.16), respectively. No significant differences were identified between our participants and the total Japanese population, except that the male participants aged 70–74 years in the ROAD study were significantly smaller in terms of body structure than the overall Japanese population ($P < 0.05$). This difference should be taken into consideration when evaluating the potential risk factors in men aged 70–74 years; factors such as body build, particularly heavy weight, are known to be associated with the occurrence of KOA [26]. Thus, our results might represent an underestimation. Conversely, a small body build is frequently associated with occurrence of OP [27]; therefore, in this case, our results might represent an overestimation.

Although care should always be taken when generalizing results obtained from the ROAD study for all similarly aged men and women, the overall BMI of the participants was basically comparable to that of the broader Japanese population. In addition, the proportion of current smokers and current drinkers (those who regularly smoked or drank more than one drink/month) in the general Japanese population was compared with that in the study population. Both proportions were significantly higher in the general Japanese population than in the study population (smokers: men, 34.8% in Japanese population, 25.3% in ROAD subjects, $P < 0.001$; women, 8.8% in Japanese population, 3.4% in ROAD subjects, $P < 0.001$; drinkers: men, 69.8% in Japanese population, 64.4% in ROAD subjects, $P < 0.01$; women, 30.8% in Japanese population, 25.5% in ROAD subjects, $P < 0.001$), suggesting that participants of the ROAD study had healthier lifestyles than the general Japanese population. This "healthy" selection bias should be taken into consideration when generalizing the results obtained from the ROAD study. Second, the age distributions of the participants among the three cohorts were different. In the urban, mountainous, and coastal areas, 99.8, 84.3, and 54.7% of the participants, respectively, were more than 60 years old. This selection bias should be considered in the analysis of regional differences of frequencies and risk factors. Third, BMD values were not collected from the participants in Itabashi Ward because of lack of available apparatus. So, our estimation of the number of patients with osteoporosis was based on the data collected in the countryside. This selection bias should always be taken into consideration when generalizing the study data to the Japanese population.

In conclusion, the prevalence of KOA, LS, and OP was clarified, and the number of people affected with these diseases in Japan was estimated, using the baseline data of the ROAD study. This study will provide the information required to develop clinical algorithms for the early identification of potential high-risk populations, as well as essential information for the development of policies for the detection and prevention of OA, OP, or osteoporotic fractures. Furthermore, establishment of the cohort will also facilitate the expansion of other studies in related areas of investigation. The knowledge gained from the ROAD study will have major implications for the understanding and management of several additional common problems of aging.

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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/m^2	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.

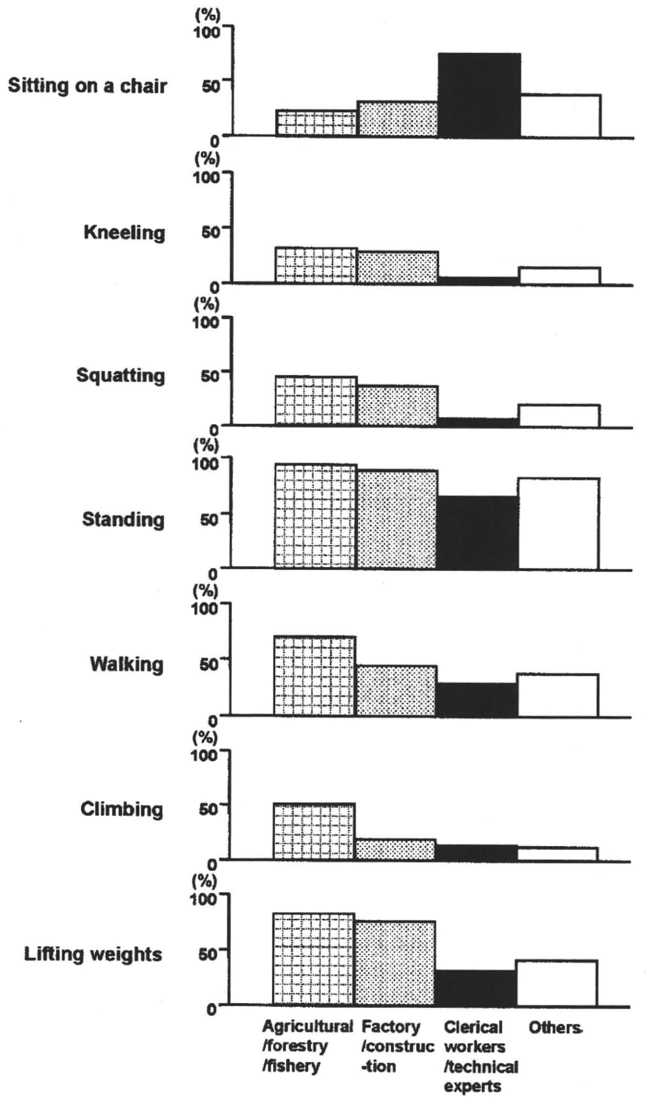

Figure 1. Percentages of participants engaged in each occupational activity: sitting on a chair ≥2 hours/day, kneeling ≥1 hour/day, squatting ≥1 hour/day, standing ≥2 hours/day, walking ≥3 km/day, climbing ≥1 hour/day, or lifting weights ≥10 kg at least once a week among agricultural, forestry, and fishery 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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Intraoperative ultrasonographic evaluation of posterior decompression via laminoplasty in patients with cervical ossification of the posterior longitudinal ligament: correlation with 2-year follow-up results

Clinical article

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Object. The aim in this prospective study was to determine the morphological limitations of laminoplasty for cervical ossification of the posterior longitudinal ligament (OPLL) by using intraoperative ultrasonography and to investigate correlations between ultrasonographic findings and 2-year follow-up results.

Methods. Included in this study were 40 patients who underwent double-door laminoplasty for cervical myelopathy due to OPLL. Intraoperative ultrasonography was used to evaluate posterior shift of the spinal cord after the posterior decompression procedure. To determine the decompression status of the cord, the authors classified ultrasonographic findings into 3 types on the basis of the presence or absence of spinal cord contact with OPLL after decompression: Type 1, noncontact; Type 2, contact and apart; and Type 3, contact. Patients were divided accordingly into Group 1, showing Type 1 or 2 findings, representing sufficient decompression; and Group 2, showing Type 3 findings with insufficient decompression. Preoperative sagittal alignment of the cervical spine (C2–7 angle) and preoperative maximal thickness of OPLL were compared between groups. The authors also investigated the morphological limitations of laminoplasty and 2-year follow-up results by using the Japanese Orthopedic Association (JOA) scoring system.

Results. According to receiver operating characteristic curve analysis, an OPLL maximal thickness > 7.2 mm was a cutoff value for insufficient decompression. However, sufficient or insufficient decompression did not correlate with 2-year results, as determined by JOA scores. The C2–7 angle had no impact on ultrasonographic findings.

Conclusions. Laminoplasty has a morphological limitation for thick OPLLs, and a thickness > 7.2 mm represents a theoretical cutoff for residual cord compression after laminoplasty. According to 2-year results, however, laminoplasty can remain the first choice for any type of multiple-level OPLL. *(DOI: 10.3171/2010.3.SPINE09680)*

Key Words • **cervical spine** • **laminoplasty** • **ultrasonography** • **ossification of the posterior longitudinal ligament**

The anterior approach for cervical OPLL is theoretically reasonable given that the lesion is anterior.[3] However, anterior surgery for multisegmental OPLL is technically demanding, and the potential for complications is higher than with posterior surgery.[5] Laminoplasty has been reported as a safe and effective procedure with few complications[1,2] and represents an alternative to the anterior technique. The choice of anterior or posterior surgery is thus controversial. To clarify whether an anterior or posterior approach is preferable for cervical OPLL, the morphological limitations of laminoplasty must be determined. Yamazaki et al.[4] reported the risk factors for unsatisfactory posterior decompression as 1) lordosis < 10° at C2–7 or kyphosis, and 2) an OPLL maximal thickness > 7 mm. Their study was conducted using postoperative CT and MR imaging for evaluation. In reality, the spinal cord is a dynamic structure, and static evaluation by CT or MR imaging does not indicate

Abbreviations used in this paper: JOA = Japanese Orthopedic Association; mJOA = motor function score according to the JOA scale; OPLL = ossification of the posterior longitudinal ligament; ROC = receiver operating characteristic; sJOA = sensory deficit score according to the JOA scale.

the dynamic decompression status of the spinal cord. Ultrasonography performed during decompression surgery is helpful to evaluate the dynamic decompression status of the spinal cord. The aim of the present study was to determine the morphological limitations of laminoplasty for cervical OPLL by using intraoperative ultrasonography and to investigate correlations between ultrasonographic findings and 2-year follow-up results.

Methods

Participants in this prospective comparative study consisted of 40 patients (25 men and 15 women) with cervical OPLL who were surgically treated with laminoplasty between February 1999 and September 2005. The mean patient age at the time of surgery was 62 ± 7 years (range 51–84 years), and the median age was 62 years. The procedure performed in all patients was a double-door laminoplasty.[2] During the same period, only 1 patient with localized OPLL who had elected to undergo anterior surgery underwent an anterior corpectomy. All 40 patients were followed up for ≥ 2 years. Outcomes were assessed based on motor function scores in the upper and lower extremities (upper and lower mJOA scores) and on sensory deficit scores in the upper and lower extremities (upper and lower sJOA scores) as defined by the JOA scale for cervical myelopathy.[1]

Following posterior decompression, we performed intraoperative ultrasonography via a water-path imaging technique to determine posterior shift of the spinal cord from the OPLL by using an HDI 5000 digital echo camera (Hitachi) and a 12.5-MHz linear array transducer. To evaluate the decompression status of the cord, ultrasonographic findings were classified into 3 types: Type 1, noncontact, retaining the presence of the subarachnoid space on the ventral side of the spinal cord; Type 2, contact and apart, with the spinal cord showing contact with and separation from the OPLL in synchrony with cord pulsations; and Type 3, contact, with the cord in continuous contact with the OPLL (Fig. 1). Patients were then categorized into Group 1 (showing Type 1 or 2 findings, representing sufficient decompression) or Group 2 (showing Type 3 findings, indicating insufficient decompression).

To investigate predictive factors for insufficient decompression, we analyzed preoperative CT and radiography, since a kyphotic cervical spine or very extensive OPLL has been considered a causative factor for insufficient posterior decompression surgery. A Cobb angle between C-2 and C-7 (cervical lordotic angle, C2–7 angle) was measured from lateral radiographs of the cervical spine. We also measured maximal thickness of the OPLL from preoperative digital CT scans. Preoperative sagittal alignment of the cervical spine (C2–7 angle) and preoperative maximal thickness of OPLL were compared between outcome Groups 1 and 2. Morphological limitations of laminoplasty and results at the 2-year follow-up (mean follow-up 2 years ± 2 weeks) were investigated.

All study protocols were approved by the institutional review board at the University of Tokyo, and each patient provided written informed consent prior to participation in the study.

Statistical Analysis

Differences in OPLL thickness and the C2–7 angle between groups were compared using the Mann-Whitney U-test. To determine cutoff points yielding the highest combined sensitivity and specificity with respect to distinguishing patients from these 2 groups, conventional ROC curve analysis was used. We also compared 2-year results for the 2 outcome groups by using postoperative upper and lower mJOA scores and score changes in the upper and lower mJOA and sJOA scores with the Mann-Whitney U-test. The SPSS, version 17, software (SPSS, Inc.) was used for all statistical analyses. A p value < 0.05 was considered significant.

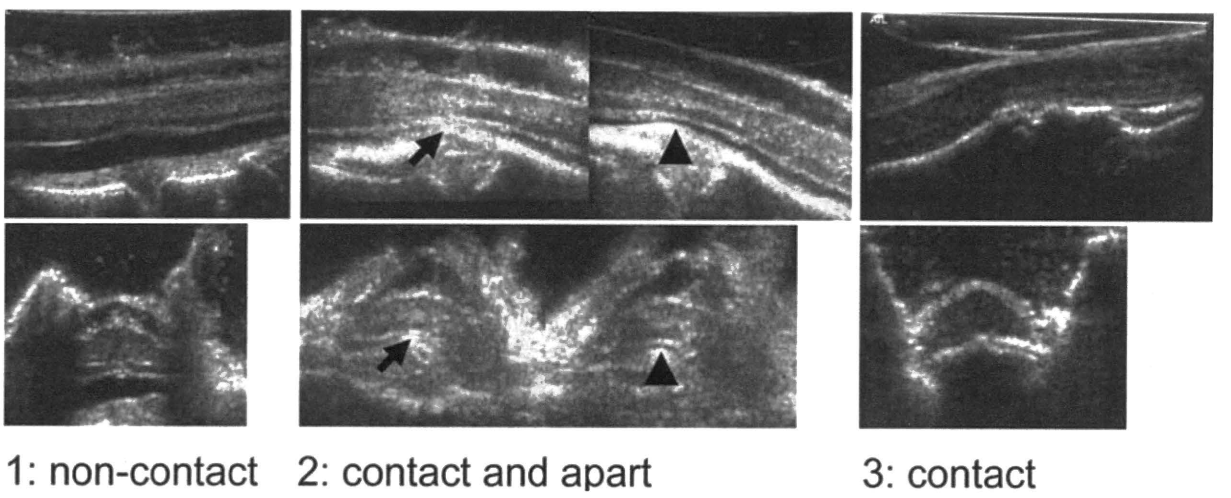

Fig. 1. Ultrasonograms illustrating 3 types of findings: Type 1, noncontact, retaining the presence of the subarachnoid space on the ventral side of the spinal cord; Type 2, contact and apart, with the spinal cord showing contact with and separation from the OPLL in synchrony with cord pulsation (*arrow* and *arrowhead*); and Type 3, contact, with the cord continuously in contact with the OPLL.

TABLE 1: Summary of clinical characteristics in 40 patients with OPLL

	Group 1 (Types 1 & 2)	Group 2 (Type 3)	p Value
mean age (yrs)	63.0 ± 8.3	61.4 ± 6.6	0.664
mean symptom duration (mos)	51 ± 79	57 ± 78	0.994
median preop mJOA score			
upper extremity	2	2	0.812
lower extremity	2	2	0.146
median postop mJOA score			
upper extremity	3	3	0.834
lower extremity	3	3	0.292
median score changes in mJOA			
upper extremity	1	1	0.834
lower extremity	1	1	0.967
OPLL thickness (mm)			
mean ± SD	5.7 ± 1.3	7.7 ± 0.7	<0.0001
range	3.1–8.6	6.5–9.5	
C2–7 angle (°)			
mean ± SD	6.6 ± 6.6	10.5 ± 6.4	0.045
range	−10.0–18.3	1.5–19.2	

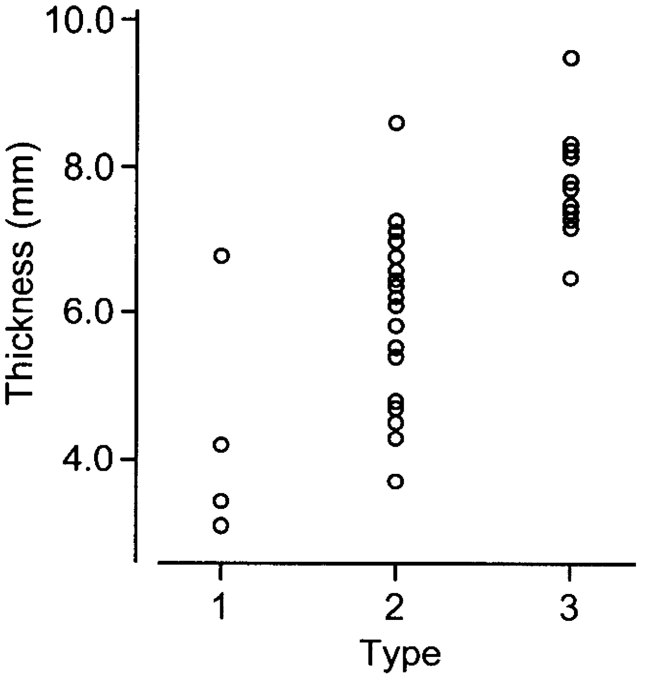

FIG. 2. Scatterplot of the maximal thickness of OPLL in the 3 types of ultrasonographic findings.

Results

Intraoperative ultrasonography showed Type 1 findings in 4 patients, Type 2 in 23, and Type 3 in 13. Statistical analysis showed no significant differences in age or symptom duration between outcome Groups 1 and 2. Demographic data for the 2 groups are shown in Table 1. No complications, including so-called C-5 nerve root palsy, occurred in either group. Postoperative changes in Cobb angles were compared between Groups 1 and 2, as this change may influence surgical results. However, no significant difference in changes to this angle was identified between groups (mean change 1.1 ± 7.8° in Group 1 and −1.1 ± 13.0° in Group 2).

Figure 2 is a scatterplot of maximal OPLL thickness for each type of finding. A significant difference in thickness was noted between Groups 1 and 2 (Fig. 3). According to the ROC curve analysis, when the preoperative OPLL maximal thickness was > 7.2 mm, sensitivity was 0.92 and specificity was 0.89. A cutoff of 7.2 mm was therefore identified for distinguishing between patient groups (Fig. 4). The area under the ROC curve was 0.919, indicating that the model offered good discriminatory power. The C2–7 angle ranged from −10.0° to 18.3° in Group 1 and from 1.5° to 19.2° in Group 2. In 1 patient from Group 1, the C2–7 angle was < 0°. Curiously, the C2–7 angle was significantly larger in patients in Group 2 ($p < 0.045$; Fig. 5). Thus, the C2–7 angle did not affect ultrasonographic findings, although only 1 patient with a severely kyphotic cervical spine was included in this study.

No significant differences in pre- or postoperative upper and lower mJOA and sJOA scores were seen between groups. Likewise, score changes for upper and lower mJOA and sJOA scores before and 2 years after surgery did not differ significantly between groups. Sufficient or insufficient decompression as recognized by intraoperative ultrasonography thus showed no significant correlation with postoperative mJOA or sJOA scores or score changes at 2 years postoperatively (Fig. 6).

Discussion

Laminoplasty has become popular, replacing anterior surgery not only for cervical spondylotic myelopathy, but also for OPLL because of the procedure's technical simplicity and reduced risk of complications. For patients with a kyphotic cervical spine or very extensive OPLL, however, laminoplasty has been considered to result in insufficient decompression.[4] Data in this study showed that laminoplasty can be effective for any type of OPLL. The present investigation included few patients with severe kyphosis of the cervical spine, and thus the effectiveness for such patients remains unclear. However, we seldom encounter such cases.

Residual cord compression can lead to poor neurological recovery or deterioration in the long-term postoperative period.[2] To determine which procedure (anterior or posterior) is preferable for cervical OPLL, the morphological limitations of posterior decompression must be clarified. Intraoperative ultrasonography provides real-time information regarding the dynamic condition of the spinal cord. This study demonstrated an OPLL thickness > 7.2 mm as a risk factor for residual contact of the OPLL

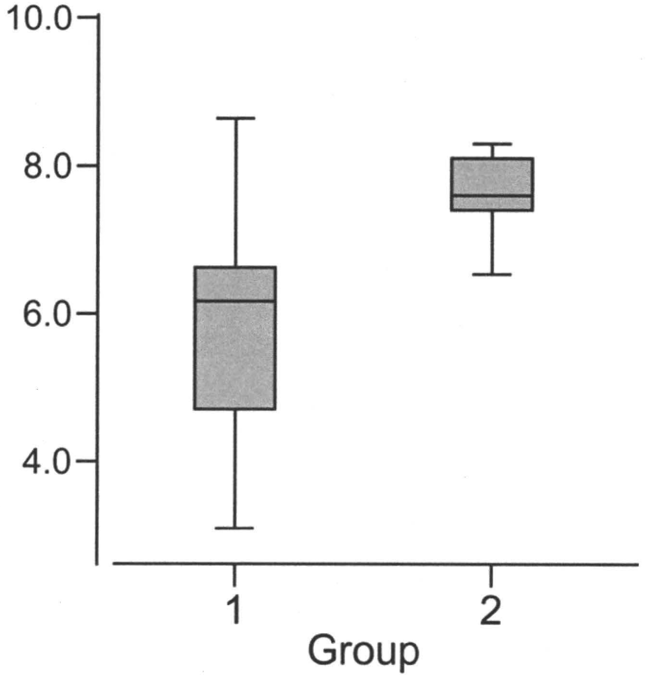

Fig. 3. Box-and-whisker plot for the maximal thickness of OPLL according to the 2 outcome groups. A significant difference was apparent between Group 1 (sufficient decompression) and Group 2 (insufficient decompression).

with the spinal cord. Ossification of the posterior longitudinal ligament less than 4 segments below the C2–3 intervertebral disc should be a theoretical candidate for anterior surgery when thickness exceeds 7.2 mm. How-

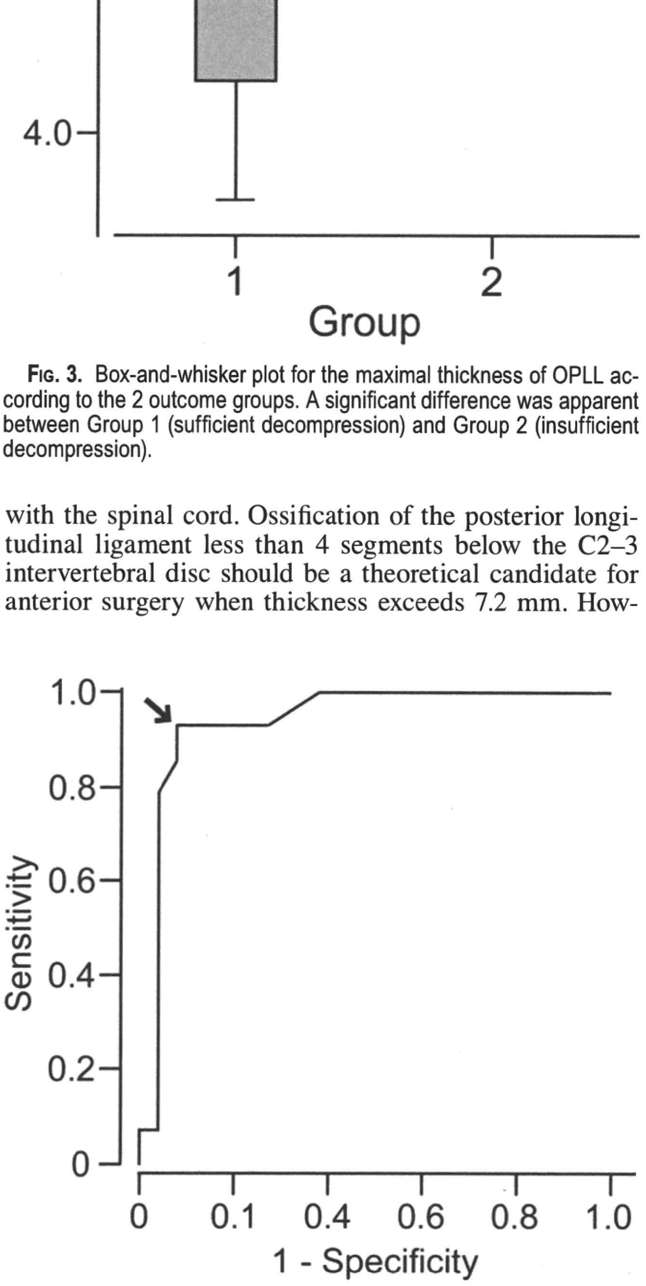

Fig. 4. Graph depicting the ROC curve to determine cutoff points of OPLL thickness. When 7.2 mm was the cutoff point, sensitivity was 0.92, specificity was 0.889, and the sum of both was maximal *(arrow)*. The area under the ROC curve was 0.0919, showing good discriminatory power.

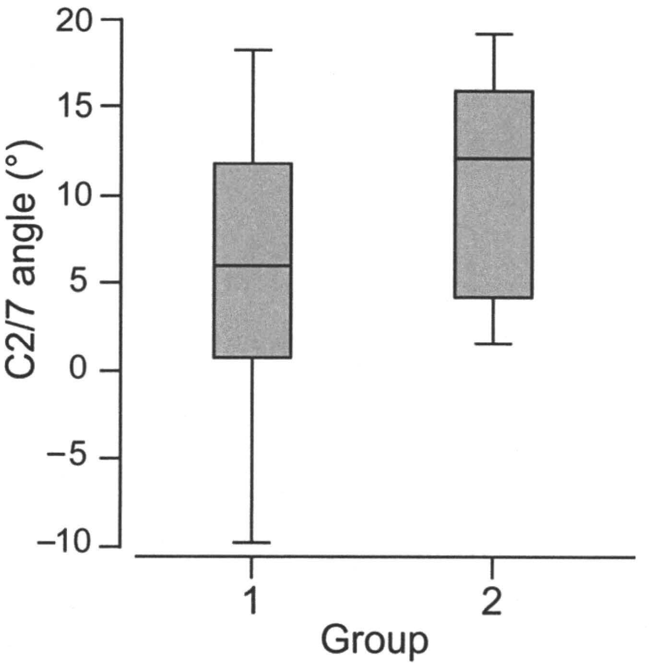

Fig. 5. Box-and-whisker plot of the C2–7 angle according to the 2 outcome groups. No significant difference was apparent between the groups.

ever, OPLL thickness showed no significant correlation with neurological outcomes as of 2 years after surgery. Thus, laminoplasty shows morphological limitations for thick OPLLs but remains the first choice for any type of multiple-level OPLL. Late deterioration after laminoplasty for thick cervical OPLL has been reported.[4] Long-term follow-up studies are thus needed to further clarify the limitations of laminoplasty and the indications for anterior surgery or posterior correction of kyphosis with instrumentation.

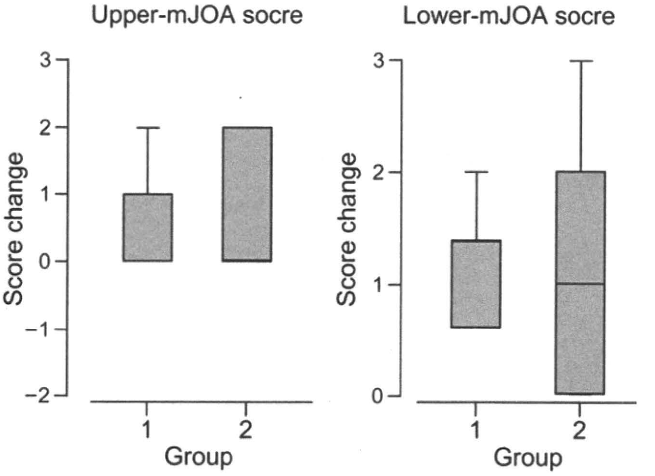

Fig. 6. Box-and-whisker plot of mJOA score changes according to the 2 outcome groups. No significant difference was seen between the 2 groups in score changes before and 2 years after surgery.