DOI 10.3109/14397595.2014.972607

Table 2. Comparison of baseline characteristics between the occurrence or nonoccurrence of each musculoskeletal disease during the 3-year follow-up period.

	Knee osteoarthritis (population at risk = 728)			Lumbar spondylosis (population at risk = 530)			Osteoporosis of lumbar spine (L2–4) (population at risk = 1,179)			Osteoporosis of femoral neck (population at risk = 1,187)		
	Occurrence (*n* = 71)	Nonoccurrence (*n* = 657)	p value (occurrence vs. nonoccurrence)	Occurrence (*n* = 182)	Nonoccurrence (*n* = 348)	p value (occurrence vs. nonoccurrence)	Occurrence (*n* = 27)	Nonoccurrence (*n* = 1,152)	p value (occurrence vs. nonoccurrence)	Occurrence (*n* = 65)	Nonoccurrence (*n* = 1,122)	p value (occurrence vs nonoccurrence)
Selected characteristics, mean (SD)												
Age, y	67.3 (8.2)	58.2 (11.8)	< 0.0001***	63.3 (10.8)	56.8 (12.5)	< 0.0001***	66.8 (8.9)	62.4 (11.8)	0.0584+	70.2 (9.0)	61.9 (11.5)	< 0.0001***
Height, cm	153.9 (7.6)	158.8 (8.6)	< 0.0001***	154.3 (9.2)	155.2 (7.9)	0.2573	151.9 (7.8)	157.0 (8.6)	0.0022**	151.4 (6.7)	157.2 (8.7)	< 0.0001***
Weight, kg	56.0 (8.8)	56.8 (11.0)	0.556	54.9 (9.7)	53.6 (9.5)	0.1477	50.6 (7.4)	57.7 (10.3)	0.0004***	49.0 (6.4)	58.1 (10.3)	< 0.0001***
BMI, kg/m^2	23.6 (2.9)	22.4 (3.2)	0.0035**	23.0 (3.1)	22.2 (3.3)	0.0107*	22.0 (3.0)	23.4 (3.3)	0.0312*	21.5 (3.2)	23.5 (3.3)	< 0.0001***
Frequency of selected characteristics, %												
Female sex	74.7	58.6	0.009**	71.4	83.1	0.002*	85.2	61.0	0.011*	84.6	60.6	< 0.001***
Residing in a coastal area	56.3	70.8	0.012*	42.3	61.5	< 0.001***	48.2	56.4	0.392	52.3	56.4	0.516
Current smoking habit (more than once a month)	7.1	16.9	0.034*	14.4	9.8	0.118	3.9	13.7	0.147	5.0	13.8	0.051+
Current alcohol consumption (more than once a month)	35.2	47.9	0.041*	38.5	39.3	0.850	40.7	44.3	0.714	20.3	45.0	< 0.001***
Prevalence of musculoskeletal diseases,%												
Knee osteoarthritis	–	–	–	44.8	30.5	0.001**	59.3	44.6	0.130	52.3	43.3	0.154
Lumbar spondylosis	67.6	51.3	0.009**	–	–	–	55.6	62.9	0.439	58.5	61.4	0.635
Osteoporosis of lumbar spine (L2–4)	14.1	10.2	0.312	18.7	14.9	0.268	–	–	–	26.2	4.9	< 0.001***
Osteoporosis of femoral neck	11.3	7.2	0.213	14.3	8.9	0.058+	25.9	4.8	< 0.001***	–	–	–
Prevalence metabolic syndrome components, %												
Obesity	9.9	7.8	0.535	11.0	6.6	0.080+	3.7	11.6	0.204	3.1	11.9	0.031*
Hypertension	85.7	55.6	< 0.001***	63.2	49.4	0.003**	77.8	66.1	0.204	81.3	65.4	0.009**
Dyslipidemia	15.5	11.6	0.333	13.2	9.8	0.232	11.1	13.7	0.697	12.3	13.6	0.776
Impaired glucose tolerance	35.2	15.8	< 0.001***	19.2	16.1	0.363	14.8	21.4	0.406	23.1	20.9	0.669

BMI body mass index.
"+$p < 0.1$, *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$".

Table 3. Comparison of baseline characteristics between the occurrence or nonoccurrence of each metabolic syndrome component during the 3-year follow-up period.

	Obesity (population at risk = 1,239)			Hypertension (population at risk = 456)			Dyslipidemia (population at risk = 1,204)			Impaired glucose tolerance (population at risk = 1,092)		
	Occurrence (n = 45)	Nonoccurrence (n = 1,194)	p value (occurrence vs nonoccurrence)	Occurrence (n = 216)	Nonoccurrence (n = 240)	p value (occurrence vs nonoccurrence)	Occurrence (n = 236)	Nonoccurrence (n = 968)	p value (occurrence vs nonoccurrence)	Occurrence (n = 146)	Nonoccurrence (n = 946)	p value (occurrence vs nonoccurrence)
Selected characteristics, mean (SD)												
Age, y	58.8 (12.5)	64.3 (11.9)	0.0024**	60.1 (11.9)	55.9 (12.8)	0.0003***	66.2 (9.5)	63.0 (12.4)	0.0002***	65.4 (10.5)	62.5 (12.3)	0.0061**
Height, cm	155.5 (7.5)	155.5 (8.3)	0.9578	156.2 (9.1)	156.9 (7.9)	0.3902	155.7 (9.1)	154.0 (8.6)	0.0094**	154.3 (9.3)	156.0 (8.9)	0.0289*
Weight, kg	63.9 (6.8)	53.8 (8.8)	< 0.0001***	54.7 (10.6)	53.1 (8.5)	0.0782+	56.5 (10.4)	55.2 (10.4)	0.1029	56.2 (12.3)	55.2 (10.2)	0.3097
BMI, kg/m^2	26.4 (1.0)	22.2 (2.5)	< 0.0001***	22.3 (3.3)	21.5 (2.6)	0.0039**	23.7 (3.2)	22.7 (3.3)	< 0.0001***	23.4 (3.7)	22.6 (3.1)	0.0041**
Frequency of selected characteristics, %												
Female sex	75.6	66.4	0.201	69.4	74.2	0.262	74.2	65.5	0.011*	72.6	67.1	0.187
Residing in a coastal area	82.2	52.3	< 0.001***	61.1	63.3	0.625	60.6	50.7	0.006**	41.8	55.5	0.002**
Current smoking habit (more than once a month)	9.1	12.2	0.533	16.4	11.4	0.126	7.4	13.4	0.012*	10.7	12.7	0.509
Current alcohol consumption (more than once a month)	33.3	40.2	0.355	36.0	42.5	0.156	28.8	44.3	< 0.001***	35.2	44.0	0.046*
Prevalence of musculoskeletal diseases, %												
Knee osteoarthritis	33.3	45.8	0.098+	41.7	25.8	< 0.001***	54.5	44.2	0.005**	51.4	43.7	0.082+
Lumbar spondylosis	57.8	60.7	0.692	50.9	42.1	0.059+	64.8	59.7	0.149	61.0	59.5	0.740
Osteoporosis of lumbar spine (L2–4)	4.4	13.2	0.086+	14.0	7.9	0.038*	16.2	11.6	0.056+	13.1	12.3	0.778
Osteoporosis of femoral neck	0.0	12.3	0.013*	13.0	7.5	0.051+	16.7	9.9	0.003**	11.7	10.6	0.685
Prevalence of metabolic syndrome components, %												
Obesity	–	–	–	6.9	2.9	0.045*	12.3	9.3	0.169	13.7	7.4	0.010*
Hypertension	75.6	64.7	0.133	–	–	–	73.2	64.1	0.008**	63.7	63.1	0.888
Dyslipidemia	22.2	12.1	0.045*	11.1	7.9	0.244	–	–	–	11.6	10.4	0.638
Impaired glucose tolerance	28.9	18.8	0.093+	13.4	9.6	0.197	26.7	16.9	0.001**	–	–	–

BMI body mass index.
+$p<0.1$, *$p<0.05$, **$p<0.01$, ***$p<0.001$.

DOI 10.3109/14397595.2014.972607

Table 4. Results of the logistic regression analyses for the occurrence of musculoskeletal diseases over a 3-year period.

		Occurrence of knee osteoarthritis			Occurrence of lumbar spondylosis			Occurrence of osteoporosis of the lumbar spine (L2–4)			Occurrence of osteoporosis of the femoral neck		
Explanatory variables	Reference (at baseline)	OR	95% CI	p value	OR	95% CI	p value	OR	95% CI	p value	OR	95% CI	p value
Musculoskeletal diseases													
Knee osteoarthritis	0: KL 0,1 vs 1: KL = 2	–	–	–	1.11	0.67–1.85	0.676	1.92	0.72–5.10	0.189	0.65	0.32–1.34	0.243
	0: KL 0,1 vs 2: KL ≥ 3	–	–	–	1.54	0.74–3.22	0.246	0.70	0.16–3.04	0.637	0.52	0.22–1.23	0.140
Lumbar spondylosis	0: KL 0,1 vs 1: KL = 2	1.25	0.61–2.58	0.546	–	–	–	0.73	0.24–2.15	0.563	0.82	0.38–1.79	0.616
	0: KL 0,1 vs 2: KL ≥ 3	1.35	0.69–2.64	0.382	–	–	–	0.52	0.19–1.44	0.209	0.54	0.27–1.08	0.086+
Osteoporosis of the lumbar spine (L2–4)	0: absent, 1: present	0.46	0.19–1.10	0.083+	0.78	0.43–1.39	0.395	–	–	–	2.19	1.01–4.79	0.047*
Osteoporosis of the femoral neck	0: absent, 1: present							4.21	1.46–12.1	0.008**	–	–	–
Metabolic syndrome components													
Obesity	0: BMI ≤ 27.5, 1: BMI > 27.5	1.59	0.59–4.30	0.357	1.97	0.99–3.92	0.053+	0.48	0.06–3.78	0.486	0.32	0.07–1.43	0.134
Hypertension	0: absent, 1: present	2.57	1.22–5.42	0.013*	1.20	0.79–1.82	0.395	1.81	0.67–4.87	0.243	1.36	0.66–2.79	0.400
Dyslipidemia	0: absent, 1: present	1.14	0.52–2.47	0.746	1.31	0.72–2.41	0.378	0.84	0.24–2.99	0.790	0.75	0.33–1.73	0.504
Impaired glucose tolerance	0: absent, 1: present	1.99	1.07–3.70	0.029*	0.73	0.43–1.24	0.243	0.65	0.21–2.03	0.456	0.90	0.45–1.80	0.773
Adjusted for:													
Age, years	+ 1 y	1.08	1.05–1.12	<0.001***	1.04	1.02–1.06	<0.001***	1.03	0.98–1.08	0.257	1.12	1.07–1.16	<0.001***
Sex	0: men, 1: women	4.73	2.22–10.1	<0.001***	0.48	0.28–0.85	0.011*	3.07	0.89–10.6	0.077+	4.75	1.91–11.9	0.001**
Residing region	0: mountainous area, 1: coastal area	0.63	0.36–1.11	0.112	0.60	0.38–0.94	0.024*	1.13	0.47–2.75	0.785	1.41	0.75–2.61	0.285
Smoking	0: ex or never smoker, 1: current smoker	1.05	0.36–3.01	0.931	1.31	0.67–2.57	0.431	0.56	0.07–4.69	0.593	1.16	0.31–4.13	0.819
Alcohol consumption	0: ex or never drinker, 1: current drinker	1.04	0.56–1.91	0.907	0.78	0.50–1.21	0.260	1.18	0.49–2.87	0.711	0.66	0.32–1.37	0.260

BMI body mass index, *CI* confidence interval, *KL* Kellgren–Lawrence grade, *OR* odds ratio.

+$p<0.1$, *$p<0.05$, **$p<0.01$, ***$p<0.001$.

Multivariate logistic regression analysis was performed for each of the outcome variables: occurrence of knee osteoarthritis (0, nonoccurrence; 1, occurrence), occurrence of lumbar spondylosis (0, absence; 1, presence), occurrence of osteoporosis of the lumbar spine (L2–4), and occurrence of osteoporosis of the femoral neck. All of the models included obesity, hypertension, dyslipidemia, and impaired glucose tolerance at baseline as explanatory variables in addition to the presence at baseline of each of the other musculoskeletal variables (knee osteoarthritis, lumbar spondylosis, osteoporosis at L2–4, osteoporosis of the femoral neck) after adjusting for age, sex, regional differences, smoking, and alcohol consumption.

Table 5. Results of the logistic regression analyses for the occurrence of metabolic components over a 3-year period.

		Occurrence of obesity			Occurrence of hypertension			Occurrence of dyslipidemia			Occurrence of impaired glucose tolerance		
Explanatory variables	Reference	OR	95% CI	p value	OR	95% CI	p value	OR	95% CI	p value	OR	95% CI	p value
Musculoskeletal diseases													
Knee osteoarthritis	0: KL 0,1 vs 1: KL = 2	0.91	0.38–2.20	0.832	1.84	1.09–3.12	0.024*	1.17	0.79–1.73	0.440	1.06	0.67–1.67	0.797
	0: KL 0,1 vs 2: KL ≥ 3	1.09	0.39–3.08	0.866	1.96	0.89–4.34	0.096+	1.66	1.05–2.61	0.029*	0.70	0.39–1.29	0.256
Lumbar spondylosis	0: KL 0,1 vs 1: KL = 2	1.32	0.55–3.16	0.532	0.82	0.47–1.42	0.479	1.08	0.71–1.65	0.720	1.11	0.68–1.82	0.673
	0: KL 0,1 vs 2: KL ≥ 3	1.20	0.55–2.62	0.655	1.44	0.88–2.34	0.143	0.95	0.64–1.39	0.779	0.90	0.57–1.44	0.670
Osteoporosis of the lumbar spine (L2–4)	0: absent, 1: present	0.47	0.11–2.06	0.314	1.52	0.77–3.01	0.231	1.20	0.75–1.92	0.446	0.73	0.40–1.33	0.302
Components of metabolic syndrome													
Obesity	0: BMI ≤ 27.5, 1: BMI > 27.5	–	–	–	3.39	1.25–9.17	0.016*	1.04	0.63–1.72	0.866	2.42	1.34–4.39	0.004**
Hypertension	0: absent, 1: present	2.99	1.35–6.59	0.007**	–	–	–	1.29	0.89–1.85	0.174	0.82	0.54–1.22	0.326
Dyslipidemia	0: absent, 1: present	1.88	0.86–4.09	0.112	1.20	0.61–2.35	0.589	–	–	–	1.17	0.66–2.05	0.598
Impaired glucose tolerance	0: absent, 1: present	2.02	0.97–4.23	0.061+	1.17	0.62–2.21	0.620	1.53	1.06–2.20	0.023*	–	–	–
Adjusted factors													
Age, y	+ 1 y	0.95	0.91–0.98	0.002**	1.01	0.99–1.04	0.162	1.02	1.00–1.03	0.087+	1.02	1.00–1.05	0.025*
Sex	0: men, 1: women	1.46	0.61–3.47	0.396	0.77	0.45–1.33	0.352	1.28	0.85–1.93	0.245	1.35	0.81–2.25	0.245
Residing region	0: mountainous area, 1: coastal area	3.30	1.38–7.92	0.007**	1.25	0.80–1.97	0.327	1.84	1.31–2.59	<0.001***	0.65	0.43–0.98	0.038*
Smoking	0: ex or never smoker, 1: current smoker	0.66	0.20–2.25	0.510	1.82	0.98–3.40	0.060+	0.79	0.44–1.41	0.425	1.11	0.59–2.09	0.747
Alcohol consumption	0: ex or never drinker, 1: current drinker	0.80	0.39–1.64	0.549	0.78	0.50–1.20	0.259	0.71	0.50–1.01	0.060+	0.69	0.45–1.07	0.096+

BMI body mass index, *CI* confidence interval, *KL* Kellgren–Lawrence grade, *OR* odds ratio.
$+p<0.1$, $*p<0.05$, $**p<0.01$, $***p<0.001$.
Multivariate logistic regression analysis was performed for each of the metabolic syndrome components: obesity, hypertension, dyslipidemia, and impaired glucose tolerance. All of the models included knee osteoarthritis (0, KL grades 0, 1; 1, KL grade 2; 2, KL grades, 3, 4), lumbar spondylosis (0, KL grades 0, 1; 1, KL grade 2; 2, KL grades 3, 4), osteoporosis (at L2–4) at baseline as explanatory variables in addition to the presence at baseline of each of the other metabolic syndrome components after adjusting for age, sex, regional differences, smoking, and alcohol consumption.

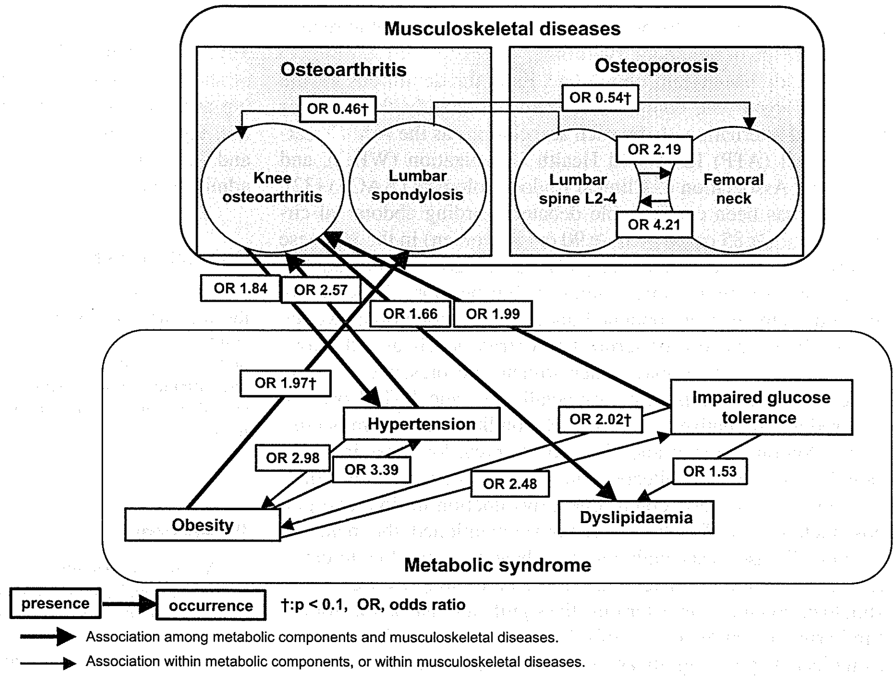

Figure 1. Summary of the mutual associations among musculoskeletal diseases and metabolic syndrome components.

was not significant. Therefore, to prevent new occurrence of KOA, the importance of body weight reduction remains unchanged.

With regard to the etiology of the association between OA and metabolic syndrome components, mechanical stress resulting from the weight-related load would be the first consideration. However, the results of the present study remained the same after the adjustment for OB. Zhuo et al. provided several explanations in their review in addition to summarizing the shared mechanisms involving inflammation, oxidative stress, common metabolites, and endothelial dysfunction that characterize the etiologies of OA and metabolic syndrome [30]. In the interest of determining whether inflammation played a role in the present study, we added baseline serum C-reactive protein (CRP) levels to the logistic regression analysis; the adjusted ORs for HT and IGT, with the outcome as the occurrence of KOA, remained unchanged. Because we used a standard method to measure CRP levels, further research is required to assess the effect of systemic inflammation on KOA using a more sensitive measurement method. With regard to oxidative stress, we plan to measure oxidative stress after we determine suitable indices and evaluate the potential role of oxidative stress as a shared risk factor for both musculoskeletal diseases and metabolic syndrome components.

The risk of the occurrence of LS was not influenced by any of the variables included in the present study; however, OB tended to increase the risk. Fewer environmental risk factors, including occupational activities, exist for LS than for KOA [31]. It is possible that lumbar osteoproliferative changes are not influenced by mechanical stress to the same extent as the knee. On the other hand, the definition in the present study of a new case of joint OA as a baseline KL grade <2 for joints and a follow-up grade ≥ 2 for at least one joint may have also influenced the findings. It is common to use a KL grade ≥ 2 for at least one joint as the criterion for the presence of OA, and, in the Japanese, a previously reported prevalence using this criterion was very high [18]. Therefore, the population at risk for the occurrence of LS was small with insufficient statistical power to detect significant relationships in the present study. However, the results were not affected when we changed the criterion to a more severe KL grade ≥ 3 for at least one joint in the logistic multivariate analysis, indicating that it is necessary to use another index to detect the risk factors for LS. We have started to measure osteophytes and minimum joint space using computer-assisted systems to enable the detection of risk factors for the development of OA of the lumbar spine.

Only the presence of OP at one site increased the risk of the occurrence of OP at the other site. Therefore, the treatment of OP at any site may prevent OP at other sites. In addition, OB tended to decrease the risk of the occurrence of OP. When we replaced OB with BMI in the logistic regression analysis, a greater BMI ($+1$ kg/m^2) significantly reduced the risk of the occurrence of OP at L2–4 and the femoral neck; it has previously been reported that emaciation increases the risk of OP [12].

We have previously reported that the presence of lumbar OP significantly reduces the risk of the occurrence of LS in a population-based cohort that consisted of 400 Japanese middle-aged and elderly people who were followed up for 10 years [17]. In the present study, LS tended to reduce the risk of the occurrence of OP at the femoral neck, and lumbar OP tended to reduce the risk of the occurrence of KOA. The low incidence of OP at both L2–4 (0.76%/year) and the femoral neck (1.83%/year) might not have resulted in sufficient statistical power to detect the risk of other musculoskeletal diseases. A longer observation period may be required to determine the significant risk factors, including musculoskeletal diseases and metabolic risk factors, for the occurrence of OP.

We also detected associations between the presence and occurrence of metabolic syndrome components, including OB and HT (reciprocal), OB and IGT (reciprocal), and IGT and DL. However, there was no significant relationship between HT and DL after adjustment for various confounders including smoking. When we replaced OB with the BMI values in the analysis, the significant associations that were present between OB and HT as well as IGT remained with BMI; furthermore, we found that BMI significantly increased the risk of the occurrence of DL (lumbar spine OP as an explanatory factor for OP, BMI $+1$ kg/m^2; OR, 1.08; 95% CI, 1.03–1.14; $p = 0.001$; femoral neck OP as an explanatory factor for OP, BMI $+1$ kg/m^2; OR, 1.09; 95% CI, 1.04–1.14; $p < 0.001$). Therefore, we emphasize that greater body composition increases the risk of other components of metabolic syndrome, and the maintenance of a healthy body composition is important to reduce the occurrence of metabolic syndrome.

This study has certain limitations. First, the definitions for the metabolic syndrome components were not exactly the same as those used internationally by such associations as the Adult Treatment Panel (ATP) III, World Health Organization (WHO), and American Association of Clinical Endocrinologists (AACE) [32]. As there has been considerable debate regarding abdominal circumference (≥ 85 cm in men, ≥ 90 cm in women) in the Japanese criteria [33], we decided to use BMI ≥ 27.5 kg/m^2 to indicate OB rather than abdominal circumference. Furthermore, because not all blood samples were obtained under fasting conditions, we did not use blood glucose or serum triglyceride levels as indicators. Therefore, our results may underestimate the presence of metabolic syndrome components, especially DL and IGT. However, we used an alternative index for each condition, as recommended by the National Health and Nutrition Survey, for cases in which samples could not be collected under fasting conditions [26]; thus, we believe our criteria could reflect dysfunction in lipid and glucose metabolisms. Finally, as previously mentioned, the incidence of some diseases, especially OP, may have been too low to detect risk factors in multivariate models. Therefore, longer observations should be conducted to determine the significant risk factors for OP. Similarly, the low incidence of OB might have biased the results, as indicated by the significant associations that were present with BMI but not OB. Because the main aim of the present study was to clarify the association between musculoskeletal diseases and metabolic components, we used the presence or occurrence of OB in the analysis. These results support the importance of body composition for the occurrence of musculoskeletal diseases or the components of metabolic syndrome, despite a lack of association with OB *per se*.

To conclude, we identified associations between the presence and occurrence of musculoskeletal diseases and metabolic syndrome components. Therefore, proactive prevention of metabolic syndrome or musculoskeletal diseases may also influence the occurrence of the other.

Acknowledgments

This work was supported by a Grant-in-Aid for H17-Men-eki-009 (Director, Kozo Nakamura), H20-Choujyu-009 (Director, Noriko Yoshimura), H23-Choujyu-002 (Director, Toru Akune), H-25-Choujyu-007 (Director, Noriko Yoshimura), and H25-Nanchitou(Men)-005 (Director, Sakae Tanaka) of the Ministry of Health, Labour and Welfare; and Scientific Research B23390172, B20390182, and Challenging Exploratory Research 24659317 to Noriko Yoshimura; B23390357 and C20591737 to Toru Akune; B23390356, C20591774, and Challenging Exploratory Research 23659580 to Shigeyuki Muraki; Challenging Exploratory Research 24659666 and 21659349 and Young Scientists A18689031 to Hiroyuki Oka; and Collaborating Research with NSF 08033011-00262 (Director, Noriko Yoshimura) from the Ministry of Education, Culture, Sports, Science and Technology in Japan. This study also was supported by grants from the Japan Osteoporosis Society (Noriko Yoshimura, Shigeyuki Muraki, Hiroyuki Oka, and Toru Akune), and research aid from the Japanese Orthopaedic Association (JOA-Subsidized Science Project Research 2006-1 & 2010-2; Director, Hiroshi Kawaguchi).

The authors wish to thank Dr. Takako Nojiri and Mr. Kazuhiro Hatanaka of the Gobo Public Health Centre; Dr. Naoki Hirabayashi of the Kawakami Clinic in Hidakagawa Town; Mrs. Tomoko Takijiri, Mrs. Rie Takiguchi, Mrs. Kyoko Maeda, and other members of the public office in Hidakagawa Town; Dr. Shinji Matsuda of the Shingu Public Health Centre; and Mrs. Tamako Tsutsumi, Mrs. Kanami Maeda, Mrs. Megumi Takino, Mrs. Shuko Okada, Mrs. Kazuyo Setoh, Mrs. Chise Ryouno, Mrs. Miki Shimosaki, Mrs. Chika Yamaguchi, Mrs. Yuki Shimoji, and other members of the public office in Taiji Town for their assistance in locating and scheduling participants for examinations. We also thank Ms. Kyoko Yoshimura, Mrs. Toki Sakurai, Mrs. Saeko Sahara, and Mr. Noriyuki Oe for their assistance in data reduction and administration.

Conflict of interest

All authors declare that (1) no author has received corporate support for the submitted work; (2) the authors have no relationships with companies that might have an interest in the submitted work in the previous 3 years; (3) the authors' spouses, partners, or children do not have financial relationships that may be relevant to the submitted work; and (4) the authors have no non-financial interests that may be relevant to the submitted work.

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Japan College of Rheumatology
MODERN RHEUMATOLOGY

http://informahealthcare.com/mor
ISSN 1439-7595 (print), 1439-7609 (online)

Mod Rheumatol, 2014; Early Online: 1–8

DOI: 10.3109/14397595.2014.883055

informa healthcare

ORIGINAL ARTICLE

Association of knee osteoarthritis with onset and resolution of pain and physical functional disability: The ROAD study

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Abstract

Objectives. To examine the onset and resolution of pain and physical functional disability using Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and their association with knee osteoarthritis (OA) in the longitudinal large-scale population of the nationwide cohort study, Research on Osteoarthritis/osteoporosis Against Disability (ROAD).
Methods. Subjects from the ROAD study who had been recruited during 2005–2007 were followed up 3 years later. A total of 1,578 subjects completed the WOMAC questionnaire at baseline and follow up, and the onset and resolution rate of pain and physical functional disability were examined. We also examined the association of onset of pain and physical functional disability and their resolution with severity of knee OA as well as age, body–mass index and grip strength.
Results. After a 3.3-year follow-up, the onset rate of pain was 35.0% and 35.3% in men and women, respectively, and the onset rate of physical functional disability was 38% and 40%, respectively. Resolution rate of pain was 20.3% and 26.2% in men and women, respectively, and resolution rate of physical functional disability was 16% and 14% in men and women, respectively. Knee OA was significantly associated with onset and resolution of pain and physical functional disability in women, but there was no significant association of knee OA with onset of pain and resolution of physical functional disability in men.
Conclusions. The present longitudinal study revealed the onset rate of pain and physical functional disability as well as their resolution, and their association with knee OA.

Keywords

Knee joint, Osteoarthritis, Epidemiology, Longitudinal studies

History

Received 9 September 2013
Accepted 10 January 2014
Published online 24 February 2014

Introduction

Knee osteoarthritis (OA), characterized by pathological features including joint space narrowing and osteophytosis, is a major public health issue causing chronic pain and disability among the elderly in most developed countries [1]. The prevalence of radiographic knee OA in Japan is high [2], with 25,300,000 subjects aged 40 years and older estimated to experience radiographic knee OA [3]. According to the recent National Livelihood Survey of the Ministry of Health, Labour and Welfare in Japan, OA is ranked fourth among diseases that cause disabilities that subsequently require support with activities of daily living [4].

The principal clinical symptoms of knee OA are pain and physical functional disability [5], but the correlation of these symptoms with radiographic severity of knee OA is controversial [2,6–8]. Thus it would be interesting to determine whether the impact of radiographic knee OA on pain and physical functional disability differs according to the severity of OA. In terms of disease-specific scales for estimating pain and physical functional disability due to knee OA, the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) has been used for Caucasians [9] and Asians [10,11], although these reports were not population-based studies. Furthermore, there is little information on the impact of knee OA on onset of pain and physical functional disability using WOMAC in Japan, although a population survey suggests that the disease pattern differs among races [12–14]. In addition, to the best of our knowledge, although pain and physical functional disability can disappear or improve, there is no information on the impact of knee OA on the resolution of pain and physical functional disability.

Grip strength is a useful marker of muscle function and sarcopenia [15]. There is growing evidence that reduced grip strength is associated with adverse outcomes including morbidity, disability, falls, higher fracture rates, increased length of hospital stay and mortality [16–18]. A previous study also showed that grip strength is related to total muscle strength [19]. Thus, the association of knee OA with pain and physical functional disability may be influenced by grip strength, but again, no studies have examined the association of knee OA and grip strength with onset of pain and disability as well as their resolution simultaneously in the same population using a longitudinal cohort study.

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The objective of the present study was to clarify the onset and resolution rate of pain and physical functional disability using WOMAC in Japanese men and women who were part of the large-scale, longitudinal, population-based cohort study known as the Research on Osteoarthritis/osteoporosis Against Disability (ROAD) study. In addition, we examined the association of body–mass index (BMI), grip strength and severity of knee OA with onset of pain and physical functional disability as well as their resolution in men and women.

Materials and methods

Subjects

The ROAD study was a nationwide prospective study for bone and joint diseases (with OA and osteoporosis as the representative bone and joint diseases) constituting population-based cohorts established in several communities in Japan. As a detailed profile of the ROAD study has already been described elsewhere [2,3,20], only a brief summary is provided here. During 2005–2007, we created a baseline database that included clinical and genetic information for 3,040 inhabitants (1,061 men; 1,979 women) aged 23–95 years (mean, 70.6 years), recruited from listings of resident registrations in three communities: an urban region in Itabashi, Tokyo; a mountainous region in Hidakagawa, Wakayama; and a coastal region in Taiji, Wakayama. All participants provided written informed consent, and the study was conducted with the approval of the ethics committees of the University of Tokyo and the Tokyo Metropolitan Institute of Gerontology. Participants completed an interviewer-administered questionnaire of 400 items that included lifestyle information such as smoking habit, alcohol consumption, family history, medical history and previous knee injury history. Furthermore, subjects were interviewed by well-experienced orthopedists regarding the treatment for knee OA, such as medication, injections, physical therapy, bracing, etc. between the baseline and follow-up study. Anthropometric measurements included height and weight, from which BMI (weight [kg]/height^2 [m^2]) was calculated. Grip strength was measured on bilateral sides using a TOEI LIGHT handgrip dynamometer (Toei Light Co., Ltd., Saitama, Japan), and the better measurement was used to represent maximum muscle strength. During 2008–2010, we attempted to trace and review all 3,040 subjects; they were invited to attend a follow-up interview. The interviews were conducted by the same trained orthopedists who undertook the baseline study during 2005–2007.

Radiographic assessment

All participants underwent radiographic examination of both knees using an anterior–posterior view with weight-bearing and foot map positioning. Fluoroscopic guidance with a horizontal anterior–posterior X-ray beam was used to properly visualize the joint space. Knee radiographs at baseline and follow-up were read in pairs without knowledge of the participant's clinical status by a single well-experienced orthopedist (S.M.), and the Kellgren Lawrence (KL) grade was defined using the KL radiographic atlas for overall knee radiographic grades [21]. In the KL grading system, radiographs are scored from grade 0 to grade 4, with the higher grades being associated with more severe OA. To evaluate the intraobserver variability of the KL grading, 100 randomly selected radiographs of the knee were scored by the same observer more than 1 month after the first reading. One hundred other radiographs were also scored by two experienced orthopedic surgeons (S.M. & H.O.) using the same atlas for interobserver variability. The intra- and inter variabilities evaluated for KL grades (0–4) were confirmed by kappa analysis to be sufficient for assessment (0.86 and 0.80, respectively).

Instruments

The WOMAC, a 24-item OA-specific index, consists of three domains: pain, stiffness and physical function. Each of these 24 items is graded on either a 5-point Likert scale or a 100-mm visual analog scale [22,9]. In the present study, we used the Likert scale (version LK 3.0). The domain score ranges from 0 to 20 for pain, 0 to 8 for stiffness and 0 to 68 for physical function. Japanese versions of the WOMAC have also been validated [23]. In the present study, onset of pain and physical functional disability were defined as WOMAC pain score = 0 at baseline and > 0 at follow up and WOMAC physical function score = 0 at baseline and > 0 at follow up, respectively. Resolution of pain and physical functional disability were defined as WOMAC pain score > 0 at baseline and = 0 at follow up and WOMAC physical function score > 0 at baseline and = 0 at follow up, respectively. Worsening pain and physical functional disability were defined as WOMAC pain and physical function at follow up was worse than at baseline, respectively.

Statistical analysis

The differences in age, height, weight, BMI, grip strength, and WOMAC pain and physical function scores at baseline and follow up between men and women were examined using a non-paired Student's t-test. The prevalence of knee OA was compared between men and women using chi-square test. Tukey's honestly significant difference test after adjustment for age and BMI was used to compare WOMAC pain and physical functional score and differences between baseline and follow up among subjects with KL = 0/1, 2 and 3/4. The non-paired Student's t test was used to compare age, BMI and grip strength between subjects with and without onset of pain and physical functional disability as well as those with and without resolution of pain and physical functional disability. Chi-square test was used to compare prevalence of knee OA between subjects with and without onset of pain and physical functional disability as well as those with and without resolution of pain and physical functional disability. Multiple logistic regression analysis after adjustment for age was also used to determine the association of severity of knee OA with onset of pain and physical functional disability as well as their resolution. In addition, to determine independent association of age, BMI, grip strength and knee OA with onset of pain and physical function as well as their resolution, multiple logistic regression analysis was used with significant variables ($p < 0.01$) in univariate analyses as explanatory variables. Data analyses were performed using SAS version 9.0 (SAS Institute Inc., Cary, NC).

Results

Of the 3,040 subjects in the baseline study during 2005–2007, 125 had died by the time of the review held 3 years later, 123 did not participate in the follow-up study due to bad health, 69 had moved away, 83 declined the invitation to attend the follow-up study, and 155 did not participate in the follow-up study for other reasons. Among the 2,485 subjects who did participate in the follow-up study, we excluded 39 subjects who were younger than 40 years at baseline. Those participating in the follow-up study were younger than those who did not survive or who did not participate for other reasons (responders 68.6 years, non-responders 75.1 years; $p < 0.0001$). The follow-up study participants also were more likely to be women (responders 66.3% women, nonresponders 61.8% women; $P = 0.03$) and were more likely to have knee OA at the baseline examination than either those who did not survive to follow-up or those who did not participate for other reasons (responders 51.5%, nonresponders 60.9%; $P < 0.0001$). Among them, 1,578 subjects provided completed WOMAC questionnaires both at baseline and follow up. We also excluded three subjects

Table 1. Characteristics of subjects.

	Overall	Men	Women	p value
N	1558	553	1005	
Age	67.0 ± 11.0	68.1 ± 10.7	66.5 ± 11.0	0.004
Height	155.2 ± 8.9	163.4 ± 6.5	150.8 ± 6.5	< 0.0001
Weight	55.5 ± 10.4	62.2 ± 10.2	51.8 ± 8.5	< 0.0001
BMI	22.9 ± 3.3	23.2 ± 3.1	22.8 ± 3.3	0.0043
Grip strength	27.2 ± 9.5	35.4 ± 8.7	22.7 ± 6.4	< 0.0001
Knee OA (%)	49.3	38.7	55.2	< 0.0001
WOMAC at baseline				
Pain	1.12 ± 2.18	1.02 ± 2.05	1.18 ± 2.25	0.157
Physical function	3.03 ± 6.63	2.56 ± 5.71	3.29 ± 7.07	0.0268
WOMAC at follow up				
Pain	1.82 ± 2.83	1.72 ± 2.67	1.88 ± 2.91	0.291
Physical function	5.59 ± 9.7	4.73 ± 8.30	6.06 ± 10.36	0.0061

Knee OA was defined as Kellgren Lawrence grade 2 or worse at baseline.
BMI, body–mass index; OA, osteoarthritis; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

who did not undergo plain radiography at knee and 17 subjects who underwent total knee arthroplasty before the follow-up study, leaving a total of 1,558 subjects (553 men and 1,005 women). The mean duration between baseline and follow up was 3.3 ± 0.6 years.

The characteristics of the 1,578 participants at baseline in the present study are shown in Table 1. Men were significantly older than women, and BMI was significantly higher in men than in women. The prevalence of knee OA was significantly higher in women than in men at baseline. WOMAC pain score was not significantly different between gender, while, physical function score was significantly worse in women than in men at baseline and follow up. The scores of WOMAC pain and physical function scores worsened at follow up compared with those at baseline in men and women ($p < 0.05$).

The scores of WOMAC pain and physical function scores and their differences between baseline and follow up according to the KL grade are shown in Supplementary Table 1 available online at http://informahealthcare.com/doi/abs/10.3109/14397595.2014.883055. In men, differences in WOMAC physical function scores were significantly larger in subjects with KL 3/4 than those with KL 0/1 after adjustment for age and BMI, while differences in WOMAC pain scores were not. In women, after adjustment for age and BMI, differences in WOMAC pain and physical function scores between baseline and follow up were significantly larger in subjects with KL 3/4 than those with KL 0/1.

Among 366 men and 634 women in subjects without pain at baseline, 128 (35.0%) men and 224 (35.3%) women had onset of pain at follow up (Table 2). In men, subjects with onset of pain tended to be older than those without pain, while BMI and grip strength were not significantly different between them. In women, age and BMI were significantly different between subjects with and without onset of pain, and grip strength tended to be higher in subjects with onset of pain than those without pain. Among 346 men and 601 subjects without physical functional disability at baseline, 132 (38.2%) men and 243 (40.4%) women had onset of physical functional disability at follow up (Table 2). Age and BMI were significantly different between subjects with and without onset of physical functional disability in both men and women, and BMI tended to be higher in subjects with onset of physical functional disability than those without it in women only.

We next examined onset of pain and physical functional disability according to KL grade (Figure 1). There were no significant differences in onset of pain among men with KL 0/1 knee, KL 2 knee OA and KL 3/4 knee OA (33.3%, 36.0% and 46.2%, respectively, $p = 0.4149$ by chi-square test), while there were significant differences in onset of pain among women with KL 0/1 knee, KL 2 knee OA and KL 3/4 knee OA (30.4%, 38.6% and 48.5%, respectively, $p = 0.0082$ by chi-square test). Multiple logistic regression analysis after adjustment for age showed that women with KL 3/4 knee OA had significant higher onset of pain compared with those with KL 0/1. There were significant differences in onset of physical functional disability among subjects with KL 0/1 knee OA, KL 2 knee OA and KL 3/4 knee OA in men and women (men 33.2%, 41.7% and 66.7%, respectively, $p = 0.0023$ by chi-square test, women 35.8%, 43.8% and 53.1%, respectively, $p = 0.0165$ by chi-square test). Multiple logistic regression analysis after adjustment for age showed that men with KL 3/4 knee OA had a significant higher onset of physical functional disability compared with those with KL 0/1.

In addition, we examined the association of age, BMI, grip strength and WOMAC pain and physical function scores at baseline with resolution of pain and physical functional disability (Table 3). Among 187 men and 371 women with WOMAC pain at baseline, pain disappeared in 38 (20.3%) men and 97 (26.2%) women at follow up. In men, WOMAC pain score at baseline was significantly different between subjects with resolution of pain and those with continuous pain. BMI tended to be higher in subjects with continuous pain than in those with resolution of pain. In women, age, BMI, grip strength and WOMAC pain score at baseline were significantly different between subjects with resolution of pain and those with continuous pain. Among 207 men and 404 women with physical functional disability at baseline,

Table 2. Age, BMI, grip strength, and WOMAC pain and physical function score according to onset of pain and physical functional disability in subjects without pain and physical functional disability at baseline.

	Pain $N = 1{,}000$			Physical function $N = 947$		
	Continuous no pain	Onset of pain	p value	Continuous no physical functional disability	Onset of physical functional disability	p value
Men						
N	238	128		214	132	
Age	65.3 ± 11.3	67.6 ± 10.8	0.056	63.3 ± 11.0	68.9 ± 10.2	< 0.0001
BMI	23.1 ± 3.1	23.1 ± 2.8	0.7981	23.1 ± 3.0	23.0 ± 3.2	0.8946
Grip strength	37.1 ± 8.8	36.6 ± 9.3	0.6531	37.4 ± 8.6	35.9 ± 9.1	0.0149
Women						
N	410	224		358	243	
Age	62.7 ± 11.0	65.4 ± 9.9	0.0017	60.2 ± 10.4	65.7 ± 10.0	< 0.0001
BMI	22.0 ± 3.1	22.7 ± 3.1	0.0023	22.2 ± 3.1	22.6 ± 3.1	0.0823
Grip strength	24.2 ± 6.4	23.3 ± 6.5	0.0948	25.3 ± 6.5	22.8 ± 5.3	< 0.0001

Values are the means ± standard deviation.
BMI, body mass index; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

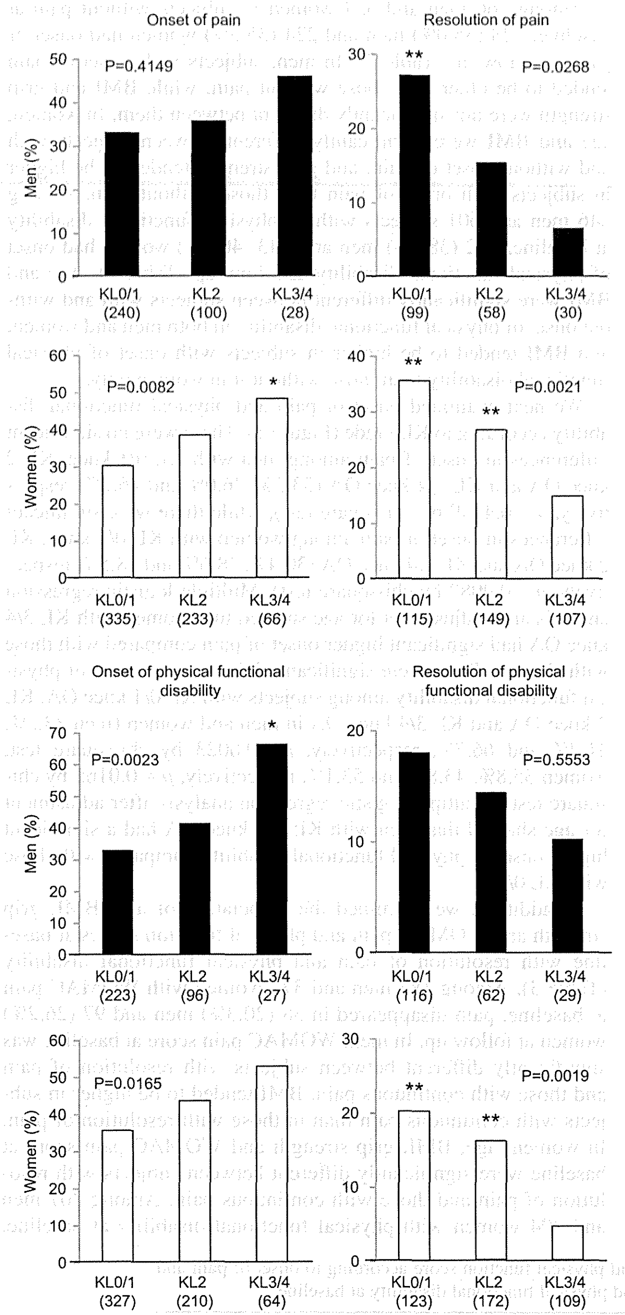

Figure 1. Onset and resolution rate of pain and physical functional disability according to Kellgren Lawrence (KL) grade in men and women. The number of subjects in each subgroup is shown in brackets. Chi-square test was used to determine the association of KL grade with onset of pain and physical functional disability as well as their resolution. $^*p < 0.05$ versus KL grade 0/1 by multiple logistic regression analysis after adjustment for age. $^{**}p < 0.05$ versus KL grade 3/4 by multiple logistic regression analysis after adjustment for age.

disability disappeared in 33 (15.9%) men and 58 (14.4%) women at follow up. In men, age and grip strength were significantly different between subjects with resolution of physical functional disability and those with continuous physical functional disability. Age, BMI, grip strength and WOMAC physical function score at baseline were significantly different between subjects with resolution of physical functional disability and those with continuous physical functional disability. In women, age, BMI, grip strength and WOMAC physical function score at baseline were significantly different between subjects with resolution of physical functional disability and those with continuous physical functional disability.

We next examined resolution of pain and physical functional disability according to KL grade (Figure 1). There were significant differences in resolution of pain among subjects with KL 0/1 knee, KL 2 knee OA and KL 3/4 knee OA in men and women (men 27.3%, 15.5% and 6.7%, respectively, $p = 0.0268$ by chi-square test; women 35.7%, 26.8% and 15.0%, respectively, $p = 0.0021$ by chi-square test). Multiple logistic regression analysis after adjustment for age showed that men with KL 3/4 knee OA had a significantly higher onset of pain compared with those with KL 0/1. Regarding resolution of physical functional disability, there were no significant differences among subjects with KL 0/1 knee, KL 2 knee OA and KL 3/4 knee OA in men (18.1%, 14.5% and 10.3%, respectively, $p = 0.5553$ by chi-square test), while there were significant differences subjects with KL 0/1 knee, KL 2 knee OA and KL 3/4 knee OA in women (20.3%, 16.3% and 4.6%, respectively, $p = 0.0019$ by chi-square test). Multiple logistic regression analysis after adjustment for age showed that women with KL 2 and 3/4 knee OA had a significantly higher onset of physical functional disability compared with those with KL 0/1.

To determine the independent association of age, BMI, grip strength and KL grade with onset of pain and physical functional disability, we next used multiple logistic regression analysis with significant variables ($p < 0.01$) by non-paired Student's t test or chi-square test shown in Table 2 and Figure 1 as explanatory variables (Table 4). Regarding onset of pain, there were no significant variables in men; thus, we did not examine the independent association with onset of pain. In women, older age and higher BMI were independently associated with onset of pain. Older age and KL 3/4 knee OA were independent risk factors for onset of physical functional disability in men, whereas older age, higher BMI and weaker grip strength were independent risk factors for onset of physical functional disability in women. The significant association of knee OA with onset of physical functional disability disappeared after adjustment age, BMI and grip strength in women.

We also examined independent associations of age, BMI, grip strength and KL grade with resolution of pain and physical functional disability (Table 5). KL 0/1 knee and lower WOMAC pain score at baseline were significantly associated with resolution of pain in men, whereas lower BMI, higher grip strength and lower WOMAC pain score were significantly associated with resolution of pain in women. Regarding physical function, only age was significantly associated with resolution of physical functional disability in men, whereas higher grip strength, KL 2 knee OA and lower WOMAC physical function score were significantly associated with resolution of physical functional disability in women. KL 01 knee also tended to be associated with resolution of physical functional disability in women. Because treatment for knee OA might affect the resolution of pain and physical functional disability, we further examined the association of treatment for knee OA with the resolution of pain and physical functional disability. Among subjects with pain at baseline, the resolution rate of pain was 36.2% in subjects who underwent treatment for knee OA, and 14.2% in subjects who did not undergo treatment for knee OA. Among subjects with physical functional disability at baseline, the resolution rate of physical functional disability was 19.3% in subjects who underwent treatment for knee OA, while, 7.2% in subjects who did not undergo treatment for knee OA. The resolution rate of pain and physical functional disability was significantly different between subjects who had and had not undergone treatment for knee OA (chi-square test, $p < 0.0001$). Thus, we examined independent associations of age, BMI, grip strength and KL grade with resolution of pain and physical functional disability after adjustment for the treatment for

Table 3. Age, BMI, grip strength, and WOMAC pain and physical function score according to resolution of pain and physical functional disability in subjects with pain and physical functional disability at baseline, respectively.

	Pain *N* = 558			Physical function *N* = 611		
	Resolution of pain	Continuous pain	p value	Resolution of physical functional disability	Continuous physical functional disability	p value
Men						
N	38	149		33	174	
Age	72.3 ± 8.9	71.9 ± 8.5	0.8	67.9 ± 11.6	73.4 ± 7.6	0.0118
BMI	22.8 ± 3.0	23.7 ± 3.3	0.08	23.4 ± 3.2	23.6 ± 3.2	0.8041
Grip strength	32.6 ± 6.4	32.4 ± 7.5	0.8694	34.9 ± 6.7	31.4 ± 7.3	0.0091
WOMAC at baseline						
Pain	1.82 ± 1.20	3.32 ± 2.69	< 0.0001	–	–	–
Physical function	–	–	–	4.85 ± 7.69	7.20 ± 7.58	0.1132
Women						
N	97	274		58	346	
Age	68.1 ± 12.6	72.4 ± 8.6	0.0022	68.1 ± 11.1	73.2 ± 8.2	0.0015
BMI	22.4 ± 3.2	24.0 ± 3.6	< 0.0001	22.3 ± 3.2	23.6 ± 3.6	0.0066
Grip strength	22.9 ± 7.2	19.8 ± 4.9	0.0002	23.7 ± 7.4	19.7 ± 5.4	0.0002
WOMAC at baseline						
Pain	1.84 ± 1.18	3.68 ± 2.90	< 0.0001	–	–	–
Physical function	–	–	–	3.33 ± 4.32	8.99 ± 9.54	< 0.0001

Values are the means ± standard deviation.
BMI, body mass index; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

knee OA. Results were similar to findings without adjustment for treatment of knee OA (Supplementary Table 2 available online at http://informahealthcare.com/doi/abs/10.3109/14397595.2014.883055). In addition, we examined associations of age, BMI, grip strength and severity of knee OA with worsening pain and physical functional disability in subjects with pain and physical functional disability at baseline (Supplementary Table 3 available online at http://informahealthcare.com/doi/abs/10.3109/14397595.2014.883055). Multiple logistic regression analysis showed that weaker grip strength was a risk factor for worsening pain, whereas KL 3/4 knee OA was a risk factor for worsening physical functional disability (Supplementary Table 4 available online at http://informahealthcare.com/doi/abs/10.3109/14397595.2014.883055).

Discussion

This is the first longitudinal population-based study to examine the onset, resolution and worsening of pain and physical functional disability using WOMAC. We also clarified the associations of age, BMI, grip strength and knee OA with the onset, resolution and worsening of pain and physical functional disability.

Our previous study showed that onset of knee pain during 3 years was approximately 20% and 30% in men and women, respectively [24]. The Chingford study also showed that more than 10% women had onset of pain during 2 years [25]. However, in these previous studies, knee pain was defined as present or absent, rather than as an established measure of pain such as WOMAC. In addition, in our previous study, we did not examine resolution of pain. In the present study, we found that 35% of men and women had onset of pain. These values were higher than onset values obtained from questionnaires in our previous study [24], indicating that WOMAC may be more powerful for detecting pain than questionnaires regarding only the presence or absence of pain. We also found that pain disappeared in approximately 20% men and 25% women using WOMAC. The Chingford study previously showed that knee pain disappeared in approximately 40% of Caucasian women during 2 years using a questionnaire on the presence and absence of pain [25], which is higher than the values

Table 4. Association of onset of pain and physical functional disability with age, BMI, grip strength, and KL grade.

	Onset of pain			Onset of physical functional disability		
	Adjusted OR	95% CI	p value	Adjusted OR	95% CI	p value
Men						
Age (+ 1 year)	–	–	–	1.05	1.02–1.08	0.0011
BMI (+ 1kg/m^2)	–	–	–	–	–	–
Grip strength (+ 1kg)	–	–	–	1.01	0.97–1.04	0.628
KL grade						
KL 0/1	–	–	–	1		
KL 2	–	–	–	1.02	0.60–1.72	0.9504
KL 3/4	–	–	–	2.7	1.14–6.69	0.0274
Women						
Age (+ 1 year)	1.02	1.003–1.04	0.023	1.05	1.03–1.07	< 0.0001
BMI (+ 1kg/m^2)	1.08	1.03–1.15	0.0047	1.08	1.02–1.14	0.0141
Grip strength (+ 1kg)	0.99	0.96–1.02	0.4977	0.96	0.92–0.99	0.0152
KL grade						
KL 0/1	1			1		
KL 2	1.09	0.74–1.61	0.6593	0.84	0.56–1.25	0.4035
KL 3/4	1.42	0.79–2.55	0.2337	1	0.54–1.82	0.9894

Multiple logistic regression analysis was used with significant variables (p < 0.01) in univariate models as explanatory variables.
BMI, body mass index; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

found in the present study. This discrepancy between our study and the Chingford study may be partly explained by age differences in addition to different estimations for pain and racial differences, because mean age was 52 years in the Chingford study compared with 67 years in the present study. Furthermore, we first found that approximately 40% men and women had onset of physical functional disability and approximately 15% men and women had resolution of physical functional disability. To our knowledge, no other community-based studies have described longitudinal patterns of physical functional disability, and the present study was the first to clarify the onset and resolution of physical functional disability using WOMAC.

Pain is the principal clinical symptom of knee OA [5], but, although much effort has been devoted to defining knee pain, the correlation with radiographic severity of the knee OA is not as strong as one would expect [2,6–8]. In the present study, we examined onset of pain according to KL grade using WOMAC. In men and women without knee OA (KL 0/1), more than 30% subjects had onset of pain. In addition, 50% of men and women with KL 3/4 knee OA had onset of pain, meaning that 50% did not have onset of pain despite having severe radiographic knee OA. In fact, in the present study, radiographic knee OA was not significantly associated with onset of pain in men, and after adjustment, the significant association of knee OA with onset of pain disappeared in women. These findings indicate that pain may arise from a variety of structures other than joint cartilage, such as menisci, synovium, ligaments, bursae, bone and bone marrow [26–30]. In addition, in the present study, the risk for onset of pain was higher with higher BMI rather than knee OA in women, indicating knee pain may be prevented by reducing obesity.

In the present study, we also examined the association of knee OA with the resolution of pain, and found that around 30% of men and women without knee OA had resolution of knee pain, which was a similar rate to onset of pain, and only 7% of men and 15% of women with severe knee OA had resolution of knee pain. These findings indicate that around 90% of subjects with severe knee OA had continuous knee pain. There were significant associations of resolution of pain with KL grade. Considering the results of onset of pain, severe knee OA may lead to difficulties with resolution of pain rather than onset of pain, particularly in men. In addition, after adjustment, resolution of pain was significantly associated with lower BMI and higher grip strength, which is a useful marker of muscle function and sarcopenia [15], rather than radiographic knee OA, indicating that improvement of obesity and performing muscle exercises may help make pain disappear. In addition, the significant association of BMI and grip strength remained after adjustment for treatment of knee OA, indicating that reducing obesity and performing muscle exercises may be as important as treatment to achieve resolution of pain due to knee OA.

We also found that severe knee OA was a risk factor for physical functional disability, particularly in men, despite the finding that severe knee OA was not significantly associated with onset of pain in men. Severe knee OA was not significantly associated with onset of physical functional disability after adjustment for age in women, despite the finding that severe knee OA was significantly associated with onset of pain. This discrepancy between gender may be partly explained by the idea that women are more susceptible to pain. In fact, our previous study showed that the prevalence of knee pain in women with KL 0/1, 2 and 3/4 knee OA was significantly higher than that in men with KL 0/1, 2 and 3/4 knee OA, respectively[2]. In addition, risk factors for onset of physical functional disability were higher BMI and weaker grip strength rather than knee OA in women in the present study. Grip strength is a useful marker of muscle function and sarcopenia [15]. A previous study also showed that grip strength is related to total muscle [19]. Results in the present study indicate that onset of physical functional disability may be prevented by improvement of obesity and muscle exercises.

In the present study, physical functional disability disappeared in 20% of women without knee OA, whereas physical functional disability disappeared only in 5% of women with severe knee OA. The association of knee OA with resolution of physical functional

Table 5. Association of resolution of pain and physical functional disability with age, BMI, grip strength, and KL grade.

	Resolution of pain			Resolution of physical functional disability		
	Adjusted OR	95% CI	p value	Adjusted OR	95% CI	p value
Men						
Age (+1 year)	–	–	–	0.95	0.90–0.9985	0.0443
BMI (+1kg/m^2)	0.92	0.80–1.04	0.1994	–	–	–
Grip strength (+1kg)	–	–	–	1.02	0.96–1.09	0.526
KL grade						
KL 3/4	1			–	–	–
KL 2	2.37	0.52–16.8	0.3042	–	–	–
KL 0/1	5.18	1.32–34.6	0.0378	–	–	–
WOMAC at baseline						
Pain	0.63	0.46–0.80	0.001	–	–	–
Physical function	–	–	–	–	–	–
Women						
Age (+1 year)	0.99	0.96–1.02	0.6031	0.98	0.95–1.02	0.4081
BMI (+1kg/m^2)	0.88	0.80–0.96	0.0034	0.93	0.84–1.02	0.1358
Grip strength (+1kg)	1.08	1.02–1.14	0.014	1.09	1.02–1.16	0.0123
KL grade						
KL 3/4	1			1		
KL 2	1.34	0.66–2.79	0.4312	3.04	1.15–9.62	0.0362
KL 0/1	1.71	0.79–3.77	0.1797	2.52	0.89–8.34	0.0997
WOMAC at baseline						
Pain	0.66	0.53–0.78	<0.0001	–	–	–
Physical function	–	–	–	0.87	0.78–0.93	0.0009

Multiple logistic regression analysis was used with significant variables ($p<0.01$) in univariate model as explanatory variables.

BMI, body mass index; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index; KL, Kellgren Lawrence grade.

disability remained significant after adjustment. This means that in women without knee OA, pain may occur, but it may disappear more easily. In addition, grip strength was also associated with resolution of physical functional disability after adjustment, indicating that muscle exercises may help make physical functional disability disappear.

The present study showed gender differences in the associations of knee OA with pain and physical functional disability. In women, knee OA was significantly associated with onset of pain and physical functional disability as well as their resolution, whereas in men, there were no significant association of knee OA with onset of pain and resolution of physical functional disability. Our previous cross-sectional study also showed that the odds ratio of knee pain for KL 3/4 knee OA was approximately twice as high in women as in men[2]. These findings may be partly explained by the lower muscle mass in women compared with men. In men, muscular strength may obscure the associations of knee OA with pain and physical functional disability.

In conclusion, the present longitudinal study revealed the onset rate of pain and physical functional disability as well as their resolution rate using WOMAC. In addition, severe knee OA was significantly associated with onset of pain and physical functional disability as well as their resolution, particularly in women. Furthermore, we also clarified that BMI and grip strength were associated with onset of pain and physical functional disability as well as their resolution in women.

Acknowledgements

This study was supported by Grants-in-Aid for Scientific Research (S19109007, B20390182, C20591737, C20591774), for Young Scientists (A18689031), and for Exploratory Research (19659305) from the Japanese Ministry of Education, Culture, Sports, Science and Technology, H17-Men-eki-009, H18-Choujyu-037, H20-Choujyu-009, H21-Chouju-Wakate-011 and H22-Chouju-Wakate-007 from the Ministry of Health, Labor and Welfare, Research Aid from the Japanese Orthopaedic Association (JOA-Subsidized Science Project Research 2006-1 & 2010-2), and Grant No.166 from the Japan Orthopaedics and Traumatology Foundation.

The authors thank Dr. Yamamoto, Dr. Ishibashi, Dr. Anamizu and members of Department of Orthopaedics, and Mr. Kutsuma and other members of Department of Radiology at Tokyo Metropolitan Geriatric Medical Center; Mrs. Tomoko Takijiri and other members of the Public Office in Hidakagawa Town; and Mrs. Tamako Tsutsumi, Mrs. Kanami Maeda and other members of the Public Office in Taiji Town, for their assistance in the location and scheduling of participants for examinations.

Conflict of interest

None.

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Supplementary material available online

Supplementary Tables 1-4.

Japan College of Rheumatology
MODERN RHEUMATOLOGY

http://informahealthcare.com/mor
ISSN 1439-7595 (print), 1439-7609 (online)

Mod Rheumatol, 2013; Early Online: 1–5

DOI: 10.3109/14397595.2013.843761

informa
healthcare

ORIGINAL ARTICLE

Prevalence, incidence and progression of lumbar spondylosis by gender and age strata

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Abstract

Objectives. To identify the prevalence, incidence and progression of radiographic lumbar spondylosis (LS).
Methods. From the Adult Health Study conducted by the Radiation Effects Research Foundation, 1,204 participants aged 44–85 years who had lumbar spine radiographs in 1990–1992 were reexamined in 1998–2000 (mean 7.9-year interval). The radiographic severity of LS was determined by Kellgren/Lawrence (KL) grading.
Results. In the overall population, the prevalence of radiographic KL $\geq$ 2 and $\geq$ 3 LS was 52.9% and 23.6%, respectively. KL $\geq$ 2 LS was more prevalent in men, whereas KL $\geq$ 3 LS was more prevalent in women. During the 8-year follow-up, the incidence of KL $\geq$ 2 LS in men and women was 65.5% and 46.6%, that of KL $\geq$ 3 LS was 27.3% and 29.5%, that of progressive LS was 31.3% and 34.0%, and multilevel LS was 44.9% and 33.4%, respectively. Body-mass index was a risk factor for both KL $\geq$ 2 and KL $\geq$ 3 LS, after adjusting for age and sex.
Conclusions. The present longitudinal study revealed the prevalence, incidence and progression of radiographic LS. Prevalence and incidence of KL $\geq$ 2 LS was higher in men than women, while those of KL $\geq$ 3 were similar between men and women.

Keywords

Incidence, Lumbar spine, Prevalence, Progression, Spondylosis

History

Received 5 April 2013
Accepted 9 July 2013
Published online 31 October 2013

Introduction

Lumbar spondylosis (LS), characterized by disc degeneration and osteophytosis [1,2], is a major public health issue in most countries and causes chronic disability among the elderly [1,3–8]. Despite the urgent need for strategies to prevent and treat this condition, epidemiologic data on LS are sparse. Past studies reported wide ranged prevalence of radiographic LS from 40% to 85% based on the limited number of study subjects in a clinical setting [9–17]. This variability may be due to the differences in age, communities, sample sizes, imaging modality and ethnic variations, yet the disorder burden remains unclear. Further, there are few studies regarding the incidence or progression of LS [7,12,15,18,19].

Plain radiography is considered the gold standard as a method that is non-invasive, inexpensive, convenient, simple and fast to use in assessing osteoarthritis (OA) severity. The most popular grading system for radiographic severity of OA is the Kellgren/Lawrence (KL) system, which is classified into five grade (0–4) scales; KL $\geq$ 2 is the conventional standard for diagnosis [20]. For LS, KL Grade 2 is defined as osteophyte formation and KL Grade 3 is defined as osteophyte formation along with disc-space narrowing. Hence, to assess osteophyte formation alone and disc-space narrowing with or without osteophyte formation, the prevalence and incidence of KL $\geq$ 2 LS as well as that of KL $\geq$ 3 LS is needed.

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In the present study, we analyzed the prevalence, incidence and progression of LS according to gender and age strata in Japan.

Materials and methods

Subjects

The Adult Health Study (AHS) was established by the Radiation Effects Research Foundation in 1958 to document the late health effects of radiation exposure among atomic-bomb survivors in Hiroshima and Nagasaki, and study subjects have been followed through biennial medical examinations. The participation rate has been over 70% throughout this period. More detail concerning recruitment and examination of participants was reported elsewhere [21].

Among AHS subjects, 1,297 subjects (363 men and 934 women) aged 44–85 years underwent radiographic examinations of the lumbar spine in Hiroshima between 1990 and 1992 (baseline). Of those 1,297 subjects, 1,204 (92.8%) subjects participated in the follow-up study between 1998 and 2000. All participants provided written informed consent, and the study was conducted with the approval of ethical committees of the Radiation Effects Research Foundation. Anthropometric measurements included height, weight and body–mass index (BMI; weight [kg]/height [m^2]) was calculated. We used individual radiation dose estimates from the Radiation Effects Research Foundation's Dosimetry System 2002 (DS02) [22].

Radiographic assessments

Plain radiographs of the lumbar spine were taken in the lateral position to assess radiographic LS. The severity of LS was

Table 1. Characteristics of participants.

	Men					Women				
	Overall	<50	50–59	60–69	≥70	Overall	<50	50–59	60–69	≥70
No. of subjects	363	56	83	158	66	934	129	217	414	174
Age, years	61.2 ± 9.4	46.4 ± 1.3	55.8 ± 3.3	63.2 ± 2.6	75.5 ± 4.1	61.6 ± 8.9	46.5 ± 1.3	55.6 ± 3.0	64.2 ± 2.8	74.2 ± 3.2
Height, cm	163.2 ± 5.8	166.6 ± 6.3	163.9 ± 5.6	163.0 ± 5.3	159.9 ± 5.2	150.7 ± 5.6*	153.4 ± 5.0*	151.9 ± 5.5*	150.7 ± 5.3*	147.3 ± 5.1*
Weight, kg	59.9 ± 8.6	61.6 ± 7.7	61.9 ± 9.1	60.1 ± 8.4	55.6 ± 7.6	52.4 ± 8.7*	54.2 ± 8.5*	54.5 ± 9.0*	52.1 ± 8.3*	49.3 ± 8.6*
BMI, kg/m^2	22.5 ± 2.8	22.2 ± 2.7	23.0 ± 2.9	22.6 ± 2.7	21.7 ± 2.8	23.1 ± 3.5*	23.1 ± 3.6	23.6 ± 3.5	22.9 ± 3.4	22.7 ± 3.6*

Data are mean ± standard deviation.
BMI, body–mass index.
*$p < 0.05$ vs. men in the corresponding group by non-paired Student's t test.

determined according to the KL grading [20] at each intervertebral level from L1/2 to L5/S1 by a well-experienced orthopedists (S.M.), who was masked to the patients' backgrounds. The KL scale defines radiographic OA in five categories: KL Grade 0, no radiographic features of OA; KL Grade 1, minimal osteophytosis only; KL Grade 2, definite osteophytosis with some sclerosis of the anterior part of the vertebral plate; KL Grade 3, marked osteophytosis and sclerosis of the vertebral plates with slight narrowing of the disc space and KL Grade 4, large osteophytes, marked sclerosis of the vertebral plates and marked narrowing of the disc space. To evaluate the intra-observer variability of the KL grading, 100 randomly selected radiographs of the lumbar spine were scored by the same observer more than a month after the first reading. A further 100 radiographs were scored by two experienced orthopedic surgeons. They used the same radiographic atlas for inter-observer variability. The intra- and inter-observer variabilities were evaluated by kappa analysis. These variabilities in the KL grading on lumbar radiographs have been shown to be sufficient for assessment (0.84 and 0.76, respectively).

For the purposes of this study, we defined four LS outcomes. First, a subject could have incident KL ≥ 2 radiographic LS if all vertebral interspaces had < Grade 2 disease at baseline, and if at least one vertebral interspace had ≥ Grade 2 disease at follow-up. Second, a subject could have incident KL ≥ 3 radiographic LS if all vertebral interspaces had < Grade 3 disease at baseline, and if at least one vertebral interspace had Grade ≥ 3 at follow-up. Third, progressive LS was defined as KL ≥ 2 LS at baseline and an increase by at least one grade in the affected vertebral interspace at follow-up. Fourth, multilevel LS was defined as KL ≥ 2 grade at two or more interspaces. A subject could have incident multilevel LS if the subject had less than two interspaces with KL ≥ 2 LS at baseline, and if he or she had two or more interspaces with KL ≥ 2 at follow-up.

Statistical analysis

We used the chi-square test to compare the prevalence and incidence with radiographic LS between men and women. Incidence was calculated as follows: the number of subjects with LS at follow-up among those without LS at baseline divided by the number of subjects without LS at baseline. The association of variables such as age, BMI and gender with the prevalence and incidence of radiographic LS was evaluated by multiple logistic regression analysis. Data analyses were performed using SAS version 9.0 (SAS Institute Inc., Cary, NC).

Results

Characteristics of the 1,297 participants at baseline are shown in Table 1. The mean age of those participating in the follow-up study was 69.1 ± 9.0 years. The interval between baseline examination and follow-up was 7.9 ± 1.1 years.

The prevalence of KL ≥ 2 LS in the overall population and subgroups classified by gender and age strata at baseline is shown in Table 2. The prevalence was significantly higher at all interspaces and at the most severe space in men compared with women in the overall population. The prevalence of multilevel LS was also significantly higher in men than in women. Logistic regression analysis showed that the prevalence of KL ≥ 2 LS at all interspaces as well as at the most severe level, and multilevel spondylosis was significantly associated with age in men and women. In men, the prevalence was highest at L3/4 at almost all age strata, whereas in women, the prevalence was highest at L4/5.

In contrast to KL ≥ 2 LS, the prevalence of KL ≥ 3 LS was significantly higher at all interspaces and at the most severe space in women than men in the overall population (Table 3). The prevalence of multilevel LS was also higher in women than in men. Logistic regression analysis showed that the prevalence of KL ≥ 3 LS at all interspaces as well as at the most severe level, and

Table 2. Number (percentage) of participants with KL ≥ 2 LS at each vertebral interspace as well as the most severe space, and multilevel KL ≥ 2 LS according to gender and age strata at baseline.

Age at baseline	L1/2	L2/3	L3/4	L4/5	L5/S	Severest	Multilevel
Overall	231 (17.8)	370 (28.5)	381 (29.4)	413 (31.8)	180 (13.9)	697 (53.8)	430 (33.2)
Men	102 (28.1)	138 (38.0)	157 (43.2)	140 (38.6)	52 (14.3)	246 (67.8)	167 (46.0)
<50	5 (8.9)	12 (21.4)	15 (26.8)	9 (16.1)	4 (7.1)	22 (39.3)	11 (19.6)
50–59	18 (21.7)	17 (20.5)	25 (30.1)	27 (32.5)	6 (7.2)	48 (57.8)	29 (34.9)
60–69	50 (31.6)	71 (44.9)	76 (48.1)	64 (40.5)	25 (15.8)	118 (74.7)	80 (50.6)
≥70	29 (43.9)	38 (57.6)	41 (62.1)	40 (60.6)	17 (25.8)	58 (87.9)	47 (71.2)
Women	129 (13.8)*	232 (24.8)*	224 (24.0)*	273 (29.2)*	128 (13.7)*	451 (48.3)*	263 (28.2)*
<50	3 (2.3)	9 (7.0)	7 (5.4)	15 (11.6)	6 (4.7)	29 (22.5)	9 (7.0)
50–59	16 (7.4)	32 (14.7)	39 (18.0)	47 (21.7)	26 (12.0)	88 (40.6)	35 (16.1)
60–69	59 (14.3)	121 (29.2)	111 (26.8)	129 (31.2)	61 (14.8)	215 (51.9)	136 (32.9)
≥70	51 (29.3)	70 (40.2)	67 (38.5)	82 (47.1)	35 (20.1)	119 (68.4)	83 (47.7)

Multilevel LS was defined as KL grade ≥ 2 at two or more interspaces.
*$p < 0.05$ vs. men by chi-square test in the overall population.

Table 3. Number (percentage) of participants with KL ≥ 3 LS at each vertebral interspace as well as the most severe space, and multilevel KL ≥ 3 LS according to gender and age strata at baseline.

Age at baseline	L1/2	L2/3	L3/4	L4/5	L5/S	Severest	Multilevel
Overall	30 (2.3)	75 (5.8)	105 (8.1)	236 (18.2)	110 (8.5)	320 (24.7)	141 (10.9)
Men	6 (1.7)	12 (3.3)	19 (5.2)	41 (11.3)	14 (3.9)	58 (16.0)	22 (6.1)
< 50	0 (0.0)	0 (0.0)	2 (3.6)	3 (5.4)	1 (1.8)	4 (7.1)	1 (1.8)
50–59	1 (1.2)	1 (1.2)	1 (1.2)	4 (4.8)	1 (1.2)	6 (7.2)	2 (2.4)
60–69	1 (6.3)	6 (3.8)	8 (5.1)	18 (11.4)	6 (3.8)	27 (17.1)	10 (6.3)
≥ 70	4 (6.1)	5 (7.6)	8 (12.1)	16 (24.2)	6 (9.1)	21 (31.8)	9 (13.6)
Women	24 (2.6)	63 (6.7)*	86 (9.2)*	195 (20.9)*	96 (10.3)*	262 (28.1)*	119 (12.8)*
< 50	0 (0.0)	2 (1.6)	2 (1.6)	10 (7.8)	5 (3.9)	16 (12.4)	3 (2.3)
50–59	1 (0.5)	7 (3.2)	12 (5.5)	30 (13.8)	19 (8.8)	47 (21.7)	14 (6.5)
60–69	10 (2.4)	23 (5.6)	38 (9.2)	88 (21.3)	43 (10.4)	116 (28.0)	55 (13.3)
≥ 70	13 (7.5)	30 (17.3)	34 (19.7)	66 (38.2)	29 (16.8)	82 (47.4)	46 (26.6)

Multilevel LS was defined as KL grade ≥ 3 at two or more interspaces.
*$p < 0.05$ (chi-square test) vs. men in the overall population.

multilevel spondylosis was significantly associated with age in men and women. The prevalence was low at L1/2 and the highest at L4/5 among all interspaces in men and women.

Table 4 shows the incidence of KL ≥ 2 and ≥ 3 LS in the overall population and subgroups classified by gender and age strata. The incidence of KL ≥ 2 LS was significantly higher in men than in women. Logistic regression analysis showed that the incidence of KL ≥ 2 LS was significantly associated with age in men and women. The incidence of KL ≥ 3 LS was significantly higher in women. When the incidence was compared among generations, the incidence of KL ≥ 3 radiographic LS tended to increase with age after the 50s in men and women, whereas that of KL ≥ 2 radiographic LS was not much different between the 40s and 50s.

We also examined progressive and multilevel LS (Table 4). Among subjects with KL = 2 LS at baseline, 31% subjects had KL = 3 LS and 9% subjects had KL = 4 LS at follow-up. Among subjects with KL = 3 LS at baseline, 31% subjects had KL = 4 LS at follow-up. The progression of LS was not associated with gender or age strata. The incidence of multilevel LS was higher in men than in women, and tended to increase with age in men and women.

We next analyzed the independent association of age, gender and BMI with the prevalence of LS by multiple logistic regression analysis (Table 5). Age and BMI were associated with an increased prevalence of KL ≥ 2 LS as well as KL ≥ 3 at the most severe space and multilevel LS. Female gender was associated with decreased prevalence for KL ≥ 2 LS at the most severe space and that of multilevel LS; it was also associated with increased prevalence for KL ≥ 3 LS.

We also analyzed the independent association of age, gender and BMI with the incidence of LS by multiple logistic regression analysis (Table 6). Age and BMI were associated with increased risk for the incidence of KL ≥ 2, KL ≥ 3 and multilevel LS, but not for progressive LS. Female gender was associated with decreased incidence for KL ≥ 2 and multilevel LS, whereas there was no significant association of gender with KL ≥ 3 and progressive LS.

No significant relationship was found between atomic-bomb radiation and prevalence and incidence of KL ≥ 2, KL ≥ 3 and multilevel LS.

Discussion

The present study revealed the prevalence of radiographic KL ≥ 2 and KL ≥ 3 LS in men and women. Although prevalence of KL ≥ 2 LS was more frequent in men than in women, KL ≥ 3 LS was more prevalent in women. Given an 8-year follow-up, we also revealed the incidence of KL ≥ 2 and KL ≥ 3 LS as well as progressive LS and multilevel LS in men and women.

Most previous epidemiologic studies on LS focused on middle-aged or younger populations, reporting the prevalence to be 40–85% [9,11–13,15,16]. This variability may be due to the differences in age, communities, sample sizes and ethnic variations. In terms of ethnic variations, we reported a different prevalence of LS in Japan and the United Kingdom in a small-scale comparative study [14], whereas our previous study of an elderly Japanese population showed a prevalence of 84.1% and 70.7% in men and women, respectively [23], which is similar to the prevalence seen in this study among subjects in their 70s.

Table 4. Incidence of KL ≥ 2 and ≥ 3 LS according to gender and age strata.

	KL ≥ 2		KL ≥ 3		Progressive LS		Multilevel LS	
Age at baseline	No. at risk	Cumulative incidence	No. at risk	Cumulative incidence	No. at risk	Cumulative incidence	No. at risk	Cumulative incidence
Overall	567	285 (50.3)	920	265 (28.8)	696	230 (33.0)	866	312 (36.0)
Men	110	72 (65.5)	286	78 (27.3)	246	77 (31.3)	196	88 (44.9)
< 50	33	18 (54.6)	49	8 (16.3)	22	8 (36.4)	45	14 (31.1)
50–59	33	20 (60.6)	74	15 (20.3)	48	11 (22.9)	54	24 (44.4)
60–69	37	28 (75.7)	125	43 (34.4)†	118	40 (33.9)	78	42 (53.8)
≥ 70	7	6 (85.7)	45	12 (26.7)	58	18 (31.0)	19	8 (42.1)
Women	457	213 (46.6)*	634	187 (29.5)	450	153 (34.0)	670	224 (33.4)
< 50	94	35 (37.2)	105	19 (18.1)	29	6 (20.7)	120	22 (18.3)
50–59	122	43 (35.3)	162	35 (21.6)	88	32 (36.4)	182	51 (28.0)
60–69	193	106 (54.9)†	288	93 (32.3)	215	79 (36.7)	277	110 (39.7)†
≥ 70	48	29 (60.4)†	91	40 (44.0)	118	36 (30.5)	91	41 (45.1)†

*$p < 0.05$ (chi-square test) vs. men in the overall population.
†$p < 0.05$ vs. the corresponding gender at < 50 years by logistic regression analysis.

Table 5. Association of age, BMI and gender with prevalence of radiographic lumbar spondylosis at baseline examination.

	Radiographic LS				Multilevel radiographic LS			
	KL ≥ 2		KL ≥ 3		KL ≥ 2		KL ≥ 3	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Age, years	1.08	1.07–1.10	1.08	1.06–1.09	1.08	1.07–1.10	1.1	1.07–1.12
BMI, kg/m^2	1.08	1.05–1.12	1.08	1.04–1.12	1.08	1.05–1.12	1.05	1.00–1.11
Women (vs. men)	0.36	0.27–0.47	1.99	1.44–2.78	0.36	0.28–0.48	2.27	1.42–3.79

BMI, body–mass index; LS, lumbar spondylosis; OR, odds ratio; CI, confidence interval.
Radiographic spondylosis was determined at the severest level among L1/2-L5/S1.
The odds ratios were calculated by logistic regression analysis.

Interestingly, KL ≥ 2 LS was more prevalent in men than in women, whereas KL ≥ 3 LS was more prevalent in women. We and others have reported that osteophytosis of the lumbar spine was more common in men than in women [12,14,23], while disc-space narrowing was more prevalent in women [14]. Based on the definition of KL grading [20], the discrepancy may be due to distinct etiologic mechanisms between osteophyte formation and disc-space narrowing. A cross-sectional study that investigated the extent, prevalence and distribution of spinal LS in women also showed that osteophytosis and disc-space narrowing were significantly correlated, but each predicted only 19% of the variation in the other [16]. Further clinical and basic research will disclose the distinct backgrounds of these two representative OA features.

We also investigated the age-specific prevalence of LS. Although KL ≥ 2 LS tended to increase with age in men and women, significant differences were not detected in the prevalence of KL ≥ 3 between the 40s and the 50s in men. In fact, the incident of KL ≥ 3 was quite low in the 40s, indicating that the incidence of disc space narrowing was low during middle age.

Most previous studies regarding LS have been cross-sectional, so incidence has not been clarified. The present study was a longitudinal study that assessed incidence and natural history of LS. In this study, KL ≥ 2 LS occurred at rates of 65.5% and 46.6% after 8-year follow-up, respectively. The only longitudinal study using KL grade reported that 45% of women deteriorated after 8.7 years follow-up [7], but deterioration was defined as an increase in KL grade at any level, which was a different definition from our study, so strict comparisons are limited. Considering the definition of KL grade, the incidence of KL ≥ 2 LS may represent osteophytosis. We also found that the incidence of LS was higher in men than in women at all ages and increased with age after the 50s, but was not much different between the 40s and 50s in men and women. In this study, among subjects with incident KL ≥ 2 LS, the percentage of those with KL ≥ 3 LS was extremely high in the 70s compared with other generations. This finding may indicate that at middle age, LS progresses slowly in subjects without LS at baseline, but it progresses faster in the elderly.

This study also clarified that the incidence of KL ≥ 3 LS was similar between men and women. Considering the definition of KL grade, the incidence of KL ≥ 3 LS may represent the occurrence of disc space narrowing. A longitudinal study regarding disc space narrowing of the lumbar spine has been performed [15], but it focused only the progression of disease and not on its incidence. Unlike KL ≥ 2 LS, the incidence of KL ≥ 3 was similar in the 40s, 50s and 60s, and was higher in women than in men at age 70 years or older. When compared among generations, the incidence was similar in the 40s and 50s and increased in the 60s in men and women. In the 70s, the incidence further increased in women, but in men, was similar to the incidence in the 60s. Elderly men generally retire from their occupations around 60–70 years of age, whereas women continue to do household chores even after the age of 70, which may partly explain the increase of incidence after age 70 in women.

We also analyzed the progression of LS. The rate of progressive LS was similar in men and women (4.5% and 4.6% per year, respectively), and was not associated with age, despite the fact that the incidence of KL ≥ 3 LS tended to increase with age. This finding may be due to the fact that the percentage of subjects with KL ≥ 3 LS was extremely high in the 70s compared with other generations among those with incident KL ≥ 2 LS, as mentioned above, which could indicate that in subjects without LS, the incidence of disc space narrowing was associated with age, but not in subjects with osteophytosis, especially in men.

There are several limitations to the present study. First, the study subjects may be biased as persons who received radiographs in both 1990–1992 and 1998–2000. In addition, this study investigated participants who lived independently, and not those who lived in institutional settings. Therefore, the calculated prevalence or incidence may be underestimated. Second, because the KL system emphasizes osteophytosis, it is unclear how to handle LS with disc-space narrowing but no osteophytosis. We are developing a computer-aided diagnostic program that enables measurement of major features of LS, including disc-space narrowing and osteophytosis, on plain radiographs. Furthermore, participants were atomic bomb survivors and thus not representative of the general Japanese population, although we adjusted for radiation, and there are no indications from earlier studies of this cohort that radiation affected BMD and fracture.

In summary, the present longitudinal study revealed the prevalence of radiographic KL ≥ 2 and ≥ 3 LS was 52.9% and 23.6%, respectively. KL ≥ 2 LS was more prevalent in men, whereas KL ≥ 3 LS was more prevalent in women. During the 8-year follow-up, the incidence of KL ≥ 2 LS in men and women was

Table 6. Association of age, BMI and gender with incidence of radiographic lumbar spondylosis.

	KL ≥ 2		KL ≥ 3		Progressive LS		Multilevel LS	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Age, years	1.05	1.03–1.07	1.05	1.04–1.07	1	0.98–1.02	1.06	1.04–1.08
BMI, kg/m^2	1.07	1.02–1.07	1.06	1.01–1.11	1	0.95–1.05	1.02	0.98–1.07
Women (vs. men)	0.37	0.23–0.58	1.09	0.80–1.51	1.08	0.76–1.52	0.5	0.35–0.71

BMI, body–mass index; LS, lumbar spondylosis; OR, odds ratio; CI, confidence interval.
Radiographic spondylosis was determined at the severest level among L1/2-L5/S1.
The odds ratios were calculated by logistic regression analysis.

65.5% and 46.6%, that of KL ≥ 3 LS was 27.3% and 29.5%, respectively. The incidence of KL ≥ 2 was higher in men than women, while, that of KL ≥ 3 was similar between men and women, indicating that different mechanisms might influence osteophytosis and disc space narrowing.

Acknowledgements

None.

Funding

The Radiation Effects Research Foundation (RERF), Hiroshima and Nagasaki, Japan is a private, non-profit foundation funded by the Japanese Ministry of Health, Labour and Welfare and the U.S. Department of Energy, the latter in part through DOE Award DE-HS0000031 to the National Academy of Sciences. This publication was supported by RERF Research Protocol RP #3–89, and by the Japanese Ministry of Health, Labour and Welfare. The views of the authors do not necessarily reflect those of the two governments.

Conflict of Interest

None.

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