Table II
Mean scores of the SF-8, EQ-5D, and WOMAC scales by KL grade in men

		Severity of knee OA			Difference in means (95% CI)	
		KL = 0 or 1 (n = 444)	KL = 2 (n = 231)	KL = 3 or 4 (n = 92)	KL = 3 or 4 vs KL = 0 or 1	KL = 3 or 4 vs KL = 2
SF-8						
PCS	Crude	48.1 ± 0.3	47.1 ± 0.4	44.7 ± 0.7	−3.3 (−5.2, −1.5)	−2.3 (−4.3, −0.4)
	Adjusted	47.8 ± 0.3	47.4 ± 0.4	45.5 ± 0.7	−2.3 (−4.2, −0.5)	−1.9 (−3.9, 0.0)
MCS	Crude	52.8 ± 0.2	53.7 ± 0.3	55.3 ± 0.5	2.5 (1.1, 3.9)	1.6 (0.1, 3.1)
	Adjusted	52.9 ± 0.3	53.7 ± 0.4	55.2 ± 0.6	2.3 (0.8, 3.8)	1.5 (−0.02, 3.1)
EQ-5D	Crude	0.92 ± 0.01	0.91 ± 0.01	0.87 ± 0.01	−0.06 (−0.10, −0.02)	−0.04 (−0.08, 0.00)
	Adjusted	0.92 ± 0.01	0.91 ± 0.01	0.89 ± 0.01	−0.03 (−0.07, 0.01)	−0.03 (−0.07, 0.01)
WOMAC						
Pain	Crude	0.92 ± 0.10	1.13 ± 0.14	2.11 ± 0.22	1.19 (0.61, 1.76)	0.97 (0.36, 1.59)
	Adjusted	1.03 ± 0.10	1.02 ± 0.14	1.75 ± 0.22	0.72 (0.14, 1.30)	0.73 (0.12, 1.34)
Stiffness	Crude	0.57 ± 0.05	0.65 ± 0.07	0.91 ± 0.11	0.34 (0.05, 0.64)	0.26 (0.05, 0.58)
	Adjusted	0.60 ± 0.05	0.61 ± 0.07	0.80 ± 0.12	0.20 (−0.10, 0.50)	0.19 (0.13, 0.51)
Function	Crude	2.83 ± 0.33	3.38 ± 0.46	6.08 ± 0.73	3.24 (1.36, 5.12)	2.70 (0.67, 4.73)
	Adjusted	3.31 ± 0.32	2.88 ± 0.45	4.66 ± 0.72	1.35 (−0.53, 3.23)	1.77 (−0.19, 3.74)

Values are mean ± standard error (SE). SF-8, Medical Outcomes Study Short Form-8.
Adjusted differences in means were calculated by Tukey HSD test after adjustment for age, BMI and grip strength.

significantly lower in subjects with symptomatic knee OA compared with those without KL = 3 or 4 knee OA (difference in mean −0.08, 95% CI −0.13 to −0.02) as well as KL = 3 or 4 knee OA without pain in men (difference in mean −0.08, 95% CI −0.15 to −0.01), but not in women.

Next, to examine the independent association of symptomatic knee OA and grip strength on QOL, multiple regression analysis was used with age, BMI, grip strength, and the presence of symptomatic knee OA as independent variables (Table IV). In men and women, symptomatic knee OA and grip strength were independently associated with PCS of the SF-8 (R^2, 0.11 and 0.17, respectively), EQ-5D utility scores (R^2, 0.08 and 0.12, respectively), and pain (R^2, 0.12 and 0.16, respectively), stiffness (R^2, 0.06 and 0.09, respectively) and physical function domains (R^2, 0.13 and 0.21, respectively) of the WOMAC.

Discussion

This is the first study to examine the association of radiographic and symptomatic knee OA with QOL measured by generic scales such as the SF-8, which is an alternate form of the SF-36, and the EQ-5D, as well as a disease-specific scale such as WOMAC in Japanese men and women using a large-scale population-based cohort study. In the present study, subjects with KL = 3 or 4 had significantly lower physical QOL than those with KL = 0 or 1 as well as KL = 2. At the same time, the MCS scores were higher in KL = 3 or 4 than KL = 0 or 1 in men and women. Furthermore, symptomatic knee OA was significantly associated with lower physical QOL compared with radiographic knee OA without pain. We further clarified the independent associations with symptomatic knee OA and grip strength. Symptomatic knee OA and grip strength were independently associated with lower QOL.

In the present study, physical QOL was significantly lower in subjects with KL = 3 or 4 compared with KL = 0 or 1 as well as KL = 2 in men and women. Samsa *et al.* reviewed the existing literature and concluded that the Minimally Clinically Important Difference (MCID) for the SF-36 is typically in the range of 3–5 points[42], implying that differences in SF-36 scores of 1–2 points are not important, but differences in scores of 3 points or more are clinically important. In this study, differences of PCS scores between subjects with KL = 3 or 4 and those with KL = 0 or 1 were 3.4 and 4.6 in men and women, respectively. The differences were similar to MCID thresholds, indicating that KL = 3 or 4 knee OA may be clinically important for physical QOL. A previous study in China

Table III
Mean scores of the SF-8, EQ-5D, and WOMAC scales by KL grade in women

		Severity of knee OA			Difference in means (95% CI)	
		KL = 0 or 1 (N = 541)	KL = 2 (N = 526)	KL = 3 or 4 (N = 292)	KL = v3 or 4 vs KL = 0 or 1	KL = 3 or 4 vs KL = 2
SF-8						
PCS	Crude	48.4 ± 0.3	46.9 ± 0.3	43.8 ± 0.4	−4.5 (−5.7, −3.4)	−3.0 (−4.2, −1.9)
	Adjusted	47.1 ± 0.3	47.4 ± 0.3	45.5 ± 0.4	−1.6 (−2.9, −0.3)	−1.9 (−3.1, −0.7)
MCS	Crude	52.1 ± 0.3	52.3 ± 0.3	53.8 ± 0.4	1.7 (0.7, 2.7)	1.4 (0.4, 1.5)
	Adjusted	51.9 ± 0.3	52.5 ± 0.3	53.8 ± 0.4	1.9 (0.7, 3.1)	1.3 (0.2, 2.4)
EQ-5D	Crude	0.92 ± 0.01	0.89 ± 0.01	0.85 ± 0.01	−0.07 (−0.09, −0.04)	−0.04 (−0.07, −0.02)
	Adjusted	0.89 ± 0.01	0.91 ± 0.01	0.89 ± 0.01	−0.003 (−0.04, 0.03)	−0.02 (−0.04, 0.01)
WOMAC						
Pain	Crude	0.96 ± 0.11	1.45 ± 0.10	2.62 ± 0.15	1.65 (1.23, 2.08)	1.16 (0.74, 1.59)
	Adjusted	1.45 ± 0.11	1.19 ± 0.11	1.99 ± 0.15	0.53 (0.07, 1.00)	0.80 (0.38, 1.21)
Stiffness	Crude	0.55 ± 0.06	0.79 ± 0.06	1.14 ± 0.08	0.59 (0.37, 0.81)	0.35 (0.12, 0.57)
	Adjusted	0.75 ± 0.06	0.68 ± 0.06	0.85 ± 0.08	0.10 (−0.15, 0.34)	0.16 (0.06, 0.39)
Function	Crude	2.41 ± 0.34	4.54 ± 0.35	8.32 ± 0.47	5.91 (4.54, 7.28)	3.78 (2.40, 5.16)
	Adjusted	4.37 ± 0.35	3.62 ± 0.33	5.79 ± 0.47	1.42 (−0.04, 2.88)	2.17 (0.85, 3.50)

Values are mean ± SE. SF-8, Medical Outcomes Study Short Form-8.
Adjusted differences in means were calculated by Tukey HSD test after adjustment for age, BMI and grip strength.

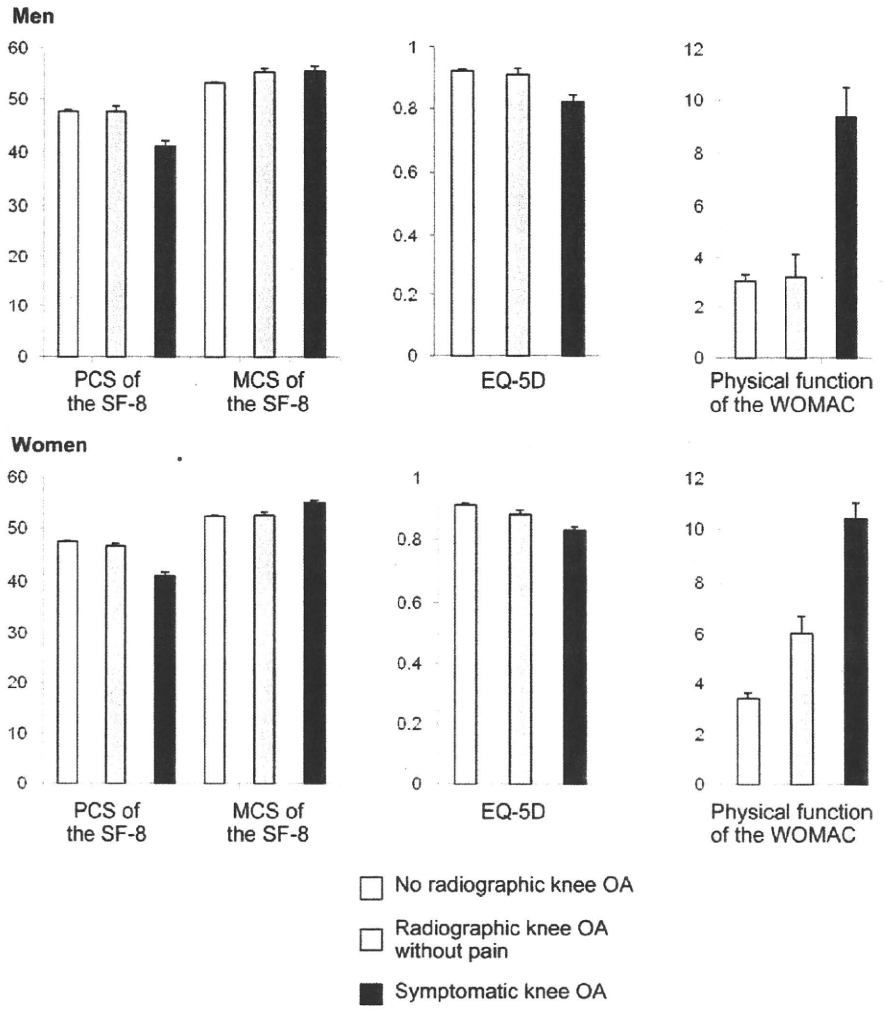

Fig. 1. Mean scores and SE of the SF-8, EQ-5D, and WOMAC scales in men and women with symptomatic knee OA ($N = 38$ and 154, respectively), radiographic knee OA without pain ($N = 53$ and 140, respectively), and no radiographic knee OA ($N = 676$ and 1065, respectively). Symptomatic knee OA was defined as KL = 3 or 4 with knee pain, radiographic knee OA without pain was defined as KL = 3 or 4 without knee pain, and no radiographic knee OA was defined as KL = 0, 1 or 2.

also showed that subjects with severe knee OA had lower QOL than those with mild knee OA[14], although their subjects were recruited from hospitals, so QOL parameters were not compared between subjects with mild knee OA and those without knee OA. The present study showed that there were no significant differences between subjects with KL = 2 and those with KL = 0 or 1. Considering the definitions of the KL grade, our findings may indicate that osteophytosis and joint space narrowing, which are representative features of knee OA, have a different impact on QOL. In other words, osteophytosis may have a weak impact on QOL, whereas joint space narrowing may have a strong impact.

Because QOL was shown to be strongly associated with pain, we next compared the impact of radiographic knee OA with and without pain on QOL. The present study showed that symptomatic knee OA was significantly associated with lower physical QOL than radiographic knee OA without pain. Differences in PCS scores among subjects with symptomatic knee OA and those without radiographic knee OA without pain were 6.6 and 6.5 in men and women, respectively. The differences were higher than the MCID; thus, symptomatic knee OA is considered clinically important for physical QOL. In addition, there were no significant differences in physical QOL between subjects with radiographic knee OA without pain and those without radiographic knee OA. This finding indicates that loss of physical QOL was more strongly associated with symptoms such as pain due to radiographic knee OA rather than radiographic changes of the knee itself. In other words, QOL may improve when pain is relieved by medical care, even if subjects have radiographic knee OA.

As measured by MCS of the SF-8, knee OA was associated with higher QOL scores in men and women, although it was also associated with lower PCS. Past studies also showed the dissociation between PCS and MCS in knee OA[43]. Several factors may contribute to this phenomenon. First, the MCS questions within the SF-8 include generic questions about energy levels, feelings of being "downhearted and blue," and interference in daily activities as a result of emotional problems. These questions are less sensitive to the presence of mental health issues than disease-specific scales such as the Kessler psychological distress scale[44]. In fact, psychological distress has been shown to be significantly more frequent in those with arthritis than those without it, although scores on the MCS were not significantly different between these two groups[45]. Second, the dissociation may be due to a disability paradox[46], which suggests that people with chronic disabilities report serious limitations in activities of daily living and problems in performing social roles, yet

Table IV
Correlations of symptomatic knee OA and grip strength with scores of the SF-8, EQ-5D, and WOMAC scales

		SF-8		EQ-5D	WOMAC		
		PCS	MCS		Pain	Stiffness	Function
Men							
Symptomatic knee OA ($N=38$)	Crude regression coefficient	−6.64 (−8.82, −4.46)	2.49 (0.77, 4.21)	−0.10 (−0.14, −0.05)	2.46 (1.78, 3.13)	0.83 (0.48, 1.18)	6.19 (3.95, 8.42)
	Adjusted regression coefficient	−6.00 (−8.17, −3.81)	2.10 (0.33, 3.88)	−0.08 (−0.12, −0.03)	2.18 (1.51, 2.86)	0.75 (0.39, 1.10)	4.88 (2.67, 7.10)
Grip strength	Crude regression coefficient	0.20 (0.15, 0.25)	−0.03 (−0.07, 0.01)	0.003 (0.002, 0.004)	−0.06 (−0.07, −0.04)	−0.02 (−0.03, −0.01)	−0.23 (−0.28, −0.17)
	Adjusted regression coefficient	0.19 (0.12, 0.26)	−0.02 (−0.08, 0.03)	0.003 (0.001, 0.004)	−0.04 (−0.06, −0.02)	−0.01 (−0.02, 0.00)	−0.19 (−0.26, −0.12)
Women							
Symptomatic knee OA ($N=154$)	Crude regression coefficient	−6.29 (−7.42, −5.16)	2.66 (1.64, 3.69)	−0.07 (−0.10, −0.05)	2.05 (1.64, 2.47)	0.80 (0.59, 1.02)	6.74 (5.40, 8.08)
	Adjusted regression coefficient	−4.36 (−5.52, −3.21)	2.52 (1.43, 3.61)	−0.03 (−0.06, −0.01)	1.44 (1.02, 1.85)	0.51 (0.29, 0.74)	3.97 (2.68, 5.27)
Grip strength	Crude regression coefficient	0.34 (0.28, 0.41)	0.06 (0.01, 0.12)	0.007 (0.006, 0.009)	−0.11 (−0.13, −0.08)	−0.04 (−0.05, −0.03)	−0.46 (−0.53, −0.39)
	Adjusted regression coefficient	0.20 (0.13, 0.27)	0.08 (0.01, 0.15)	0.004 (0.003, 0.006)	−0.04 (−0.07, −0.02)	−0.01 (−0.03, 0.00)	−0.21 (−0.30, −0.13)

Adjusted regression coefficient is calculated by multiple regression analysis with age, BMI, grip strength, and the presence of symptomatic knee OA as independent variables.
SF-8, Medical Outcomes Study Short Form-8.

state that they have excellent or good QOL. Many subjects with knee OA had knee pain, which may lead to functional impairment. Particularly in elderly individuals, pain or functional impairment may be considered a natural consequence of being elderly. Knee OA was thus not associated with lower scores for MCS in the SF-8.

In the present study, grip strength was independently associated with QOL measured by almost all domains of the three scales. Previous reports showed that low muscle mass was associated with reduced QOL[32,33]. There is increasing recognition that grip strength is a useful clinical marker of sarcopenia, and recent work has validated this approach, demonstrating that grip strength is more strongly associated with age and is a better predictor of poor mobility than other potential markers such as calf muscle area[31]. The independent association of grip strength with QOL suggests that QOL may improve with increase of muscle power in subjects with symptomatic knee OA, although longitudinal studies will be required to clarify this finding.

The present study showed that the association of radiographic and symptomatic knee OA with QOL differed among the SF-8, the WOMAC, and the EQ-5D. Radiographic and symptomatic knee OA were significantly associated with physical QOL in men and women, but not with EQ-5D utility scores. The reason for this difference may be explained by the fact that in the EQ-5D, all five domains are combined to analyze the association with knee OA, whereas the PCS and MCS of the SF-8 are analyzed separately. In fact, associations of knee OA differed between PCS and MCS of the SF-8, so when all domains were combined, the results may differ. For WOMAC, previous studies have found that WOMAC discriminates better among individuals with knee OA, whereas the SF-36 discriminates better among individuals with varying levels of self-reported general health status and comorbidities[47]. In addition, WOMAC was shown to be a more responsive measure than SF-36 in documenting changes after surgery[7,10]. Although our survey is not strictly comparable in design, it would appear that in our Japanese population, the PCS of the SF-8 and physical function domains of the WOMAC are able to discriminate among individuals with knee OA. It has been suggested that these two scales provide complementary information and may be useful in assessing both generic and disease-specific aspects of OA. However, this was a cross-sectional study, so the efficacy of these scales for knee OA in a longitudinal analysis could not be clarified. In longitudinal studies, generic measures such as the SF-8 may be much less useful than disease-specific measures such as the WOMAC because the generic measures pick up a lot of "noise" from comorbidities and may therefore be relatively unresponsive.

There are several limitations to the present study. First, this is a large-scale, population-based study, with a cross-sectional study of baseline data. Thus, causal relationships could not be determined. The ROAD study is a longitudinal survey, so further progress may help elucidate any causal relationships. Second, we did not include other weight-bearing OAs, such as hip OA, in the analysis, although this disorder may also affect QOL. However, the prevalence of KL = 3 or 4 hip was 1.4% and 3.5% in Japanese men and women[48], respectively, which was smaller compared with KL = 3 or 4 knee in the present study. Thus it is possible that hip OA would not strongly affect the results in the present study. Third, among the 2995 subjects ≥40 years old in the ROAD study, 2126 subjects had completed questionnaires for the SF-8, the EQ-5D, and the WOMAC, for a response rate of 71.0%. Subjects who completed questionnaires may have had better QOL than those who did not, so our results regarding QOL may have represented overestimations of QOL.

In conclusion, the present cross-sectional study using a large-scale population from the ROAD study revealed that KL = 3 or 4 OA was significantly associated with lower physical QOL scores, whereas KL = 2 OA was not. Symptomatic knee OA was more strongly associated with QOL than radiographic knee OA without pain. Further studies, along with continued longitudinal surveys in the ROAD study, will help to elucidate the background of knee OA and relations with QOL.

Author contributions

All authors have made substantial contributions to all three of sections (1), (2) and (3) below;

(1) the conception and design of the study, or acquisition of data, or analysis and interpretation of data
(2) drafting the article or revising it critically for important intellectual content
(3) final approval of the version to be submitted.

Conflicts of interest

There are no conflicts of interest.

Acknowledgements

This study was supported by a Grant-in-Aid for Scientific Research (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, and H20-Choujyu-009 from the Ministry of Health, Labor and Welfare, the Research Aid from the Japanese Orthopaedic Association and Grant of Japan Orthopedics and Traumatology Foundation, Inc., No. 166. The sponsors had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

The authors wish to thank Dr Anamizu and members of the Department of Orthopedics; Mr Kutsuma and other members of the 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.

References

1. Sharma L, Kapoor D. Epidemiology of osteoarthritis. In: Moskowitz RW, Altman RD, Hochberg MC, Buckwalter JA, Goldberg VM, Eds. Osteoarthritis: Diagnosis and Medical/Surgical Management. 4th edn. Philadelphia: Lippincott Williams & Wilkins; 2007:3–26.
2. Guccione AA, Felson DT, Anderson JJ, Anthony JM, Zhang Y, Wilson PW, *et al.* The effects of specific medical conditions on the functional limitations of elders in the Framingham Study. Am J Public Health 1994;84:351–8.
3. Felson DT, Zhang Y. An update on the epidemiology of knee and hip osteoarthritis with a view to prevention. Arthritis Rheum 1998;41:1343–55.
4. Muraki S, Oka H, Akune T, Mabuchi A, En-yo Y, Yoshida M, *et al.* Prevalence of radiographic knee osteoarthritis and its association with knee pain in the elderly of Japanese population-based cohorts: the ROAD study. Osteoarthritis Cartilage 2009;17:1137–43.
5. Yoshimura N, Muraki S, Oka H, Mabuchi A, En-yo Y, Yoshida M, *et al.* Prevalence of knee osteoarthritis, lumbar spondylosis and osteoporosis in Japanese men and women: the Research on Osteoarthritis/osteoporosis Against Disability (ROAD). J Bone Miner Metab 2009;27:620–8.
6. Ministry of Health, Labour and Welfare. The outline of the results of National Livelihood Survey 2007. Available at: http://www.mhlw.go.jp/toukei/list/20-19-1.html.
7. Brazier JE, Harper R, Munro J, Walters SJ, Snaith ML. Generic and condition-specific outcome measures for people with osteoarthritis of the knee. Rheumatology (Oxford) 1999;38:870–7.
8. Fransen M, Edmonds J. Reliability and validity of the EuroQol in patients with osteoarthritis of the knee. Rheumatology (Oxford) 1999;38:807–13.
9. March LM, Cross MJ, Lapsley H, Brnabic AJ, Tribe KL, Bachmeier CJ, *et al.* Outcomes after hip or knee replacement surgery. Med J Aust 1999;171:235–8.
10. Bachmeier CJ, March LM, Cross MJ, Lapsley HM, Tribe KL, Courtenay BG, *et al.* A comparison of outcomes in osteoarthritis patients undergoing total hip and knee replacement surgery. Osteoarthritis Cartilage 2001;9:137–46.
11. Hill CL, Parsons J, Taylor A, Leach G. Health related quality of life in a population sample with arthritis. J Rheumatol 1999;26:2029–35.
12. Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. J Rheumatol 1988;15:1833–40.
13. Thumboo J, Chew LH, Soh CH. Validation of the Western Ontario and McMaster University osteoarthritis index in Asians with osteoarthritis in Singapore. Osteoarthritis Cartilage 2001;9:440–6.
14. Woo J, Lau E, Lee P, Kwok T, Lau WC, Chan C, *et al.* Impact of osteoarthritis on quality of life in a Hong Kong Chinese population. J Rheumatol 2004;31:2433–8.
15. Dillon CF, Rasch EK, Gu Q, Hirsch R. Prevalence of knee osteoarthritis in the United States: arthritis data from the Third National Health and Nutrition Examination Survey 1991–94. J Rheumatol 2006;33:2271–9.
16. Jordan JM, Helmick CG, Renner JB, Luta G, Dragomir AD, Woodard J, *et al.* Prevalence of knee symptoms and radiographic and symptomatic knee osteoarthritis in African Americans and Caucasians: the Johnston County Osteoarthritis Project. J Rheumatol 2007;34:172–80.
17. Yoshida S, Aoyagi K, Felson DT, Aliabadi P, Shindo H, Takemoto T. Comparison of the prevalence of radiographic osteoarthritis of the knee and hand between Japan and the United States. J Rheumatol 2002;29:1454–8.
18. Felson DT, Naimark A, Anderson J, Kazis L, Castelli W, Meenan RF. The prevalence of knee osteoarthritis in the elderly. The Framingham osteoarthritis study. Arthritis Rheum 1987;30:914–8.
19. Coggon D, Croft P, Kellingray S, Barrett D, McLaren M, Cooper C. Occupational physical activities and osteoarthritis of the knee. Arthritis Rheum 2000;43:1443–9.
20. Muraki S, Akune T, Oka H, Mabuchi A, En-yo Y, Yoshida M, *et al.* Association of occupational activity with radiographic knee osteoarthritis and lumbar spondylosis in elderly patients of population-based cohorts: a large-scale population-based study. Arthritis Rheum 2009;61:779–86.
21. Linaker CH, Walker-Bone K, Palmer K, Cooper C. Frequency and impact of regional musculoskeletal disorders. Baillieres Clin Rheumatol 1999;13:197–215.
22. Duncan R, Peat G, Thomas E, Hay E, McCall I. Croft P symptoms and radiographic osteoarthritis: not as discordant as they are made out to be? Ann Rheum Dis 2007;66:86–91.
23. Hannan MT, Felson DT, Pincus T. Analysis of the discordance between radiographic changes and knee pain in osteoarthritis of the knee. J Rheumatol 2000;27:1513–7.
24. Neogi T, Felson D, Niu J, Nevitt M, Lewis CE, Aliabadi P, *et al.* Association between radiographic features of knee osteoarthritis and pain: results from two cohort studies. BMJ 2009;339:b2844.
25. Roubenoff R. Sarcopenia: a major modifiable cause of frailty in the elderly. J Nutr Health Aging 2000;4:4140–2.
26. Sayer AA, Syddall HE, Dennison EM, Martin HJ, Phillips DI, Cooper C, *et al.* Grip strength and the metabolic syndrome: findings from the Hertfordshire Cohort Study. QJM 2007;100:707–13.
27. Bohannon RW. Hand-grip dynamometry predicts future outcomes in aging adults. J Geriatr Phys Ther 2008;31:3–10.
28. Sirola J, Rikkonen T, Tuppurainen M, Jurvelin JS, Kroger H. Association of grip strength change with menopausal bone loss and related fractures: a population based follow-up study. Calcif Tissue Int 2006;78:218–26.
29. Kerr A, Syddall HE, Cooper C, Turner GF, Briggs RS, Sayer AA. Does admission grip strength predict length of stay in hospitalised older patients? Age Ageing 2006;35:82–4.

30. Wind AE, Takken T, Helders PJ, Engelbert RH. Is grip strength a predictor for total muscle strength in healthy children, adolescents, and young adults? Eur J Pediatr 2010;169:281–7.
31. Lauretani F, Russo CR, Bandinelli S, Bartali B, Cavazzini C, Di Iorio A, *et al.* Age-associated changes in skeletal muscles and their effect on mobility: an operational diagnosis of sarcopenia. J Appl Physiol 2003;95:1851–60.
32. Iannuzzi-Sucich M, Prestwood KM, Kenny AM. Prevalence of sarcopenia and predictors of skeletal muscle mass in healthy, older men and women. J Gerontol A Biol Sci Med Sci 2002;57:M772–7.
33. Sayer AA, Syddall HE, Martin HJ, Dennison EM, Roberts HC, Cooper C. Is grip strength associated with health-related quality of life? Findings from the Hertfordshire Cohort Study. Age Ageing 2006;35:409–15.
34. Yoshimura N, Muraki S, Oka H, Kawaguchi H, Nakamura K, Akune T. Cohort profile: research on osteoarthritis/osteoporosis against disability study. Int J Epidemiol (In press).
35. Kellgren JH, Lawrence JS, Eds. The Epidemiology of Chronic Rheumatism: Atlas of Standard Radiographs of Arthritis. Oxford: Blackwell Scientific; 1963.
36. Fukuhara S, Bito S, Hsiano A, Green J, Kurokawa K. Translation, adaptation, and validation of the SF-36 health survey for use in Japan. J Clin Epidemiol 1998;51:1045–53.
37. Fukuhara S, Suzukamo Y. Manual of the SF-8 Japanese Version (In Japanese). Kyoto: Institute for Health Outcomes & Process Evaluation Research; 2004.
38. Dolan P. Modeling valuations for EuroQol health states. Med Care 1997;35:1095–108.
39. Japanese EuroQOL Translation Team. The development of the Japanese EuroQOL instrument. J Health Care Soc 1998;8:109–1123.
40. Barr S, Bellamy N, Buchanan WW, Chalmers A, Ford PM, Kean WF, *et al.* A comparative study of signal versus aggregate methods of outcome measurement based on the WOMAC osteoarthritis index. J Rheumatol 1994;21:2106–12.
41. Hashimoto H, Hanyu T, Sledge CB, Lingard EA. Validation of a Japanese patient-derived outcome scale for assessing total knee arthroplasty: comparison with Western Ontario and McMaster Universities osteoarthritis index (WOMAC). J Orthop Sci 2003;8:288–93.
42. Samsa G, Edelman D, Rothman ML, Williams GR, Lipscomb J, Matchar D. Determining clinically important differences in health status measures: a general approach with illustration to the Health Utilities Index Mark II. Pharmacoeconomics 1999;15:141–55.
43. Boutron I, Rannou F, Jardinaud-Lopez M, Meric G, Revel M, Poiraudeau S. Disability and quality of life of patients with knee or hip osteoarthritis in the primary care setting and factors associated with general practitioners' indication for prosthetic replacement within 1 year. Osteoarthritis Cartilage 2008;16:1024–31.
44. Kessler RC, Andrews G, Colpe LJ, Hiripi E, Mroczek DK, Normand SL, *et al.* Short screening scales to monitor population prevalences and trends in non-specific psychological distress. Psychol Med 2002;32:959–76.
45. Hill CL, Gill T, Taylor AW, Daly A, Grande ED, Adams RJ. Psychological factors and quality of life in arthritis: a population-based study. Clin Rheumatol 2007;26:1049–54.
46. Albrecht G, Devlieger P. The disability paradox: high quality of life against all odds. Soc Sci Med 1999;48:977–88.
47. Hawker G, Melfi C, Paul J, Green R, Bombardier C. Comparison of a generic (SF-36) and a disease specific (WOMAC) (Western Ontario and McMaster Universities Osteoarthritis Index) instrument in the measurement of outcomes after knee replacement surgery. J Rheumatol 1995;22:1193–6.
48. Inoue K, Wicart P, Kawasaki T, Huang J, Ushiyama T, Hukuda S, *et al.* Prevalence of hip osteoarthritis and acetabular dysplasia in french and japanese adults. Rheumatology (Oxford) 2000;39:745–8.

Published by Oxford University Press on behalf of the International Epidemiological Association
© The Author 2009; all rights reserved. Advance Access publication 11 September 2009

International Journal of Epidemiology 2010;**39**:988–995
doi:10.1093/ije/dyp276

COHORT PROFILE

Cohort Profile: Research on Osteoarthritis/ Osteoporosis Against Disability study

Noriko Yoshimura,[1]* Shigeyuki Muraki,[2] Hiroyuki Oka,[1] Hiroshi Kawaguchi,[3] Kozo Nakamura[3] and Toru Akune[2]

Accepted 15 July 2009

How did the study come about?

Since the proportion of the ageing population in Japan is increasing, a comprehensive and evidence-based strategy is urgently required for the prevention of musculoskeletal diseases, including osteoarthritis (OA) and osteoporosis (OP), both of which affect the activities of daily living (ADL) and quality of life (QOL) and increase morbidity and mortality.[1–4] However, few prospective, longitudinal studies for the purpose of developing such a strategy have been conducted, and little information is available regarding the prevalence and incidence of musculoskeletal disorders, including OA and OP, as well as pain and disability in the Japanese population.[5–10] It is difficult to design rational clinical and public health approaches for the diagnosis, evaluation and prevention of OA and OP without such epidemiological data.

The Research on Osteoarthritis/osteoporosis Against Disability (ROAD) study was established in 2005 by N.Y., T.A., H.O., S.M., H.K. and K.N. (principal investigators). The principal investigators are affiliated with the 22nd Century Medical and Research Center, University of Tokyo.

What does the ROAD study cover?

The ROAD study is a multi-centre prospective observational study that aims to elucidate the environmental and genetic background of bone and joint diseases (with OA and OP as the representative bone and joint diseases). It is designed to examine the extent to which risk factors for these diseases are related to the clinical features of the diseases, laboratory and radiographic findings, bone mass, bone geometry, lifestyle, nutritional factors, anthropometric and neuromuscular measures and fall propensity. It also aims to determine how these diseases affect the ADL and QOL of Japanese men and women.

The study will provide the information required to develop clinical algorithms for the early identification of potential high-risk populations. It will also provide information required to develop policies for the detection and prevention of OA, OP and osteoporotic fractures. The immediate goal of this study is to establish a representative population of elderly people, principally for the study of bone and joint health. The establishment of this cohort will also facilitate the expansion of other studies in related areas of investigation. Moreover, the knowledge gained from the ROAD study will have major implications for understanding and managing several other common problems of ageing.

Who are in the sample?

The subjects were residents of any one of the three communities that have different characteristics: an urban region in Itabashi, Tokyo; a mountainous region in Hidakagawa, Wakayama; and a coastal region in Taiji, Wakayama (Figure 1). The inclusion criteria, apart from residence in the communities mentioned above, were the ability to (i) walk to the survey site, (ii) report data and (iii) understand and sign an informed consent form. The age of the participants recruited from the urban region was $\geqslant 60$ years, and that of the participants from the other

[1] Department of Joint Disease Research, 22nd Century Medical and Research Centre, Graduate School of Medicine, University of Tokyo, Tokyo, Japan.
[2] Department of Clinical Motor System Medicine, 22nd Century Medical and Research Centre, Graduate School of Medicine, University of Tokyo, Tokyo, Japan.
[3] Department of Orthopedic Surgery, Faculty of Medicine, University of Tokyo, Tokyo, Japan.

* Corresponding author. Department of Joint Disease Research, 22nd Century Medical and Research Centre, Graduate School of Medicine, University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8655, Japan. E-mail: YOSHIMURAN-ORT@h.u-tokyo.ac.jp

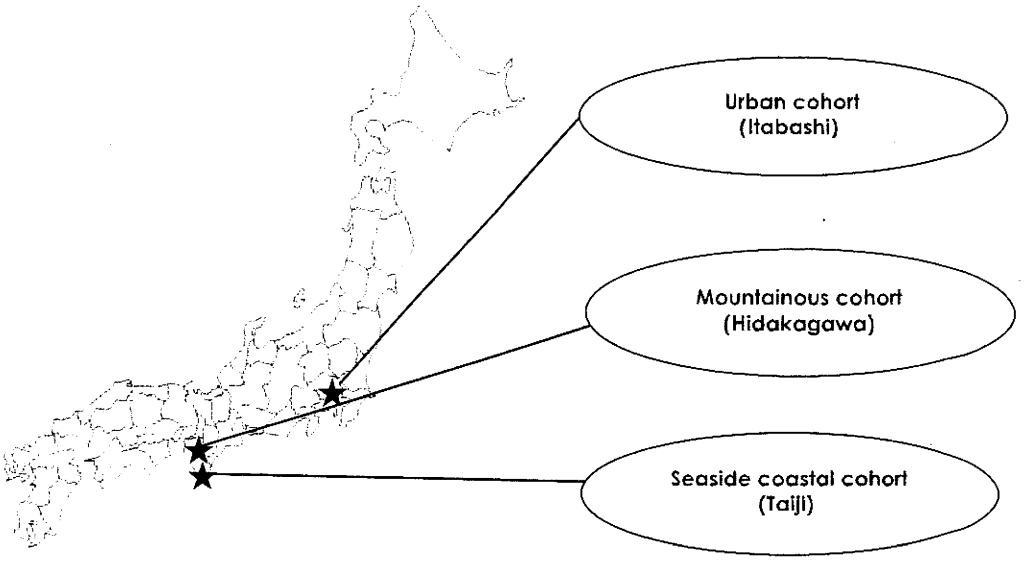

Figure 1 Locations of the three regions from which the study cohort was derived

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

Age strata (years)	Men				Women			
	Total	Urban	Mountainous	Coastal	Total	Urban	Mountainous	Coastal
⩽39	14	0	2	12	31	0	7	24
40–49	44	0	7	37	105	0	17	88
50–59	107	0	36	71	211	2	67	142
60–69	168	11	93	64	385	60	183	142
70–79	535	315	150	70	913	594	196	123
⩾80	193	139	31	23	334	229	75	30
Total	1061	465	319	277	1979	885	545	549
Age (years)	71.0 (10.7)	77.2 (4.3)	69.5 (9.1)	62.6 (13.2)	69.9 (11.2)	76.3 (5.0)	68.6 (10.4)	60.8 (12.5)
Height (cm)	162.5 (6.7)	161.3 (5.9)	161.4 (6.9)	165.8 (6.8)	149.8 (6.5)	148.5 (5.6)	148.2 (6.7)	153.2 (6.2)
Weight (kg)	61.3 (10.0)	60.0 (8.5)	60.0 (10.2)	64.8 (11.0)	51.5 (8.6)	50.8 (8.3)	50.5 (8.6)	53.5 (8.8)
BMI (kg/m^2)	23.1 (3.0)	23.0 (2.8)	23.0 (3.0)	23.5 (3.4)	22.9 (3.5)	23.0 (3.4)	23.0 (3.4)	22.8 (3.6)
Current smoker (%)	25.9	19.0	28.9	31.1	3.5	2.9	4.7	2.9
Current drinker (%)	64.4	60.5	69.8	63.2	25.9	27.4	26.1	24.2

BMI = body mass index.

two regions was ⩾40 years. In the urban region, invitation letters were distributed only to the inhabitants whose name was on a list of community-dwelling people that was prepared in 2002.[11]

Subjects from each area who were willing to attend the study were invited to participate. Despite being younger (58 years) than the age limit defined in the inclusion criteria, 2 inhabitants from the urban area, 9 from the mountainous area and 36 from the coastal area were included in the study because they were very keen to participate. Over the 1.5-year period from October 2005 to March 2007, 3040 of 5785 candidates were enrolled from the three regions (participation rate, 52.5%).

Selected characteristics of the study population, including age, height, weight, BMI and proportions of participants who smoked and consumed alcohol, are shown in Table 1. In the urban, mountainous and coastal areas, 99.8, 84.3 and 54.7% of the participants, respectively, were >60 years of age. Two-thirds of the participants were women, and their mean age was 1 year less than that of the male

participants. No significant differences were observed in BMI values between the genders, but the proportions of both current smokers and alcohol consumers were significantly higher among men than among women.

All participants provided written informed consent, and the study was conducted with the approval of the ethics committees of the University of Tokyo (nos 1264 and 1326) and the Tokyo Metropolitan Institute of Gerontology (no. 5). Careful consideration was given to ensure a safe experience for the participants during the examination and during any other study procedures.

How often have they been followed up?

We intend to follow-up the three population-based cohorts of the ROAD study for at least 10 years. In October 2008, after a follow-up period of 3 years, a second comprehensive clinical examination was started and is ongoing. We will repeat the baseline measurements during the second examination. A third and fourth examination will be performed at 6 and 10 years, respectively, after the baseline examination.

What has been measured?

The baseline examination of the ROAD study consisted of the following: interviewer-administered questionnaire, dietary assessment, anthropometric measurements, visual and neuromuscular function assessment, biochemical measurements, medical history taking, radiographic assessment and bone mineral density (BMD) measurement (Table 2).

Interviewer-administered questionnaire

A questionnaire was prepared by modifying the questionnaire used in the Osteoporotic Fractures in Men Study (MrOS),[12] and adding some new items to the modified questionnaire. Knee symptoms were

Table 2 Summary of data collected in the ROAD study

Interviewer-administrated questionnaire	
Cigarette smoking, alcohol consumption	
Medical history, medications	
Reproductive variables, lactation	
Dietary history, history of falls and fractures	
Physical activity using PASE	
Family history	
Evaluation of knee symptoms using WOMAC	
Health-related QOL (EQ5D, SF-8)	
Dietary assessment	
Nutrient intake calculated using BDHQ	
Anthropometric measurements	
Height, weight, arm span, grip strengths	
Circumference of both wrists, circumference of waist	
Heart rate, systolic and diastolic blood pressure	
Visual and neuromuscular function	
Visual acuity	
Walking speed with tandem walking 6 m x 20 cm	
Rise from a chair	
Biochemical measurements	
Blood samples	Blood counts, haemoglobin, haemoglobin A1C, blood sugar
Sera	Total protein, AST, ALT, GGT, total cholesterol, HDL-cholesterol, triglyceride BUN, uric acid, creatinine
DNA samples extracted	
Urine samples	Urinary protein, occult blood, sugar, urobilinogen
Medical information	
Pain in back, lumbar, knee and hip	
Swelling and range of motion of the joints	
Tendon reflexes	
Cognigitve function used by Mini-Mental Status Examination	
Radiographic assessment	
Anteroposterior and lateral views of lumbar spine	
Anteroposterior view of both knees	
Anteroposterior view of both hips	
BMD measurements	
Lumbar spine and proximal femur (mountainous and coastal areas)	

AST = aspartate aminotransferase; ALT = alanine aminotransferase; GGT = γ-glutamyltranspeptidase; HDL = high-density lipoprotein; BUN = blood urea nitrogen; BDHQ = Brief Diet History Questionnaire; PASE = Physical Activity Scale for the Elderly; WOMAC = Western Ontario and McMaster University Osteoarthritis Index; EQ5D = European QOL-5 dimensions instrument; SF-8 = Medical Outcomes Study 8-item Short Form.

evaluated using the WOMAC.[13] The health-related QOL was evaluated using the EuroQOL, EQ5D[14] and the SF-8.[15] The study staff recorded all the medications administered and their doses. Physical activity was quantified using the PASE.[16]

Dietary assessment

Dietary assessment was made using a BDHQ, and the dietary intakes of nutrients during the previous month were determined. Each participant received a questionnaire that included detailed explanations. Well-trained interviewers clarified any unclear sections in the questionnaire, which was to be completed by the participants at their leisure. The BDHQ is a four-page structured questionnaire that includes questions about the frequency of consumption of 80 principal foods. The serving sizes of the foods are described as normal portions, i.e. the standard weight and volume of servings commonly consumed by the general Japanese population. The BDHQ was modified from a comprehensive, 16-page version of a validated self-administered diet history questionnaire.[17] A total of 141 components, including dietary energy and nutrient intakes, were calculated using an *ad hoc* computer algorithm for the BDHQ.

Anthropometric measurements

Anthropometric factors were measured by well-trained medical nurses. The height and weight of the participants at age 25 years were also noted. BMI [weight in kilograms/(height in metres)^2] was calculated on the basis of the current height and weight.

Visual and neuromuscular function

Visual acuity was assessed by the Landolt ring test. Walking speed was determined by recording the time taken by a subject to walk 6 m at the fastest possible speed. The time required for tandem walking across a 6-m long and 20-cm wide path was used to determine balance. The ability to rise from a chair without using the arms (chair stand) and the ability to perform five chair stands was evaluated; the time required to complete the tasks was noted.

Biochemical measurements

Blood and urine samples were obtained from each participant for biochemical and genomic examinations. Urinary protein, occult blood, sugar and urobilinogen were tested using disposable reagent strips (uro-hema-combi sticks; Siemens Medical Solutions Diagnostics, Tokyo, Japan). Residual blood, plasma, serum and urine specimens were processed and stored in a deep freezer (−80°C). DNA was extracted from stored whole-blood specimens, and biochemical markers of bone turnover and cartilage will be measured using these stored serum and urine samples.

Medical history

Medical history was obtained by experienced orthopaedic surgeons (S.M. and H.O.). To quantify cognitive function, the participants were instructed to complete the modified Mini-Mental Status Examination—Japanese version.[18] Physicians explained any unclear sections of this questionnaire to the participants and assessed the participants' cognitive status on the basis of the completed questionnaire.

Radiographic assessment

The severity of OA was radiographically determined according to the Kellgren–Lawrence (KL) grading system as follows[19]: KL0—normal joint; KL1—slight osteophytes; KL2—definite osteophytes; KL3—disc-space narrowing and large osteophytes; and KL4—bone sclerosis, disc-space narrowing and large osteophytes. In the ROAD study, joints that exhibited only disc-space narrowing and no large osteophytes were graded as KL3. The radiographs were examined by a single, experienced orthopaedic surgeon (S.M.), who was blinded to the clinical status of the participants. If at least one knee joint was graded as KL2 or higher, the participant was diagnosed with radiographic knee OA. Similarly, if at least one intervertebral joint of the lumbar spine was graded as KL2 or higher, the participant was diagnosed with radiographic lumbar spondylosis.

BMD measurement

In the mountainous and coastal areas, the BMD of the lumbar spine and proximal femur was measured using dual energy X-ray absorptiometry (DXA) (Hologic Discovery; Hologic, Waltham, MA, USA) during the baseline examination. Another BMD measurement was scheduled for the second examination.

To maintain the quality of measurement, the same DXA equipment was used, and the same spine phantom was scanned daily to monitor the machine's performance in study populations from different regions. The BMD of the phantom was adjusted to 1.032 ± 0.016 g/cm^2 ($\pm 1.5\%$) during all examinations. In addition, to exclude inter-observer variability, the same physician (N.Y.) examined all participants. In another study, N.Y. had measured the intra-observer variability in both *in vitro* and *in vivo* experiments using Lunar DPX.[20] In the case of the *in vitro* experiment, the coefficient of variance (CV) for the BMD of the L2–L4 vertebrae was 0.35%. In the case of the *in vivo* experiments, which were performed on five male volunteers, the CVs for the BMDs of the L2–L4 vertebrae, the proximal femur, Ward's triangle and the trochanter were 0.61–0.90, 1.02–2.57, 1.97–5.45 and 1.77–4.17%, respectively.

OP was defined on the basis of the World Health Organization (WHO) criteria; specifically, it was diagnosed when the BMD T-scores were lower than the mean lumbar peak bone mass minus 2.5 SDs.[21]

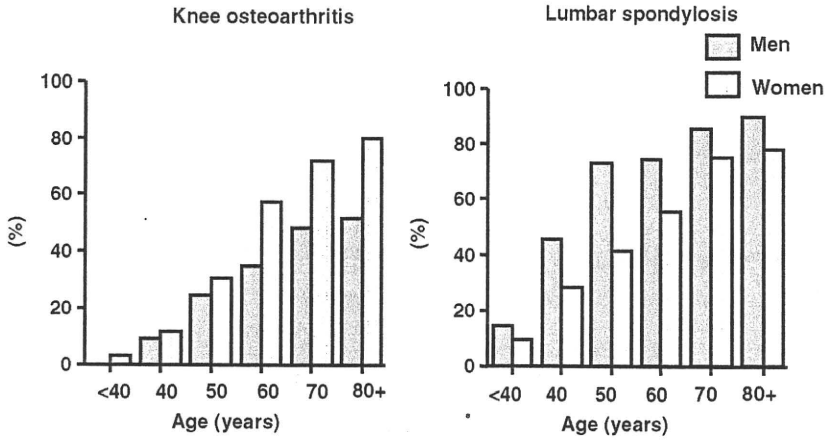

Figure 2 Prevalence of radiographic knee osteoarthritis and lumbar spondylosis, classified by age and gender

In Japan, the mean BMD of the L2–L4 vertebrae among both young male and female adults has been measured using Hologic DXA.[22] These indices were used in the present study; lumbar spine BMD $<0.714\,g/cm^2$ (in case of both men and women), and femoral neck BMD $<0.546\,g/cm^2$ (men) or $0.515\,g/cm^2$ (women) were considered to indicate OP.

All assessments performed in the baseline study will be repeated at the first, second and third follow-ups.

What is attrition like?

The first follow-up (second examination) commenced on October 2008, 3 years from baseline assessment. By the end of 2008, follow-up was completed in Hidakagawa, the mountainous region. Of the 864 participants (319 men and 545 women) in the baseline study, 635 subjects (224 men and 411 women) attended the second examination. The response rate for the second examination in the mountainous area was 73.5%. The most common reasons for non-participation were illness and difficulty in visiting the clinic (43% of the dropouts). Further, 26 people (12% of the dropouts) who participated in the baseline study died during the 3-year period following the initial assessment. In other two areas, the follow-ups are on going. The total attrition will be determined at the end of March 2010.

What has the ROAD study found?

By analysing the data from the baseline study, we have determined the prevalence of OA and OP.

OA

The age–sex distribution of radiographic knee OA and lumbar spondylosis was calculated (Figure 2); both conditions were diagnosed at KL grades of $\geqslant 2$. In the overall population, the prevalence of radiographic knee OA and lumbar spondylosis was 54.6% (42.0% in men and 61.5% in women) and 70.2% (80.6% in men and 64.6% in women), respectively. Thus, both the overall and sex-specific prevalence of lumbar spondylosis were higher than those of knee OA.[23]

OP

The prevalence of OP was calculated for the participants from mountainous and coastal regions in the ROAD study (Figure 3). The prevalence of OP of the lumbar spine and femoral neck in women was 6- and 5-fold, respectively, than in men. The differences were significant ($P < 0.001$).[23]

What are the main strengths and weaknesses of the ROAD study?

Strengths

In Japan, little epidemiological information is available of musculoskeletal diseases such as OA and OP. The ROAD study is the first large population-based prospective study conducted on the Japanese population and is designed to supply essential information, chiefly of OA and OP.

We confirmed the high prevalence of OA and OP among the ROAD study participants, and we will conduct follow-up examinations for at least 10 years in order to clarify the relationships of OA, OP and osteoporotic fractures with the following parameters: lifestyle, anthropometric and neuromuscular measurements, bone mass, bone geometry and fall propensity. Further, we will determine how these impairments affect QOL and mortality. We also expect to assess the similarities and differences in the risk factors of OA and OP. In addition, we will clarify the incident morbidity of other lifestyle-related disorders,

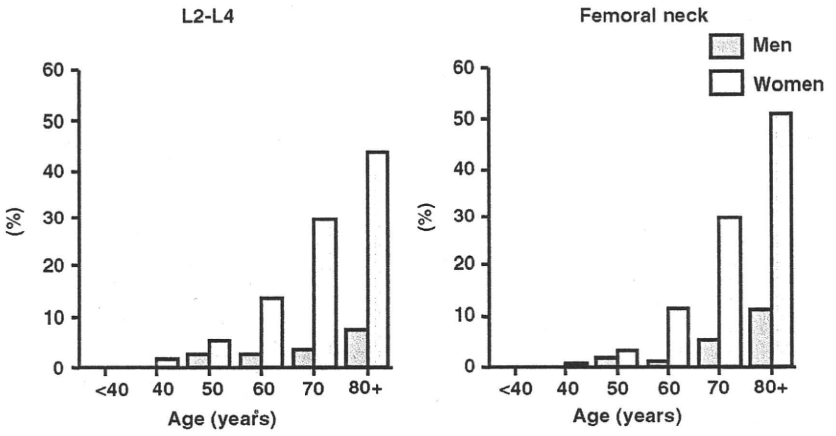

Figure 3 Prevalence of osteoporosis of the lumbar spine and femoral neck

such as obesity, hypertension, diabetes mellitus, cardiovascular and metabolic diseases and dementia.

The ROAD study data will facilitate the development of clinical guidelines for the detection and prevention of osteoporotic fractures in other countries. This study was designed such that it would be similar to the Study of Osteoporotic Fractures, a large observational study on the determinants of fractures in older women,[24] and to MrOS, a large observational study on the determinants of fractures in older men[25] in the USA.

Finally, the completion of the ROAD study will provide unique opportunities for the study of other conditions that are common among older men and women, such as obesity, diabetes, cardiovascular disease, cognitive disorders and frailty. The blood, plasma, serum and urine specimens stored during the ROAD study will enable the clarification of a variety of new biochemical and genetic factors associated with musculoskeletal disorders and the aforementioned diseases.

Weaknesses

Although the ROAD study includes a large number of subjects (more than 3000), these subjects are voluntary participants and have been recruited from only three areas; hence, they do not truly represent the general population. The 'healthy' and 'regional' selection biases should be confirmed.[26] We could not directly compare the baseline characteristics between the responders and non-responders owing to lack of data regarding the non-responders. Hence, to determine whether a selection bias existed in the ROAD study, we compared the anthropometric measurements and frequencies of smoking and alcohol drinking between the participants and the general Japanese population. The values for the general population were obtained from the 2005 National Health and Nutrition Survey conducted by the Ministry of Health, Labour and Welfare, Japan, which is an annual survey to clarify the health status of the Japanese population and is conducted on approximately 18 000 inhabitants from 6000 randomly selected families.[27]

The BMIs of ROAD study participants and the Japanese population were compared (Table 3). No significant differences were identified, except that the male participants aged 70–74 years were significantly smaller in build than men of this age group in the overall Japanese population ($P < 0.05$).

The proportion of current smokers and current drinkers (those who regularly smoked or drank more than once a month) in the general Japanese population was compared with that in the study population (Figure 4). Both proportions were significantly higher in the general Japanese population than in the study population (smokers: men, $P < 0.001$ and women, $P < 0.001$; drinkers: men, $P < 0.01$ and women, $P < 0.001$), suggesting that participants of the ROAD study had healthier lifestyles than the general Japanese population. This bias due to the selection of 'healthy' individuals should be taken into consideration while generalizing the results of the ROAD study.

Further, BMD was measured only in the participants from the mountainous and coastal areas. The total number of participants from these two areas (1690) may be large enough to accurately estimate the incidence and evaluate risk factors. Nevertheless, regional bias should be taken into account while generalizing the results.

Can I get hold of the data? Where can I find out more?

The ROAD study group welcomes specific and detailed proposals for new collaborations. Initial enquiries should be addressed to N.Y. Some information about the ROAD study is available on the website of the Department of Joint Disease Research, 22nd Century Medical and Research Centre,

Table 3 Comparison of BMI (SD) (kg/m^2) of the participants with general Japanese population

Age strata (years)	Men		Women	
	ROAD	Japanese	ROAD	Japanese
40–49	24.5 (4.4)	24.0 (3.3)	21.9 (4.1)	22.4 (3.5)
50–59	23.6 (2.9)	23.7 (3.1)	23.0 (3.3)	23.1 (3.4)
60–69	23.8 (3.2)	23.8 (2.9)	23.3 (3.2)	23.5 (3.7)
70–74	23.1 (2.8)	23.7 (3.2)	23.4 (3.5)	23.2 (3.4)
75–79	22.8(2.9)	23.3 (3.0)	23.0 (3.7)	23.4 (3.5)
⩾80	22.6 (2.9)	22.3 (2.6)	22.2 (3.2)	22.5 (4.0)

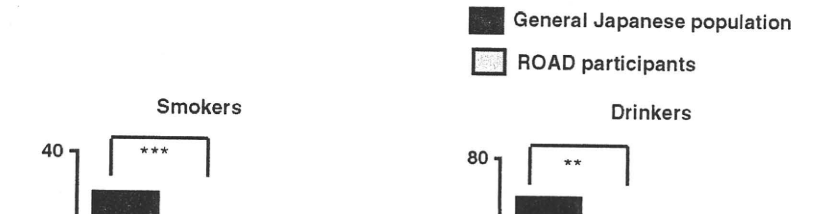

Figure 4 Comparison of the proportion of current smokers and drinkers between the participants of the ROAD study and the general Japanese population. $^{**}P < 0.01$, $^{***}P < 0.001$

University of Tokyo Hospital (http://www.h.u-tokyo.ac.jp/center22/kansetu.html).

Funding

Grant-in-Aid for Scientific Research [B20390182] to N.Y., [C20591737] to T.A. and [C20591774] to S.M. Young Scientists [A18689031] to H.O.; collaborating Research with National Science Foundation (NSF) [08033011-00262] (Director, N.Y.); the Ministry of Education, Culture, Sports and Science and Technology [H17-Men-eki-009] (Director, K.N.), [H18-Choujyu-037] (Director, T.N.) and [H20-Choujyu-009] (Director, N.Y.); and the Ministry of Health, Labour and Welfare in Japan. Japan Osteoporosis Society and Nakatomi Foundation to N.Y. and research aid from the Japanese Orthopaedic Association (Director, H.K.).

Acknowledgements

The authors wish to thank Mrs Tomoko Takijiri, Mrs Kumiko Shinou and other staff of the public office in Hidakagawa town, and Mrs Tamako Tsutsumi, Mrs Kanami Maeda and other staff of the public office in Taiji town for their assistance in locating participants and scheduling examinations.

Conflict of interest: None declared.

References

1 Ministry of Health, Labour and Welfare. Outline of the results of National Livelihood Survey 2004. http://www.mhlw.go.jp/toukei/saikin/hw/k-tyosa/k-tyosa04/4-2.html (5 August 2009, date last accessed).

2 Yamamoto I. Estimation for the number of patients of Osteoporosis in Japan. *Osteoporosis Jpn* 1999;**7**:10–11 (in Japanese).

3 Muraki S, Yamamoto S, Ishibashi H, Nakamura K. Factors associated with mortality following hip fracture in Japan. *J Bone Miner Metab* 2006;**24**:100–4.

4 Jornell O, Kanis JA, Oden A *et al.* Mortality after osteoporotic fractures. *Osteoporosis Int* 2004;**15**:38–42.

5 Yoshimura N, Dennison E, Wilman C, Hashimoto T, Cooper C. Epidemiology of chronic disc degeneration and osteoarthritis of the lumbar spine in Britain

and Japan: a comparative study. *J Rheumatol* 2000;**27:** 429–33.

[6] Yoshida S, Aoyagi K, Felson DT, Aliabadi P, Shindo H, Takemoto T. Comparison of the prevalence of radiographic osteoarthritis of the knee and hand between Japan and the United States. *J Rheumatol* 2002;**29:** 1454–58.

[7] Yoshimura N, Hashimoto T, Morioka S, Sakata K, Kasamatsu T, Cooper C. Determinants of bone loss in a rural Japanese community. The Taiji Study. *Osteoporosis Int* 1998;**8:**604–10.

[8] Yoshimura N, Kinoshita H, Danjoh S *et al.* Bone loss at the lumbar spine and the proximal femur in a rural Japanese community, 1990–2000: the Miyama study. *Osteoporos Int* 2002;**13:**803–88.

[9] Fujiwara S, Kasagi F, Masunari N, Naito K, Suzuki G, Fukunaga M. Fracture prediction from bone mineral density in Japanese men and women. *J Bone Miner Res* 2003; **18:**1547–53.

[10] Kwon J, Suzuki T, Yoshida H *et al.* Association between change in bone mineral density and decline in usual walking speed in elderly community-dwelling Japanese women during 2 years of follow-up. *J Am Geriatr Soc* 2007;**55:**240–44.

[11] Shimada H, Lord SR, Yoshida H, Kim H, Suzuki T. Predictors of cessation of regular leisure-time physical activity in community-dwelling elderly people. *Gerontology* 2007;**53:**293–97.

[12] Orwoll E, Blank JB, Barrett-Connor E *et al.* Design and baseline characteristics of the osteoporotic fractures in men (MrOS) study: a large observational study of the determinants of fracture in older men. *Contemp Clin Trials* 2005;**26:**569–85.

[13] Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC. a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. *J Rheum* 1998;**15:**1833–40.

[14] Johnson JA, Coons SJ, Ergo A, Szava-Kovats G. Valuation of EuroQOL (EQ-5D) health states in an adult US sample. *Pharmacoeconomics* 1998;**13:**421–33.

[15] Fukuhara S, Suzukao Y. Manual of the SF-8 Japanese version. *Institute for Health Outcomes and Process Evaluation Research*. Kyoto, 2004.

[16] Washburn RA, Smith KW, Jette AM, Janney CA. The physical activity scale for the elderly (PASE): development and evaluation. *J Clin Epidemiol* 1993;**46:** 153–62.

[17] Sasaki S, Yanagibori R, Amano K. Self-administered diet history questionnaire developed for health education: a relative validation of the test-version by comparison with 3-day diet record in women. *J Epidemiol* 1998;**8:** 203–15.

[18] Teng EL, Chui HC. The modified mini-mental state (3MS) examination. *J Clin Psychiatry* 1987;**48:**314–18.

[19] Kellgren JH, Lawrence LS. Radiological assessment of osteo-arthrosis. *Ann Rheum Dis* 1957;**16:**494–502.

[20] Yoshimura N, Kakimoto T, Nishioka M *et al.* Evaluation of reproducibility of bone mineral density measured by dual energy X-ray absorptiometry (Lunar DPX-L). *J Wakayama Med Soc* 1997;**48:**461–66.

[21] World Health Organization. Assessment of fracture risk and its application to screening for postmenopausal Osteoporosis. *WHO Technical Report Series 843*. Geneva: WHO, 1994.

[22] Orimo H, Hayashi Y, Fukunaga M *et al.* Osteoporosis diagnostic criteria review committee: Japanese society for bone and mineral research. Diagnostic criteria for primary Osteoporosis: year 2000 revision. *J Bone Miner Metab* 2001;**19:**331–37.

[23] Yoshimura N, Muraki S, Oka H *et al.* Prevalence of knee osteoarthritis, lumbar spondylosis and Osteoporosis in Japanese men and women: the research on osteoarthritis/Osteoporosis against disability (ROAD). *J Bone Miner Metab* 2009;**27** (in press). Available at (http://www.springerlink.com/openurl.asp?genre=article&id=doi:10.1007/s00774-009-0080-8).

[24] Cummings SR, Nevitt MC, Browner WS *et al.* Risk factors for hip fracture in white women. *N Engl J Med* 1995;**332:** 767–74.

[25] Cummings SR, Cawthon PM, Ensrud KE, Cauley JA, Fink HA, Orwoll ES. Osteoporotic fractures in men (MrOS) research groups. Study of osteoporotic fractures research groups. BMD and risk of hip and nonvertebral fractures in older men: a prospective study and comparison with older women. *J Bone Miner Res* 2006;**21:**1550–60.

[26] Coggon D, Rose G, Barker DJP (eds). *Epidemiology for the Uninitiated*. 4th edn. BMJ Publishing Group, 1997. Available at http://bmj.bmjjournals.com/epidem/epid.html. (5 August 2009, date last accessed).

[27] Ministry of Health, Labour and Welfare. The Report of National Health and Nutrition Survey 2005. http://www.mhlw.go.jp/bunya/kenkou/eiyou07/01.html.

Mod Rheumatol (2010) 20:444–451
DOI 10.1007/s10165-010-0307-5

ORIGINAL ARTICLE

Impact of knee and low back pain on health-related quality of life in Japanese women: the Research on Osteoarthritis Against Disability (ROAD)

Shigeyuki Muraki · Toru Akune · Hiroyuki Oka · Yoshio En-yo · Munehito Yoshida · Akihiko Saika · Takao Suzuki · Hideyo Yoshida · Hideaki Ishibashi · Fumiaki Tokimura · Seizo Yamamoto · Kozo Nakamura · Hiroshi Kawaguchi · Noriko Yoshimura

Received: 22 December 2009 / Accepted: 6 April 2010 / Published online: 14 May 2010

Abstract Although knee and low back pain are major public health issues, little information is available on their impact on the quality of life (QOL). We have investigated the impact of knee and low back pain on the QOL in Japanese women by assessing the associations between knee pain and low back pain and various QOL domains using measures such as the Medical Outcomes Study Short Form-8, EuroQOL, and the Western Ontario and McMaster Universities Osteoarthritis Index. From the 3,040 Japanese women participating in the Research on Osteoarthritis Against Disability (ROAD) study, we analyzed data on 1,369 women >40 years old (mean age 68.4 years). We further examined the associations of Kellgren–Lawrence (KL) grade at the knee and lumbar spine and the presence of vertebral fracture (VFx) with the magnitude of QOL loss in women with knee pain and low back pain, respectively. Knee pain and low back pain were found to be significantly associated with lower QOL scores among the women comprising the study cohort. In women with knee pain KL = 4, knee osteoarthritis was strongly associated with the magnitude of QOL loss. For women with low back pain, no significant associations were found between KL grade and magnitude of QOL loss, while there was a moderate association between the latter and VFx.

Keywords Epidemiology · Knee · Pain · Osteoarthritis · Quality of life

S. Muraki (✉) · T. Akune
Department of Clinical Motor System Medicine, Faculty of Medicine, 22nd Century Medical and Research Center, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8655, Japan
e-mail: murakis-ort@h.u-tokyo.ac.jp

H. Oka · N. Yoshimura
Department of Joint Disease Research, Faculty of Medicine, 22nd Century Medical and Research Center, The University of Tokyo, Tokyo, Japan

Y. En-yo · M. Yoshida · A. Saika
Department of Orthopaedic Surgery, Wakayama Medical University, Wakayama, Japan

T. Suzuki · H. Yoshida · H. Ishibashi · F. Tokimura · S. Yamamoto
Tokyo Metropolitan Institute of Gerontology, Tokyo, Japan

K. Nakamura · H. Kawaguchi
Department of Sensory and Motor System Medicine, Faculty of Medicine, The University of Tokyo, Tokyo, Japan

Introduction

Knee pain and low back pain are major public health issues and important causes of physical impairment among the elderly populations of most developed countries [1–3]. The prevalence of knee pain and low back pain is quite high among elderly women in Japan [1, 3]. However, although it is important to determine the impact of knee pain and low back pain on the quality of life (QOL), few studies have assessed the association between knee pain and QOL [4]. Several studies have focused on the association between low back pain and QOL in Caucasian populations [5–8], but the results of a subsequent population survey suggested that disease patterns differ according to ethnicity [9]. Therefore, clarification of the impact of knee pain and low back pain on the QOL of the Japanese elderly would be of interest. Furthermore, although the association of knee pain and low back pain with QOL may not be independent, to date, no population-based studies have examined the impact of knee pain and low back pain on QOL in the same population using the same QOL assessment tools.

A significant causal factor of knee pain is knee osteoarthritis (OA) [10, 11], and the prevalence of knee pain also increases with increasing severity of knee OA [3]. The impact of knee pain on QOL may thus differ according to the severity of knee OA, but there is a lack of population-based studies on possible associations between knee pain and QOL according to the severity of knee OA. Among the elderly, one of the main causes of low back pain is vertebral fracture (VFx), leading to impaired physical functioning, immobility, loss of self-esteem, and depression [12]. Low back pain is also believed to be a principal clinical symptom of lumbar spondylosis, but there has as yet been no population-based studies that have examined the associations between low back pain and QOL according to the presence of VFx or lumbar spondylosis.

Gender differences have also been observed in knee pain and low back pain, with the prevalence of both conditions being higher in women than in men [1, 3]. The associations of these kinds of pain with lumbar spondylosis and knee OA also differ between genders [1, 3]. Consequently, the impact of these diseases on QOL may also differ between genders. Although a number of studies have examined the association of knee pain [4] or low back pain [5–8] with QOL, men and women were not assessed separately in most of these studies [4–6], and only two large-scale population-based studies have examined these kinds of pain specifically in women [7, 8].

In the study reported here, we first investigated the impact of knee pain and low back pain on QOL among 1,369 women who were participating in the Research on Osteoarthritis Against Disability (ROAD) study, a nationwide prospective study on bone and joint diseases involving population-based cohorts from several communities in Japan. Secondly, we investigated the impact of pain on QOL in women according to the presence and severity of various diseases, such as VFx, lumbar spondylosis, and knee OA.

Materials and methods

Materials

Recruitment for the ROAD study has been described in detail elsewhere [13, 14]. To date, we have completed the creation of a baseline database that includes clinical and genetic information on 3,040 Japanese inhabitants (1,061 men, 1,979 women) in the age range of 23–95 years (mean 70.6 years), who were recruited from listings of resident registration in three communities. 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 consisting of 400 items, which included questions on lifestyle, such as smoking habits, alcohol consumption, family history, past history, physical activity, reproductive variables, and health-related QOL. Anthropometric measurements included height, weight, bilateral grip strength, and body mass index (BMI), which was calculated as weight in kilograms divided by the square of height in meters. All subjects were interviewed by well-experienced orthopedists on aspects related to knee pain and low back pain, who asked, "In the past month, have you experienced knee pain on most days?" and "In the past month, have you experienced low back pain on most days?", respectively. Those respondents who answered "yes" were defined as having pain. From the baseline data compiled on all ROAD participants, we extracted data on 1,369 Japanese women ≥40 years old who had completed the questionnaire comprising the Medical Outcomes Study Short Form-8 (SF-8) health survey [15], the EuroQOL (EQ-5D) [16], and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) [17, 18].

Radiographic assessment

All participants underwent radiographic examination of both knees, both anteroposterior and lateral views, with weight-bearing and foot-map positioning, and of the lumbar spine, including intervertebral levels from L1/2 to L5/S, both anteroposterior and lateral views. Knee and lumbar spine radiographs by a single well-experienced orthopedist (S.M.) blinded to the participant's clinical status. VFx was assessed by lateral radiography of the lumbar spine (L1–L5) using a semiquantitative method [19]. Lumbar spondylosis and knee OA were assessed using the Kellgren–Lawrence (KL) radiographic atlas, and severity was determined by KL grading [20] (Fig. 1). For this study, we defined lumbar spondylosis and knee OA as KL $\geq$ 2 in at least one knee and one intervertebral level, respectively.

Assessment instruments

To carry out the QOL assessment, we used the SF-8, a new generic eight-item assessment that generates a health profile consisting of eight scales and two summary measures describing health-related QOL. The SF-8 is an alternate form to the SF-36 health survey (SF-36) [21], which is worldwide the most intensively used patient-based health status survey. The SF-8 uses one question to measure each of the eight SF-36 domains. Japanese versions of the SF-8 have been well-validated [15]. In the SF-8, each of the eight items assesses a different dimension of health: general health (GH); physical functioning (PF); role physical

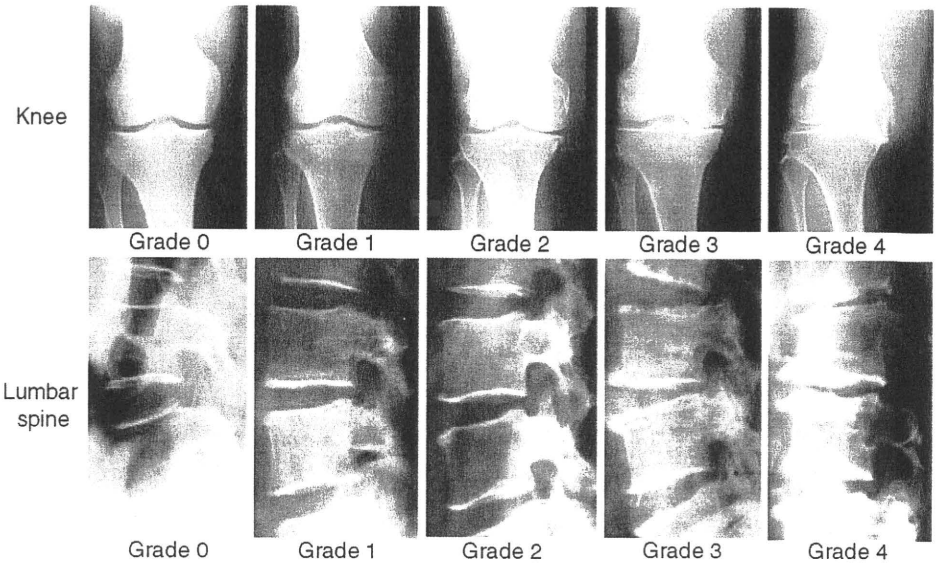

Fig. 1 Kellgren–Lawrence (KL) grade at knee and lumbar spine. *Knee*: *Grade 1* Doubtful narrowing of the joint space and possible osteophytic lipping, *Grade 2* definite osteophytes and possible narrowing of the joint space, *Grade 3* multiple moderate osteophytes, definite narrowing of the joint space, some sclerosis, and possible deformity of bone ends, *Grade 4* large osteophytes, marked narrowing of the joint space, severe sclerosis, and definite deformity of bone ends. *Lumbar spine*: *Grade 1* Minimal osteophytosis only, *Grade 2* definite osteophytosis with some sclerosis of the anterior part of the vertebral plates, *Grade 3* marked osteophytosis and sclerosis of the vertebral plates with slight narrowing of the disk space, *Grade 4* large osteophytes, marked sclerosis of the vertebral plates, and marked narrowing of the disk space

(RP); bodily pain (BP); vitality (VT); social functioning (SF); mental health (MH); role emotional (RE). The SF-8 provides two summary scores for physical and mental health [physical component summary (PCS) and mental component summary (MCS)]. The EQ-5D questionnaire [16] translated into Japanese was also used [22]. This five-dimensional healthcare classification includes questions on the status of morbidity, self-care, usual activities, pain/discomfort, and anxiety/depression. Participants were asked to indicate current health status by checking off the most appropriate of three statements on each of five QOL dimensions. Each statement represents an increasing degree of severity. These results were coded and converted to a score of utility using the tables of values. For disease-specific scales, the WOMAC (version LK 3.0) [17, 18], a 24-item OA-specific index, was utilized. The WOMAC consists of three domains: pain; stiffness; physical function. Domain scores range from 0 to 20 for pain, 0 to 8 for stiffness, and 0 to 68 for physical function. Japanese versions of the WOMAC have been validated [23].

Statistical analysis

We performed a non-paired Student's *t* test to examine differences between subjects with and without knee pain and low back pain. The impact of knee pain and low back pain on QOL was analyzed by multiple regression analysis after adjusting for age and BMI. We also examined the association of KL grade at the knee with the magnitude of QOL loss in subjects with knee pain using the Tukey honestly significant difference (HSD) test. If a subject showed pain in both knees, the more severe KL grade was designated as that of the subject. The Tukey HSD test was also used to examine the association of the presence of VFx and lumbar spondylosis with the magnitude of QOL loss in subjects with low back pain. For the lumbar spine, the most severe KL grade among all intervertebral spaces was designated as that of the subject. Data analyses were performed using SAS ver. 9.0 software (SAS Institute, Cary, NC).

Results

Characteristics of the 1,369 women ≥40 years old enrolled in the ROAD study are shown in Table 1. The prevalence of knee pain was higher than that of low back pain, while the prevalence of knee OA and lumbar spondylosis was similar and substantially higher than that of VFx.

Table 2 shows the mean scores for all QOL domains in the SF-8 and EQ-5D utility score according to the presence of knee pain and low back pain. We further examined the independent association of knee pain and low back pain with QOL using multiple regression analysis after

Table 1 Characteristics of the participants

Clinical/demographic/QOL characteristics of study cohort	Values
n	1,369
Age (years)	68.4 ± 11.1
Height (cm)	150.0 ± 6.9
Weight (kg)	51.4 ± 9.0
BMI (kg/m^2)	22.8 ± 3.7
Knee pain (%)	27.9
Low back pain (%)	17.3
VFx (%)	7.7
Knee OA (%)	60.2
Lumbar spondylosis (%)	61.3
SF-8 score	
GH	49.5 ± 5.8
PF	49.5 ± 6.3
RP	49.8 ± 6.5
BP	49.1 ± 9.6
VT	49.3 ± 5.9
SF	51.9 ± 6.2
MH	53.3 ± 6.4
RE	51.4 ± 5.7
PCS	46.8 ± 7.0
MCS	52.5 ± 6.1
EQ-5D score	0.90 ± 0.15
WOMAC index	
Pain (0–20)	1.50 ± 2.57
Stiffness (0–8)	0.77 ± 1.33
Function (0–68)	4.49 ± 8.37

Unless indicated otherwise, values represent the mean ± standard deviation (SD)

QOL Quality of life,*BMI* body mass index, *VFx* vertebral fracture, *OA* osteoarthritis, *SF-8* Medical Outcomes Study Short Form-8 health survey, *GH* general health, *PF* physical function, *RP* role physical, *BP* bodily pain, *VT* vitality, *SF* social function, *MH* mental health, *RE* role emotional, *PCS* physical component summary, *MCS* mental component summary, *EQ-5D* EuroQOL questionnaire, *WOMAC* the Western Ontario and McMaster Universities Osteoarthritis Index

adjustment for age and BMI. Knee pain was significantly associated with lower QOL scores in all domains of the SF-8, with the exception of MH, RE, MCS, and also with lower EQ-5D utility scores. Low back pain was significantly associated with lower QOL scores in almost all domains of the SF-8, except for MCS, and with lower EQ-5D utility scores. The impact of low back pain was greater than that of knee pain in almost all QOL domains.

Scores of the SF-8, EQ-5D, and WOMAC by KL grade of knee in women with knee pain are shown in Table 3. The Tukey HSD test revealed that compared with women with KL = 0/1, PCS in the SF-8 and pain in the WOMAC were significantly lower in women with KL = 3 knee OA, while PF, RP, BP, and PCS in the SF-8 and all domains of the WOMAC were significantly lower in women with KL = 4 knee OA. After adjusting for age and BMI, PCS in the SF-8 and pain and physical function in the WOMAC were also significantly lower in women with KL = 4 knee OA compared with those with KL = 0/1.

Table 4 shows the association of KL grade for the lumbar spine and presence of VFx with QOL in subjects with low back pain. In women with low back pain, no associations were seen between KL grade and any of the domains of the SF-8 or EQ-5D utility scores, while PF, RP, RE, and PCS were significantly lower in subjects with VFx than in those without VFx.

To compare the magnitude of impact on PCS between knee pain graded as KL = 4 knee OA and low back pain with vertebral fracture, we then used multiple regression analysis after adjusting for age and BMI. The impact of knee pain graded as KL = 4 knee OA on PCS was larger than that of low back pain with VFx (beta: −0.11 and −0.09, $p < 0.0001$, respectively).

Discussion

Few previous studies have examined the associations of knee pain with QOL [4], and there have been no studies published to date on the impact of knee pain and low back pain on QOL in women. The results of our study reveal that among our study cohort of 1,369 Japanese women ≥40 years of age, knee pain and low back pain were significantly associated with lower QOL scores. The multiple regression analysis showed that the impact of knee pain on QOL was weaker than that of low back pain; however, knee pain with severe knee OA had a strong, negative impact on QOL that was greater than that of low back pain with VFx. In fact, the severity of knee OA was significantly associated with the magnitude of QOL loss in subjects with knee pain. In other words, the Tukey HSD test after adjustment for age and BMI showed that in subjects with KL = 4 knee OA, PCS in the SF-8 was significantly lower and pain and physical function in the WOMAC were both significantly higher, while QOL scores of subjects with KL = 2 knee OA were similar to those of subjects with KL = 0/1. These results indicate not only that the prevalence of knee pain is higher but also that the magnitude of knee pain may be more severe in subjects with severe knee OA, whereas the magnitude of knee pain may be similar in subjects with moderate knee OA and in those without knee OA. However, the two features of knee OA, joint space narrowing and osteophytosis, cannot be assessed separately using the KL grade, so we were unable to clarify the independent effects of these two features to the association

Table 2 Scores for QOL in participants with and without knee pain and low back pain and associations with knee and low back pain by multiple regression analysis after adjusting for age, BMI, knee pain, and low back pain

QOL assessment domain	Knee pain			Low back pain		
	No	Yes	Adjusted beta[a]	No	Yes	Adjusted beta[a]
SF-8						
GH	49.9 ± 5.8	48.8 ± 5.8[b]	−0.043[c]	50.1 ± 5.7	47.1 ± 5.5[b]	−0.152[c]
PF	50.1 ± 6.0	47.9 ± 6.8[b]	−0.064[c]	50.2 ± 5.9	46.0 ± 6.9[b]	−0.180[c]
RP	50.4 ± 6.3	48.4 ± 6.9[b]	−0.058[c]	50.6 ± 6.1	47.3 ± 7.5[b]	−0.182[c]
BP	50.4 ± 9.4	45.6 ± 9.2[b]	−0.163[c]	50.3 ± 9.5	43.3 ± 7.7[b]	−0.223[c]
VT	49.7 ± 5.9	48.4 ± 5.8[b]	−0.059[c]	49.7 ± 5.9	47.2 ± 5.0[b]	−0.134[c]
SF	52.4 ± 5.6	50.8 ± 7.3	−0.077[c]	52.4 ± 5.7	49.8 ± 8.0[b]	−0.111[c]
MH	53.6 ± 6.1	52.7 ± 6.8	−0.039	53.7 ± 6.2	51.4 ± 6.9[b]	−0.128[c]
RE	51.8 ± 5.4	50.8 ± 6.4	−0.038	51.9 ± 5.3	49.4 ± 7.1[b]	−0.131[c]
PCS	47.7 ± 6.9	44.5 ± 7.0[b]	−0.113[c]	47.8 ± 6.7	42.4 ± 7.0[b]	−0.218[c]
MCS	52.6 ± 5.9	52.6 ± 6.7	−0.004	52.7 ± 5.9	51.9 ± 7.3	−0.0052
EQ-5D	0.92 ± 0.14	0.85 ± 0.17[b]	−0.127[c]	0.91 ± 0.14	0.82 ± 0.17[b]	−0.150[c]

[a] Adjusted beta values are shown using multiple regression analysis after adjusting for age, BMI, knee pain and low back pain

[b] $p < 0.05$ vs. subjects without the corresponding pain by non-paired t test

[c] $p < 0.05$

Table 3 Scores for SF-8, EQ-5D, and WOMAC by Kellgren–Lawrence (KL) grade in participants with knee pain

Variables	KL 0/1	KL 2	KL 3	KL 4
Prevalence (%)	26.8	37.5	22.8	12.9
SF-8				
GH	49.3 ± 5.9	49.1 ± 5.7	48.5 ± 6.3	47.2 ± 5.3
PF	49.3 ± 6.8	48.3 ± 6.1	47.2 ± 7.6	45.0 ± 6.3[a]
RP	49.8 ± 6.4	48.4 ± 6.4	48.1 ± 7.8	46.1 ± 7.3[a]
BP	46.7 ± 8.9	46.9 ± 9.2	44.2 ± 9.2	42.0 ± 8.7[a]
VT	49.2 ± 6.0	49.0 ± 5.5	47.2 ± 6.2	46.8 ± 4.9
SF	51.6 ± 6.8	50.4 ± 7.2	50.5 ± 8.0	50.8 ± 7.3
MH	52.6 ± 7.6	52.5 ± 6.5	52.8 ± 6.8	53.6 ± 6.2
RE	51.4 ± 6.5	50.6 ± 5.9	50.6 ± 7.0	50.3 ± 6.7
PCS	46.1 ± 6.5	45.4 ± 6.4	43.5 ± 7.9[a]	40.6 ± 6.1[a,b]
MCS	52.5 ± 7.2	52.0 ± 6.1	52.7 ± 7.2	54.2 ± 6.3
EQ-5D	0.89 ± 0.15	0.84 ± 0.19	0.84 ± 0.16	0.81 ± 0.18[a]
WOMAC				
Pain	1.67 ± 2.72	2.33 ± 2.99	2.80 ± 2.76[a]	4.38 ± 3.29[a,b]
Stiffness	0.96 ± 1.59	1.14 ± 1.61	1.34 ± 1.50	1.88 ± 2.20[a]
Function	4.58 ± 9.38	6.95 ± 9.80	8.05 ± 9.56	14.94 ± 12.46[a,b]

Except where indicated otherwise, values represent the mean ± SD

[a] $p < 0.05$ vs. KL 0/1 in the corresponding group by the Tukey HSD test

[b] $p < 0.05$ vs. KL 0/1 in the corresponding group by the Tukey HSD test after adjustment for age and BMI

of knee pain with QOL. Furthermore, radiographic joint space narrowing represents not only joint cartilage destruction but also meniscal loss or extrusion. In addition, knee pain may arise from a variety of structures other than joint cartilage, including menisci, synovium, ligaments, bursae, bone, and bone marrow [24–28]. Comprehensive mechanistic studies of knee pain taking various tissues in and around the knee joint into consideration are thus needed to elucidate the relationships between radiographic OA and QOL.

The results of our previous study showed that lumbar spondylosis is weakly associated with low back pain. In the

Table 4 Scores for SF-8 and EQ-5D by KL grade and VFx in subjects with low back pain

Variables	Lumbar spondylosis				VFx	
	KL 0/1	KL 2	KL 3	KL 4	No	Yes
Prevalence (%)	28.3	12.9	26.6	32.2	10.7	89.3
SF-8						
GH	48.1 ± 5.6	47.1 ± 5.7	46.4 ± 5.7	46.9 ± 5.1	47.2 ± 5.5	46.1 ± 5.4
PF	46.8 ± 7.4	45.9 ± 6.7	44.7 ± 6.7	46.3 ± 6.6	46.2 ± 6.9	43.9 ± 6.3[a]
RP	47.2 ± 7.4	47.1 ± 6.9	44.7 ± 8.2	46.7 ± 7.2	46.7 ± 7.4	43.4 ± 7.6[a]
BP	43.8 ± 8.0	44.1 ± 8.3	43.4 ± 7.9	42.6 ± 7.2	43.6 ± 7.7	41.1 ± 7.4
VT	48.3 ± 5.3	45.6 ± 6.7	47.3 ± 5.5	46.9 ± 5.0	47.3 ± 5.6	46.3 ± 3.9
SF	51.4 ± 6.6	50.8 ± 6.5	47.8 ± 9.8	49.7 ± 7.9	50.0 ± 7.9	48.3 ± 8.7
MH	52.8 ± 6.0	52.0 ± 7.4	50.0 ± 7.5	51.2 ± 6.8	51.5 ± 6.9	49.8 ± 7.0
RE	50.7 ± 5.9	51.2 ± 5.2	47.8 ± 8.8	49.0 ± 6.7	49.7 ± 7.0	46.9 ± 7.1[a]
PCS	42.9 ± 7.7	42.3 ± 7.2	41.8 ± 7.0	42.4 ± 6.3	42.6 ± 7.0	40.2 ± 6.2[a]
MCS	53.5 ± 6.0	52.8 ± 6.7	50.3 ± 8.6	51.5 ± 7.1	52.0 ± 7.3	50.6 ± 6.8
EQ-5D	0.86 ± 0.15	0.87 ± 0.18	0.77 ± 0.18[a]	0.81 ± 0.17	0.83 ± 0.17	0.80 ± 0.21

Except where indicated otherwise, values represent the mean score ± SD

[a] $p < 0.05$ vs. KL 0/1 in the corresponding group by the Tukey HSD test

present study, we found that low back pain was strongly associated with lower QOL scores, while the severity of lumbar spondylosis was not significantly associated with the magnitude of QOL loss in women with low back pain. These results may be partly explained by the weak association between lumbar spondylosis and low back pain, as reported by us and other researchers [1, 29, 30]. KL grade encompasses assessments of both osteophytosis and disk space narrowing, but not of narrowing of the spinal canal, spondylolisthesis, or scoliosis, all of which are associated with low back pain. In addition, low back pain arises from a number of disorders other than disc space narrowing, such as nociceptive stimuli, inflammation, muscle weakness, and abnormal load on muscles, ligaments, or capsular tissues [31]. Indeed, disc degeneration was detected by magnetic resonance imaging (MRI) at at least one lumbar level in all but one asymptomatic volunteer in a 60- to 80-year-old age group [32]. Pain is also influenced by psychological status, such as depression, since significant associations between low back pain and depression have been confirmed in many longitudinal studies [33, 34]. In terms of VFx, previous studies have shown strong effects of clinical VFx on QOL in clinical studies [35, 36], and associations of subclinical vertebral deformity with QOL were found in women in a population-based study [37]. The results of our also show that VFx was significantly associated with the magnitude of QOL loss as measured by the PF, RP, RE, and PCS of the SF-8 in subjects with low back pain, indicating that low back pain with VFx has a strong impact on QOL in women.

Knee pain and low back pain were not significantly associated with lower scores for the MCS of the SF-8 in this study. MCS questions within the SF-8 include generic questions on energy levels, feelings of being "downhearted and blue", and interference with daily activities as a result of emotional problems. As such, this summary score is less sensitive to the presence of mental health issues than disease-specific scales such as the Kessler psychological distress scale [38]. In fact, although in one study psychological distress was significantly more frequent in individuals with pain than in those without [39], the MCS score did not differ significantly between these two groups [40]. Whether the MCS is not associated with knee pain and low back pain is thus unclear. A further complication is that previous research has shown that chronic pain patients who accept their diagnosis display lower levels of pain and affective distress than those who are uncertain [41, 42], which may be one reason why in our study MCS was not associated with pain. The ROAD study is a longitudinal survey, and analysis of its data over time may elucidate the association of QOL measured by MCS and pain.

This study has several limitations. First, it was a large-scaled population-based study, but the baseline data were cross-sectional, so causal relationships could not be determined. The ROAD study is a longitudinal survey that will eventually shed light on the causal relationships. Second, we only used a semi-quantitative method to assess VFx. In addition, the KL system was used for knee OA and lumbar spondylosis. The KL system is the most conventional grading system to detect the radiographic severity of knee OA, but joint space narrowing and osteophyte formation cannot be assessed separately in this categorical system. In addition, since the KL system emphasizes osteophytosis, the handling of data on lumbar spondylosis

with disc space narrowing but no osteophytosis is unclear. In addition, in terms of the lumbar spine, we did not include lumbar spinal canal stenosis (LSCS), scoliosis, spondylolisthesis, or narrowing of the nerve canal in our analysis, although these changes are also associated with QOL. To determine the associations of these changes of the lumbar spine and knee with QOL, we are currently developing a computer-aided diagnostic program to enable automatic measurement of the major features of VFx, disc space narrowing, osteophytosis, LSCS, scoliosis, spondylosis, and narrowing of the nerve canal in the lumbar spine, and of joint space narrowing and osteophytosis at the knee on plain radiographs [43]. Third, we did not include the onset of VFx in the analysis, although the severity of low back pain often appears to be associated with the interval from the onset of VFx. With respect to clinical fractures, we examined the history of fracture, including vertebral fracture, in the ROAD study by self-report, and no clinical vertebral fractures occurred within 1 month prior to baseline examination. However, we could not compare radiographs of the lumbar spine at baseline examination with those before the examination as the subjects had not undergone radiography of the lumbar spine prior to that examination. We were therefore unable to assess the incidence of subclinical fracture within the month prior to the baseline examination. Both clinical and subclinical vertebral fractures are associated with lower QOL in women [44], but the association between the severity of low back pain and the interval from onset of subclinical VFx may be weaker than that for clinical VFx; consequently, the absence of data on the incidence of subclinical VFx may not strongly affect the present results.

In conclusion, the results of our cross-sectional study using a large-scale population (1,369 Japanese women ≥40 years of age) from the ROAD study reveal that knee pain and low back pain were significantly associated with the QOL of these women. In women with knee pain, KL = 4 knee OA was strongly associated with QOL loss. In women with low back pain, no significant associations were seen between KL grade and QOL, while VFx may have some associations with QOL loss. The impact of knee pain with KL = 4 knee OA for PCS was larger than that of low back pain with VFx. Future studies, along with the continued longitudinal survey in the ROAD study, will elucidate the environmental and genetic backgrounds of knee pain and low back pain.

Acknowledgments This study was supported by a Grant-in-Aid for Scientific Research (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, and H20-Choujyu-009 from the Ministry of Health, Labor and Welfare, Research Aid from the Japanese Orthopaedic Association, and Grant No. 166 from the Japan Orthopaedics and Traumatology Foundation. The authors wish to thank Dr. Anamizu and members of the Department of Orthopaedics, Mr. Kutsuma and other members of the Department of Radiology at Tokyo Metropolitan Geriatric Medical Center, Ms. Tomoko Takijiri and other members of the Public Office in Hidakagawa Town, and Ms. Tamako Tsutsumi, Ms. Kanami Maeda, and other members of the Public Office in Taiji Town for their assistance in locating and scheduling participants for examinations.

Conflict of interest statement None.

References

1. Muraki S, Oka H, Mabuchi A, Akune T, En-yo Y, Yoshida M, et al. Prevalence of radiographic lumbar spondylosis and its association with low back pain in the elderly of population-based cohorts: the ROAD study. Ann Rheum Dis. 2009;68:1401–6.
2. Dawson J, Linsell L, Zondervan K, Rose P, Carr A, Randall T, et al. Impact of persistent hip or knee pain on overall health status in elderly people: a longitudinal population study. Arthritis Rheum. 2005;53:368–74.
3. Muraki S, Oka H, Akune T, Mabuchi A, En-yo Y, Yoshida M, et al. Prevalence of radiographic knee osteoarthritis and its association with knee pain in the elderly of Japanese population-based cohorts: the ROAD study. Osteoarthritis Cartil. 2009;17:1137–43.
4. Hopman-Rock M, Kraaimaat FW, Bijlsma JW. Quality of life in elderly subjects with pain in the hip or knee. Qual Life Res. 1997;6:67–76.
5. Horng YS, Hwang YH, Wu HC, Liang HW, Mhe YJ, Twu FC, et al. Predicting health-related quality of life in patients with low back pain. Spine. 2005;30(5):551–5.
6. Kovacs FM, Abraira V, Zamora J, Teresa Gil del Real M, Llobera J, Fernandez C, et al. Correlation between pain, disability, and quality of life in patients with common low back pain. Spine. 2004;29(2):206–10.
7. Leidig-Bruckner G, Minne HW, Schlaich C, Wagner G, Scheidt-Nave C, Bruckner T, et al. Clinical grading of spinal osteoporosis: quality of life components and spinal deformity in women with chronic low back pain and women with vertebral osteoporosis. J Bone Miner Res. 1997;12(4):663–75.
8. Silverman SL, Piziak VK, Chen P, Misurski DA, Wagman RB. Relationship of health related quality of life to prevalent and new or worsening back pain in postmenopausal women with osteoporosis. J Rheumatol. 2005;32(12):2405–9.
9. Hardt J, Jacobsen C, Goldberg J, Nickel R, Buchwald D. Prevalence of chronic pain in a representative sample in the United States. Pain Med. 2008;9(7):803–12.
10. Bagge E, Bjelle A, Eden S, Svanborg A. Osteoarthritis in the elderly: clinical and radiographic findings in 79 and 85 year olds. Ann Rheum Dis. 1991;50:535–9.
11. Dekker J, Boot B, van der Woude LHV, Bijlsma JWJ. Pain and disability in osteoarthritis: a review of biobehavioral mechanisms. J Behav Med. 1992;15:189–214.
12. Ross PD. Clinical consequences of vertebral fractures. Am J Med. 1997;103:30S–42S.
13. Yoshimura N, Muraki S, Oka H, Mabuch A, En-yo Y, Yoshida M, et al. Prevalence of knee osteoarthritis, lumbar spondylosis and osteoporosis in Japanese men and women: the research on osteoarthritis/osteoporosis against disability (ROAD). J Bone Miner Metab. 2009;27:620–8.
14. Yoshimura N, Muraki S, Oka H, Kawaguchi H, Nakamura K. Cohort profile: Research on Osteoarthritis/Osteoporosis Against