

Prevalence of radiographic lumbar spondylosis and its association with low back pain in the elderly 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 the elderly, few epidemiologic studies have been performed. We investigated the prevalence of radiographic lumbar spondylosis using a large-scale population, and examined the association with low back pain.

Methods: From a nationwide cohort study ROAD (Research on Osteoarthritis Against Disability), 2,288 participants (≥ 60 years; 818 men and 1,470 women) living in urban, mountainous and seacoast communities were analyzed. The radiographic severity at lumbar intervertebral levels from L1/2 to L5/S was determined by the Kellgren/Lawrence (KL) grading.

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

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

Key words: Osteoarthritis, spondylosis, lumbar spine, prevalence, pain

INTRODUCTION

Lumbar spondylosis is considered a major public health issue causing chronic disability of the elderly in most developed countries (1,2). Despite the urgent need for strategies for the prevention and treatment of this condition, the epidemiologic data on lumbar spondylosis such as its prevalence and association with symptoms are sparse. With the goal of establishing epidemiologic indexes to evaluate clinical evidence for the development of the 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 seacoast communities of Japan.

Lumbar spondylosis is characterized by disc degeneration and osteophytosis (2,3). Although this disorder has been widely studied in a clinical setting, few population-based radiologic 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 of age. Hence, the present study initially investigated the prevalence and distribution of this disorder according to age, gender and community using cohorts of 2,288 participants 60 years or older 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 (0-4) scales, and $KL \geq 2$ 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 there are few epidemiologic studies which have applied the KL system to evaluate the lumbar spine (5, 6, 9). Hence, to assess osteophyte formation alone and disc space narrowing with or without osteophytosis separately, the present study examined not only the prevalence of $KL \geq 2$ spondylosis but also that of $KL \geq 3$ spondylosis.

Although low back pain is believed to be the principal clinical symptom of lumbar spondylosis, its association with the radiographic severity remains unclarified. The correlation was not as strong as one would expect, and there is often a disconnect 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 the radiographic severity and low back pain.

METHODS

Participants

The ROAD study is a nationwide prospective cohort study for bone and joint diseases constituted of population-based cohorts established in several communities in Japan. To date, we have completed creation of a baseline database including clinical and genomic information of 3,040 inhabitants (men 1,061, women 1,979) 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 seacoast region in Taiji, Wakayama. Participants in the urban region were recruited from those of a cohort study (13) in which the participants were randomly drawn from the Itabashi-ward residents register database and the response rate in the age groups of 60 years or older were 75.6%. Participants in the mountainous and seacoast regions were recruited from

listings of resident registration and the response rates in the age groups of 60 years or older were 68.4 and 29.3%, respectively. All participants provided written informed consent, and the study was conducted with approval of ethical committees of the University of Tokyo and the Tokyo Metropolitan Institute of Gerontology. 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; weight [kg] / height [m²]). Medical information was taken by well-experienced orthopaedic surgeons (S.M. and H.O.) on systemic, local and mental status including information of 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 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). Height was 162.5 and 149.7 cm in men and women, respectively, in the ROAD study vs. 162.6 and 149.9 cm in the Japanese general population. Weight was 61.3 and 51.8 kg vs. 61.6 and 53.8 kg. Percentage of population with a smoking habit was 26.4 and 3.2% vs. 29.4 and 4.0%. From the baseline data of the overall participants, the present study analyzed 2,288 (818 men and 1,470 women) who were 60 years or older.

Radiographic assessment

Plain radiographs of the lumbar spine were taken at anteroposterior and lateral position, and the images were downloaded into Digital Imaging and Communication in Medicine (DICOM) format files to assess radiographic spondylosis. We used contrast-adjusted images to detect osteophytes and intervertebral spaces when the original images were obscure. Osteophytes were analyzed 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 well-experienced orthopaedist (S.M.) who was masked to the patients' backgrounds. To evaluate the intraobserver variability of the KL grading, 100 randomly selected radiographs of the lumbar spine were scored by the same observer more than one month after the first reading. Furthermore, 100 other radiographs were scored by two experienced orthopaedic surgeons (S.M. & H.O.) using the same radiographic atlas for interobserver variability. The intra- and interobserver variabilities were evaluated by the kappa analysis. These variabilities of the KL grading on lumbar radiographs have been shown to be sufficient for assessment (0.84 and 0.76, respectively).

Statistical analysis

The non-paired t-test was used to examine the difference of age and BMI between men and women. To compare the percentage of patients with radiographic spondylosis (KL grade ≥ 2 or ≥ 3 at the severest level) and low back pain between men and women, we performed a logistic regression analysis after adjustment for age and BMI. The differences of prevalence among the age-groups were determined using the 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 the radiographic spondylosis and low back pain was evaluated by the multivariate logistic regression analysis. The association of radiographic spondylosis at each intervertebral level with low back pain was determined by the logistic regression analysis after adjustment for age and BMI. The association of the number of intervertebral level with $KL \geq 3$ 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 Inc. NC).

RESULTS

Table 1 shows the overall characteristics of the 2,288 participants 60 years or older in the three cohorts of the ROAD study. Although men were significantly older than women in the overall population and in some communities, BMI was comparable between genders.

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, prevalence of radiographic spondylosis with $KL \geq 2$ 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 lumbar spine was 10.7%. Logistic regression analysis after adjustment for age and BMI revealed that the prevalence of radiographic spondylosis with $KL \geq 2$ was higher in men than in women. Meanwhile, that of $KL \geq 3$ radiographic spondylosis and low back pain was higher in women than in men. When the prevalence was compared among the generations, radiographic spondylosis ($KL \geq 2$ and ≥ 3) and low back pain tended to increase with age. Interestingly, the difference was greater between <70 and 70-79 than between 70-79 and ≥ 80 .

To identify risk factors for the radiographic spondylosis and low back pain, we further performed the logistic regression analysis to estimate odds ratios and confidence intervals (Table 3). Age and BMI were significantly associated with radiographic spondylosis. Male sex was confirmed to be a risk factor for $KL \geq 2$ spondylosis while female sex for $KL \geq 3$ and low back pain. Among the communities, mountainous area residents had a lower risk for $KL \geq 3$ spondylosis than urban residents.

We then examined the association between radiographic spondylosis and low back pain. Considering that intervertebral levels other than the severest level of radiographic spondylosis might possibly cause low back pain, the spondylosis at all intervertebral levels from L1/2 to L5/S was evaluated; $KL \geq 2$ spondylosis was found to be comparably prevalent at L2/3, L3/4 and L4/5, while $KL \geq 3$ spondylosis was remarkably prevalent at L4/5 in both men and women (Table 4). In fact, among the five levels L4/5 was most frequently determined to be the severest level in both genders (men: L1/2 49.4%, L2/3 59.5%, L3/4 58.0%, L4/5 64.5%, L5/S 48.3%, women: L1/2 49.5%, L2/3 58.0%, L3/4 58.6%, L4/5 65.5%, L5/S 44.3%). We then looked at the percentage of subjects with low back pain in three groups: $KL=0$ or 1, $KL=2$, and $KL \geq 3$, at each intervertebral level and the severest level in the overall population and the three communities (Figure 1). When odds ratios of $KL=2$ and $KL \geq 3$ spondylosis as compared to $KL=0$ or 1 for the pain were estimated by logistic regression analysis after adjustment for age and BMI, $KL=2$ spondylosis was not significantly associated with the pain in either gender at any intervertebral level (Table 5). However, $KL \geq 3$ spondylosis was related at all levels in women while in none of the levels in men. Further, the number of intervertebral level with $KL \geq 3$ spondylosis was significantly associated with low back pain in women ($p < 0.01$), but not in men by multiple regression analysis after adjustment for age and BMI. The association between $KL \geq 3$ spondylosis at the severest level and low back pain in women was conspicuous in younger

generations (<70 and 70-79) (Supplementary Table 1) and in the urban community (Supplementary Table 2).

DISCUSSION

The present study revealed that the prevalence of radiographic lumbar spondylosis with $KL \geq 2$ and $KL \geq 3$ in the elderly (≥ 60 years) was 75.8 and 50.4% respectively, and that of low back pain was 28.8% in the overall population. Although the $KL \geq 2$ spondylosis was more prevalent in men (84.1%) than in women (70.7%), the $KL \geq 2$ spondylosis and low back pain were more prevalent in women. This study also showed that $KL=2$ spondylosis was not significantly associated with low back pain compared to $KL=0$ or 1, while $KL \geq 3$ spondylosis was related to the pain only in women.

Most previous epidemiologic studies on lumbar spondylosis were focused on the middle-aged or younger populations, reporting the prevalence to be 46.5-83.7% (4,6-8,10,11). Our previous small-scale study on a younger population has shown that to be 76.3 and 37.4% (9). Interestingly, the subjects were living in a mountainous area in Japan, which was shown to have a lower risk for spondylosis in the present study. The variability may therefore be due to the differences of age, community, the sample size and ethnic variation. In fact, a study on the elderly (≥ 65 years) showed that the prevalence of $KL \geq 2$ spondylosis was 84.8 and 70.6%, similar to the present results, although in a relatively small number of subjects (5). We have reported different prevalence of lumbar spondylosis in Japan and the United Kingdom by a small-scale comparative study (9), which may in part relate to ethnic variation. It should be noticed that this is the first population-based study that investigated the age-related prevalence of lumbar spondylosis in the elderly. Although $KL \geq 2$ and $KL \geq 3$ spondylosis tended to increase with age, significant difference was detected between the sixties and the seventies, but not thereafter. However, this cross-sectional analysis, of course, does not lead to the conclusion that individual lumbar spondylosis hardly progresses after 80 years. Since the ROAD study is a prospective cohort study for more than ten years, the follow-up data will clarify the progression with aging. Furthermore, there was a difference of the prevalence between urban and mountainous communities. Considering that lumbar spondylosis is a common disease whose progression is governed by environmental and genetic factors, the regional difference is inevitable, as previously reported (6). Although age and obesity are known to be representative risk factors for lumbar spondylosis (2), the difference between communities in the present study was significant even after adjustment for age and BMI, indicating the involvement of other factors. Here again, further longitudinal survey in the ROAD study that collects database including detailed environmental and genomic information will elucidate the underlying backgrounds.

Interestingly, $KL \geq 2$ spondylosis was more prevalent in men than in women, while $KL \geq 3$ spondylosis was more prevalent in women. We and others also have reported that osteophytosis of lumbar spine was more common in men than in women (8,9), while disc space narrowing was prevalent in women (9). Based on the definition of the KL grading (12), the discrepancy may be due to distinct etiologic mechanisms between osteophyte formation and disc space narrowing. A cross-sectional study which investigated the extent, prevalence and distribution of spinal spondylosis in women also showed that osteophytosis and disc space narrowing were significantly correlated, but each predicted only 19% of the variation in the other (11). A previous prospective study in knee joints using a famous cohort, the Chingford Study, has

reported that there was no association between osteophyte formation and joint space narrowing (14). A recent study using quantitative magnetic resonance imaging (MRI) in knee joints has also shown that osteophyte formation was unrelated to cartilage loss (15). Furthermore, in an experimental mouse knee OA model, we have identified a cartilage specific molecule carminerin that induces only osteophyte formation without affecting cartilage degeneration during the OA progression (16,17). Further clinical and basic research will disclose the distinct backgrounds of these two representative OA features.

Symptomatic low back pain was solely associated with $KL \geq 3$ spondylosis in women, but not $KL \geq 2$ spondylosis in either gender or $KL \geq 3$ spondylosis in men. Considering the definition of KL grading again, this may suggest that disc space narrowing, but not osteophytosis, of the lumbar spine contributes to low back pain in consistency with previous reports (18). Difference of the association between genders might possibly be dependent on muscle strength to compensate the spinal instability due to disc space narrowing, since men are known to have greater muscle strength than women in all decades (19). However, approximately 30% of participants without definite radiographic lumbar spondylosis ($KL=0$ or 1) actually had low back pain, and the odds ratio of $KL \geq 3$ spondylosis for the pain was 1.44 and 1.80 in men and women, respectively, which is much lower than the previously reported odds ratio 8.5 of $KL \geq 3$ osteoarthritis in the knee joint for knee pain (20). This may be because low back pain arises from a number of disorders other than disc space narrowing, like nociceptive stimuli, inflammation, muscle weakness, and abnormal load on muscle, ligament or capsular tissues (21). Indeed, disc degeneration was reported to be detected by MRI in at least one lumbar level in all but one of asymptomatic volunteers in a 60-80 age group (22). Furthermore, pain is also influenced by psychological status like depression, since significant association between low back pain and depression has been confirmed in many longitudinal studies (23-25). A recent psychophysical study has shown that anxiety was linked to self-reported and induced low back pain for men, but not for women (26). This might be an alternative reason for lower association between radiographic spondylosis and low back pain in men.

There are several limitations in the present study. First, prevalence figures in this study using a large-scale population based sample of the elderly may be generalized to the Japanese population. However, this study investigated elderly participants who lived independently, not those who lived in institutional settings. Therefore, the calculated prevalence may be underestimated. Second, the definition of low back pain in the present study did not determine the severity. The association of lumbar spondylosis with the severity of low back pain could not be examined in this study. Third, analyses did not include facet joint osteoarthritis nor vertebral fracture, which would likely be associated with low back pain. This is the next task in the ROAD study to be investigated. Fourth, since the KL system emphasizes osteophytosis, it is unclear how to handle lumbar spondylosis with disc space narrowing but no osteophytosis. Since quantitative MRI is still too laborious and expensive to perform in general clinical practice, we are now developing a computer-aided diagnostic program which enables a fully automatic measurement of major features of lumbar spondylosis including disc space narrowing and osteophytosis on plain radiographs.

In conclusion, the present cross-sectional study using a large-scale population from the ROAD study revealed a high prevalence of radiographic lumbar spondylosis in the elderly. The prevalence differed to some extent by age, gender, and community. Gender seems to be distinctly associated with $KL \geq 2$ and $KL \geq 3$ lumbar spondylosis, and disc space narrowing with

or without osteophytosis in women may be a risk factor for low back pain. Further progress, along with continued longitudinal survey in the ROAD study, will elucidate the environmental and genetic backgrounds of lumbar spondylosis and its relation with low back pain.

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Conflict of interest/disclosure

There are no conflicts of interest or disclosures regarding the present manuscript.

Figure Legends

Figure 1. The percentage of subjects with low back pain according to the Kellgren/Lawrence grade in the overall population, and urban, mountainous and seacoast communities.

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Table 1. Characteristics of participants

	Men				Women			
	Overall	Urban	Mountainous	Seacoast	Overall	Urban	Mountainous	Seacoast
No. of subjects	818	397	266	155	1,470	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	146.6 ± 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 means ± SD. *p<0.05 vs. men in the corresponding group by the non-paired t-test.
BMI = Body mass index

Table 2. Number (percentage) of participants with radiographic lumbar spondylosis and low back pain according to gender and age

		Radiographic lumbar spondylosis		Low back pain
		KL≥2	KL≥3	
Overall	2,288	1,728 (75.8)	1,149 (50.4)	659 (28.8)
Men	818	688 (84.1)	383 (46.8)	201 (24.6)
<70	154	114 (74.0)	51 (33.1)	35 (22.7)
70-79	491	419 (85.3)*	232 (47.3)*	119 (24.2)
80≤	173	155 (89.6)*	100 (57.8)*	47 (27.2)
Women	1,470	1,040 (70.7)†	766 (52.1)†	458 (31.2)†
<70	356	196 (55.1)	128 (36.0)	80 (22.5)
70-79	818	612 (74.8)*	456 (55.7)*	273 (33.4)*
80≤	296	232 (78.3)*	182 (61.5)*	105 (35.5)*

Radiographic spondylosis was determined at the severest level among L1/2-L5/S1.

*p<0.05 vs. subjects aged <70 by Scheffe's test after adjustment for BMI.

There was no significant difference between 70-79 and ≤80 in both genders.

†p<0.05 vs. men by logistic regression analysis after adjustment for age and BMI.

Table 3. Association of gender and community with radiographic lumbar spondylosis and low back pain

	Radiographic lumbar spondylosis				Low back pain	
	KL \geq 2		KL \geq 3		OR	95%CI
	OR	95%CI	OR	95%CI		
Age, years	1.07	1.06-1.09†	1.05	1.04-1.07†	1.02	1.00-1.04*
BMI, kg/m ²	1.06	1.03-1.09†	1.04	1.01-1.06†	1.02	0.99-1.05
Women (vs. Men)	0.68	0.61-0.76†	1.13	1.03-1.23†	1.19	1.08-1.31†
Community (vs. Urban)						
Mountainous	0.82	0.65-1.04	0.56	0.45-0.69†	0.87	0.69-1.08
Seacoast	1.24	0.93-1.66	1.06	0.84-1.34	0.86	0.66-1.11

Radiographic spondylosis was determined at the severest level among L1/2-L5/S1.

The odds ratios were calculated by logistic regression analysis after adjustment for all other variables.

* $p < 0.05$, † $p < 0.01$

OR = odds ratio, CI = confidence interval

Table 4. Number (percentage) of subjects with radiographic lumbar spondylosis at each intervertebral level in all cohorts

	KL \geq 2		KL \geq 3	
	Men	Women	Men	Women
L1/2	474 (57.9)	609 (41.4)	116 (14.2)	254 (17.3)
L2/3	541 (66.1)	749 (51.0)	164 (20.1)	355 (24.2)
L3/4	554 (67.7)	735 (50.0)	194 (23.7)	419 (28.5)
L4/5	523 (63.9)	736 (50.1)	306 (37.5)	605 (41.2)
L5/S	400 (48.9)	576 (39.2)	197 (24.2)	413 (28.1)

Table 5. Association of KL grade at each intervertebral level with low back pain

	L1/2		L2/3		L3/4		L4/5		L5/S		Severest	
	OR	95%CI	OR	95%CI								
Men												
KL=2	1.30	0.92-1.84	0.94	0.65-1.36	1.43	0.98-2.11	1.24	0.82-1.89	1.12	0.75-1.65	1.15	0.70-1.92
KL≥3	1.30	0.79-2.11	1.25	0.80-1.94	1.49	0.96-2.32	1.42	0.97-2.08	1.22	0.82-1.81	1.44	0.89-2.38
Women												
KL=2	1.20	0.91-1.57	0.99	0.75-1.31	0.96	0.71-1.30	1.25	0.82-1.88	1.07	0.73-1.54	0.99	0.69-1.42
KL≥3	1.66	1.23-2.24*	1.74	1.32-2.30*	2.10	1.62-2.72*	1.88	1.48-2.38*	1.60	1.25-2.06*	1.80	1.38-2.37*

The odds ratio was calculated by logistic regression analysis compared with subjects with KL grade 0 or 1 after adjustment for age and BMI. *p<0.01

OR = odds ratio, CI = confidence interval

Supplementary Table 1. Association of KL grade at the severest level with low back pain according to age

	Overall		<70		70-79		80≤	
	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI
Men								
KL=2	1.15	0.70-1.92	0.94	0.49-1.86	2.78	0.96-9.38	0.70	0.23-2.37
KL≥3	1.44	0.89-2.38	1.37	0.74-2.62	2.50	0.82-8.71	0.80	0.28-2.53
Women								
KL=2	0.99	0.69-1.42	1.11	0.69-1.79	1.18	0.57-2.39	0.59	0.24-1.36
KL≥3	1.80	1.38-2.37†	1.93	1.34-2.80†	1.82	1.03-3.22*	1.39	0.77-2.57

The odds ratio was calculated by logistic regression analysis compared with subjects with KL grade 0 or 1 after adjustment for BMI. *p<0.05, †p<0.01
OR = odds ratio, CI = confidence interval

Supplementary Table 2. Association of KL grade at the severest level with low back pain according to community

	Overall		Urban		Mountainous		Seacoast	
	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI
Men								
KL=2	1.15	0.70-1.92	1.96	0.87-4.88	0.54	0.25-1.16	1.75	0.48-8.46
KL≥3	1.44	0.89-2.38	2.49	1.16-6.01*	0.68	0.31-1.48	2.24	0.64-10.53
Women								
KL=2	0.99	0.69-1.42	1.15	0.68-1.93	0.72	0.39-1.31	1.21	0.49-2.88
KL≥3	1.80	1.38-2.37†	1.94	1.32-2.88†	1.52	0.93-2.51	1.80	0.94-3.56

The odds ratio was calculated by logistic regression analysis compared with subjects with KL grade 0 or 1 after adjustment for BMI. *p<0.05, †p<0.01
OR = odds ratio, CI = confidence interval

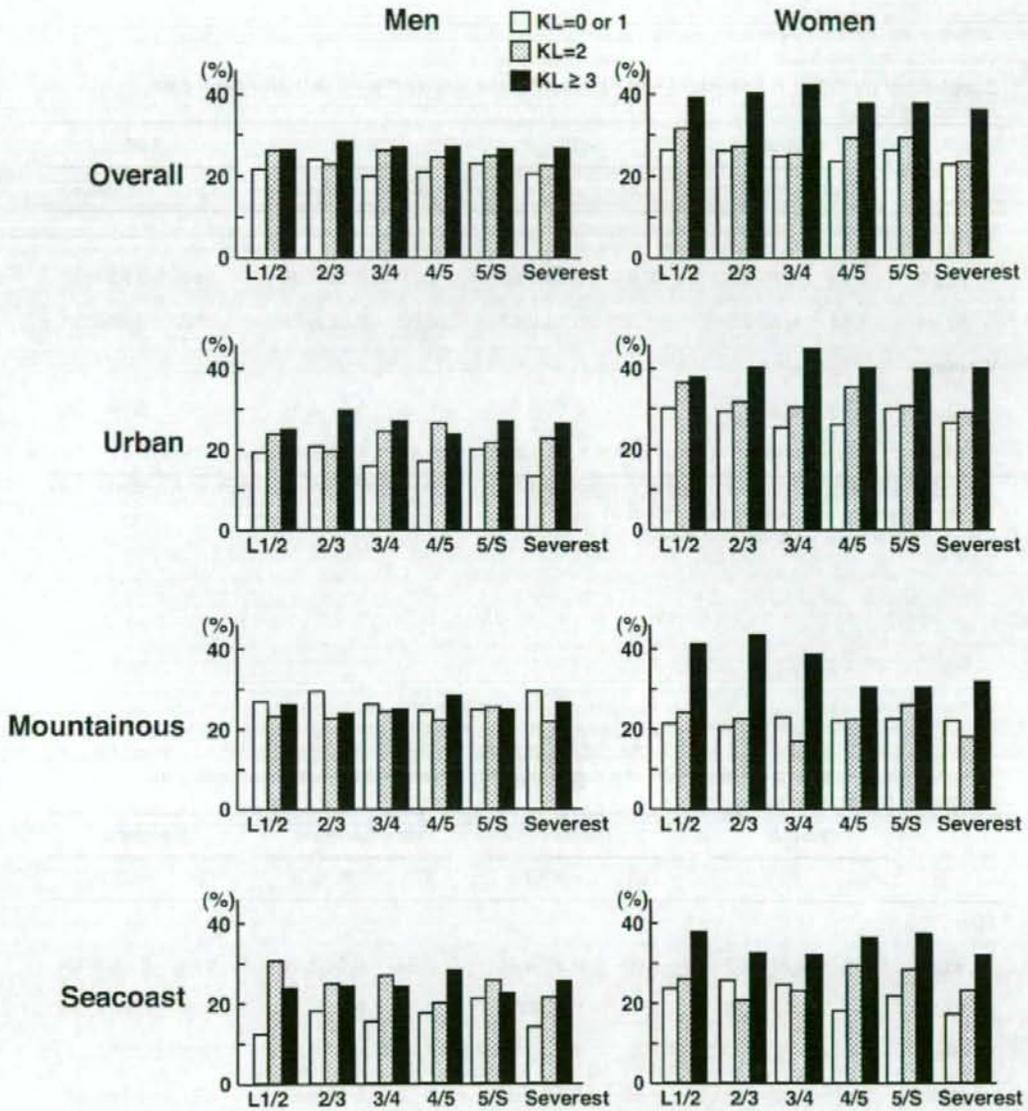


Figure 1

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.

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

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 circumferences 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/cm² (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/cm² while the SD is 0.146 g/cm² [22]. The present study therefore defined OP at the lumbar spine as L2–4

BMD $<0.827 \text{ g/cm}^2$. 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 $<0.617 \text{ g/cm}^2$. 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 ³)
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 \pm 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

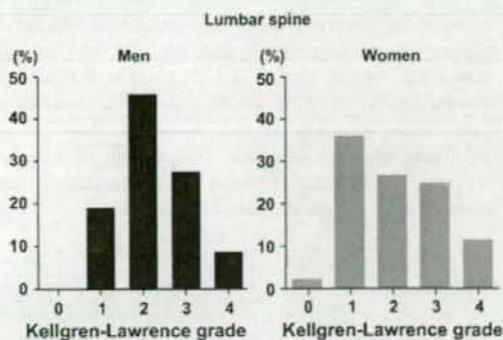


Fig. 1 Distribution of Kellgren-Lawrence grades at the lumbar spine by gender at the baseline in the Miyama population

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 (%) Osteoporosis Osteoarthritis ^a	Age strata (years)	Number of participants	Prevalence (%) 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