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Association of radiographic and symptomatic knee osteoarthritis with health-related quality of life in a population-based cohort study in Japan: the ROAD study

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SUMMARY

Objective: Knee osteoarthritis (OA) is a major public health issue causing chronic pain and disability. However, there is little information on the impact of this disease on quality of life (QOL) in Japanese men and women. The objective of the present study was to clarify the impact of radiographic and symptomatic knee OA on QOL in Japan.

Methods: This study examined the association of radiographic and symptomatic knee OA with QOL parameters such as the Medical Outcomes Study Short Form-8 (SF-8), EuroQOL (EQ-5D) and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). Radiographic knee OA was defined according to Kellgren/Lawrence (KL) grades, and symptomatic knee OA was defined as KL = 3 or 4 with knee pain. We also examined the independent association of symptomatic knee OA and grip strength with QOL.

Results: From the 3040 participants in the Research on Osteoarthritis Against Disability (ROAD) study, the present study analyzed 2126 subjects older than 40 years who completed the questionnaires (767 men and 1359 women; mean age, 68.9 ± 10.9 years). Subjects with KL = 3 or 4 had significantly lower physical QOL as measured by the physical component summary (PCS) score of the SF-8 and pain domains of the WOMAC, whereas mental QOL, as measured by the mental component summary (MCS) score of the SF-8, was higher in subjects with KL = 3 or 4 than KL = 0 or 1. Symptomatic knee OA was significantly more likely than radiographic knee OA without pain to be associated with physical QOL loss as measured by the PCS score and physical domains of the WOMAC. Symptomatic knee OA and grip strength were independently associated with physical QOL.

Conclusion: This cross-sectional study revealed that subjects with symptomatic knee OA had significantly lower physical QOL than subjects without it.

Introduction

Knee osteoarthritis (OA) is a major public health issue that causes chronic pain and disability[1–3]. The prevalence of radiographic knee OA is high in Japan[4], with 25,300,000 subjects aged 40 years and older estimated to experience radiographic knee OA[5]. 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[6].

Quality of life (QOL) measurements in patients with chronic diseases are useful tools for estimating disease impact; these QOL scales may be generic or disease specific. Among the generic scales, the EuroQOL (EQ-5D) has been widely used to measure health-related QOL (HRQOL) in patients with OA[7,8], and several studies have used the Medical Outcomes Study Short Form-36 (SF-36) in

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Caucasian patients with OA[9–11]. However, almost all of these studies include only patients with knee OA, and there are few population-based studies regarding knee OA and QOL[11]. A previous population-based study in Caucasians showed that arthritis has a major impact on the HRQOL measured by the SF-36 in a community setting[11], although arthritis was examined by self-reported means and not by radiographs. In terms of disease-specific scales for knee OA, the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) has been used for Caucasians[12] and Asians[13,14], although these reports were not population-based studies. Furthermore, there is little information on the impact of knee OA with QOL in Japan, although a population survey suggests that the disease pattern differs among races[15–17]. In fact, the prevalence of knee OA in Japan[4] was much higher than that of previous epidemiologic studies in elderly Caucasians[16,18]. Furthermore, in terms of risk factors, studies in Caucasians have suggested that occupational activities that include kneeling and squatting were associated with knee OA[19], whereas these activities were not associated with Kellgren/Lawrence (KL) grades ≥ 2 OA in our previous study in Japan[20]. Therefore, the impact of knee OA on QOL also appears to differ in different populations. It would thus be of interest to clarify the impact of OA on QOL in a Japanese population.

The principal clinical symptom of knee OA is pain[21], but the correlation with the radiographic severity of knee OA is controversial[4,22–24]. Thus it would be interesting to determine whether the impact of radiographic knee OA on QOL differs according to the severity of OA. Furthermore, pain is strongly associated with QOL, so it would be of interest to clarify the impact of symptomatic OA as well as radiographic knee OA on QOL.

Gender differences have also been observed in knee OA. The prevalence of knee OA is higher in women than men[4], and the association of knee pain with knee OA also differs by gender[4]. Thus, the impact of these diseases on QOL may also differ between genders. However, to the best of our knowledge, there are no population-based studies that assess the association of knee OA with QOL in men and women separately.

Grip strength is a useful marker of muscle function and sarcopenia[25]. There is growing evidence that reduced grip strength is associated with adverse outcomes including morbidity[26], disability[27], falls[27], higher fracture rates[28], increased length of hospital stay[29], and mortality[27]. A previous study also showed that grip strength is related to total muscle strength[30]. Furthermore, 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]. Previous reports have shown that low muscle mass was also associated with reduced QOL[32,33]; thus, the association of knee OA with QOL may be influenced by grip strength, but again, no studies have examined the association of knee OA and grip strength with QOL simultaneously in the same population.

The first objective of this study is to clarify the association of radiographic severity of knee OA with QOL among Japanese men and women using the large-scale, population-based cohort study called the Research on Osteoarthritis Against Disability (ROAD). Because pain is strongly associated with QOL, we also examined the association of symptomatic knee OA with QOL. Finally, we analyzed the independent associations of knee OA and grip strength with QOL.

Subjects and methods

Subjects

The ROAD study is a nationwide prospective study designed to establish epidemiologic indexes for evaluation of clinical evidence for the development of a disease-modifying treatment for bone and joint diseases (with OA and osteoporosis as the representative bone and joint diseases). It consists of population-based cohorts in several communities in Japan. A detailed profile of the ROAD study has been described in detail elsewhere[4,5,34]; a brief summary is provided here. To date, we have completed creation of a baseline database including clinical and genetic information for 3040 inhabitants (1061 men and 1979 women) ranging in age from 23 to 95 years (mean, 70.6 years), who were recruited from resident registration listings in three communities: an urban region in Itabashi, Tokyo, a mountainous region in Hidakagawa, Wakayama, and a seacoast 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. Anthropometric measurements included height and weight, and body mass index (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 characterize maximum muscle strength. Among 2995 subjects aged 40 years or older in the ROAD study, 2243 (74.9%), 2245 (75.0%) and 2222 (74.2%) subjects completed the SF-8, the EQ-5D and the WOMAC, respectively, and 2126 (71.0%) subjects completed all three questionnaires. The present study analyzed 2126 subjects (767 men and 1359 women) aged 40 years (mean, 68.9 $\pm$ 10.9 years) or older who had completed the SF-8, the EQ-5D, and the WOMAC.

Radiographic assessment

All participants had radiographic examination of both knees using anterior–posterior and lateral views with weight-bearing and foot map positioning. Knee radiographs were read without knowledge of participant clinical status by a single well-experienced orthopaedist (SM) using the KL radiographic atlas for overall knee radiographic grades[35]. In KL grade, radiographs are scored as grade 0 through 4, with higher grades being associated with more severe OA. The higher KL grade in both knees was designated as that of the participant. Symptomatic knee OA was defined as: (1) a subject reporting knee pain lasting at least 1 month with pain having last occurred within the current or previous year; and (2) KL = 3 or 4 OA in the painful knee. To evaluate the intra-observer variability of 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 orthopaedic surgeons (SM & HO) using the same atlas for inter-observer variability. The evaluated intra- and inter-observer variabilities were confirmed by kappa analysis to be sufficient for assessment (0.86 and 0.80, respectively).

Instruments

The SF-8 generates a health profile consisting of eight scales and two summary measures describing HRQOL. The SF-8 is an alternate form to the SF-36, which is the most widely used patient-based health status survey, translated into more than 40 languages; the Japanese version of the SF-36 has been well validated[36]. The SF-8 uses a single question to measure each of the eight SF-36 domains. In the SF-8, each of the eight items assesses a different dimension of health: General Health (GH), Physical Functioning (PF), Role Physical (RP), Bodily Pain (BP), Vitality (VT), Social Functioning (SF), Mental Health (MH) and Role Emotional (RE). The SF-8 was scored by assigning the mean SF-36 scale score from the 2002 general Japanese population to each response category of the SF-8 measuring the same concept, and then weighting each SF-8 item to

compute aggregate physical component summary (PCS) and mental component summary (MCS) scores. The SF-8 may be scored using a published algorithm for Japanese versions of the SF-8, which has been well validated[37]. The EQ-5D self-report questionnaire measures five domains of HRQOL, including mobility, self-care, usual activities, pain/discomfort, and anxiety/depression[38]. Each of the five domains is assessed by a single question with three response levels (no problem, some problems, and extreme problems), so the EQ-5D defines a total of 243 health states. These results were coded and converted to a score of utility using the tables of values[39]. The EQ-5D scoring algorithm was first developed using time trade off-based preference scores for a sample of these health states from a representative sample of the UK general population[38]; the Japanese version of the EQ-5D has been validated[39]. This EQ-5D algorithm is used worldwide and generates scores ranging from −0.111 to 1.000, with negative scores representing health states worse than being dead, 0 representing being dead, and 1.00 representing a state of full health. 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 five-point Likert scale or a 100-mm visual analogue scale[12,40]. 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[41].

Table I
Characteristics of participants

	Overall	Men	Women	*P*-Values
Number of subjects	2126	767	1359	
Age, years	68.9 ± 10.9	69.7 ± 10.5	68.4 ± 11.1	0.006
Height, cm	154.6 ± 9.2	162.8 ± 6.7	150.0 ± 6.9	<0.0001
Weight, kg	55.0 ± 10.9	61.5 ± 10.8	51.4 ± 9.0	<0.0001
BMI, kg/m^2	22.9 ± 3.6	23.1 ± 3.4	22.8 ± 3.7	0.03
Grip strength, kg	25.5 ± 9.3	33.2 ± 8.9	21.2 ± 6.3	<0.0001
Radiographic knee OA, %	17.9	11.6	21.5	<0.0001
Symptomatic knee OA, %	9.0	5.0	11.3	<0.0001
SF-8				
PCS	47.0 ± 7.0	47.4 ± 6.8	46.8 ± 7.0	0.03
MCS	52.8 ± 5.9	53.4 ± 5.3	52.5 ± 6.1	0.0009
EQ-5D	0.90 ± 0.15	0.91 ± 0.14	0.90 ± 0.15	0.03
WOMAC				
Pain (0–20)	1.37 ± 2.44	1.13 ± 2.16	1.50 ± 2.57	0.0003
Stiffness (0–8)	0.71 ± 1.25	0.63 ± 1.09	0.77 ± 1.33	0.01
Function (0–68)	4.08 ± 7.93	3.35 ± 7.06	4.49 ± 8.37	0.001

Except where otherwise indicated, values are the mean ± SD.
The differences between men and women were examined by the Student's *t* test except for the prevalence of radiographic and symptomatic knee OA.
The prevalence of radiographic and symptomatic knee OA was compared between men and women using the chi-square test.
Radiographic knee OA was defined as KL grade 3 or 4.
Symptomatic knee OA was defined as KL grade 3 or 4 with knee pain.
SF-8, Medical Outcomes Study Short Form-8.

Statistical analysis

The differences in age, height, weight, BMI, grip strength, and QOL measurements between men and women were examined by the Student's *t* test. The prevalence of radiographic and symptomatic knee OA was compared between men and women using the chi-square test. We also used the chi-square test to analyze whether subjects with one symptomatic knee were likely to have symptomatic OA in the other knee. According to KL grade[35], KL = 2 was defined as definite osteophytosis but no definite joint space narrowing, and KL = 3 and 4 included definite joint space narrowing. We thus categorized KL grade in KL = 0 or 1, KL = 2, or KL = 3 or 4, and differences among each KL grade with QOL measurements were determined using the Tukey Honestly Significant Difference (HSD) test without adjustment and after adjustment for age, BMI, and grip strength in men and women. We further classified subjects into those with symptomatic knee OA, those with KL = 3 or 4 knee OA without pain, and those without KL = 3 or 4 knee OA, and compared their association with QOL using the Tukey HSD test after adjustment for age, BMI, and grip strength. To determine the independent association of symptomatic knee OA and grip strength with QOL, we used multiple regression analysis without adjustment and after adjustment for age and BMI. Data analyses were performed using SAS version 9.0 (SAS Institute Inc., Cary, NC).

Results

The characteristics of the 2126 participants in the present study are shown in Table I. The prevalence of knee OA was significantly higher in women than men. The prevalence of bilateral and unilateral symptomatic knee OA was 2.0% and 3.0% in men, and 5.6% and 5.8% in women, respectively. Chi-square test showed that when the right knee had symptomatic knee OA, the odds ratio for the left knee to have symptomatic knee OA was 86.3 and 59.7 in men and women, respectively. The PCS and MCS of the SF-8 and the EQ-5D utility scores were significantly higher and the all domains of WOMAC were significantly lower in men than women, indicating that the QOL scores were higher in men than women.

The scores for PCS and MCS in the SF-8, the EQ-5D utility scores, and all domains in the WOMAC by KL grade of knee OA in men and women are shown in Tables II and III. The associations of age, BMI, and grip strength with each QOL parameter were significant in men and women by linear regression analysis ($P < 0.01$), except for the association of age with the MCS of the SF-8. Thus, we used the Tukey HSD test after adjustment for age, BMI, and grip strength to determine the association of radiographic severity of knee OA with QOL. Men and women with KL = 3 or 4 had significantly lower QOL measured by PCS of the SF-8 and pain domains of the WOMAC than those with KL = 0 or 1 as well as KL = 2. In addition, the MCS scores were higher in men and women with KL = 3 or 4 compared with KL = 0 or 1. The EQ-5D utility scores were not significantly associated with the KL grade of the knee after adjustment for age, BMI and grip strength.

Next, to determine impact of symptoms of radiographic knee OA with QOL, we classified subjects into those with symptomatic knee OA, defined as KL = 3 or 4 with knee pain, those with KL = 3 or 4 without pain, and those without KL = 3 or 4 and compared the impact of each type of OA on QOL using the Tukey HSD test after adjustment for age, BMI, and grip strength (Fig. 1). In men and women, PCS of the SF-8 and physical function domain of the WOMAC were significantly lower in subjects with symptomatic knee OA compared with those without KL = 3 or 4 knee OA (men: difference in mean −5.9, 95% CI −8.6 to −3.2 and difference in mean 4.9, 95% CI 2.2 to 7.6, respectively; women: difference in mean −4.3, 95% CI −5.7 to −2.9 and difference in mean 3.9, 95% CI 2.3 to 5.5, respectively) as well as KL = 3 or 4 knee OA without pain (men: difference in mean −6.3, 95% CI −9.7 to −3.0 and difference in mean 5.7, 95% CI 2.3 to 9.1, respectively; women: difference in mean −4.9, 95% CI −6.7 to −3.1 and difference in mean 3.9, 95% CI 1.8 to 5.9, respectively), whereas among those with KL = 3 or 4 knee OA without pain and no KL = 3 or 4 knee OA, there were no significant differences in PCS of the SF-8 and physical function domain of the WOMAC. In women, MCS of the SF-8 was significantly higher in subjects with symptomatic knee OA compared with those without KL = 3 or 4 knee OA (difference in mean 2.6, 95% CI 1.3 to 4.0) as well as KL = 3 or 4 knee OA without pain (difference in mean 2.3, 95% CI 0.6 to 4.0). The EQ-5D utility score was

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.

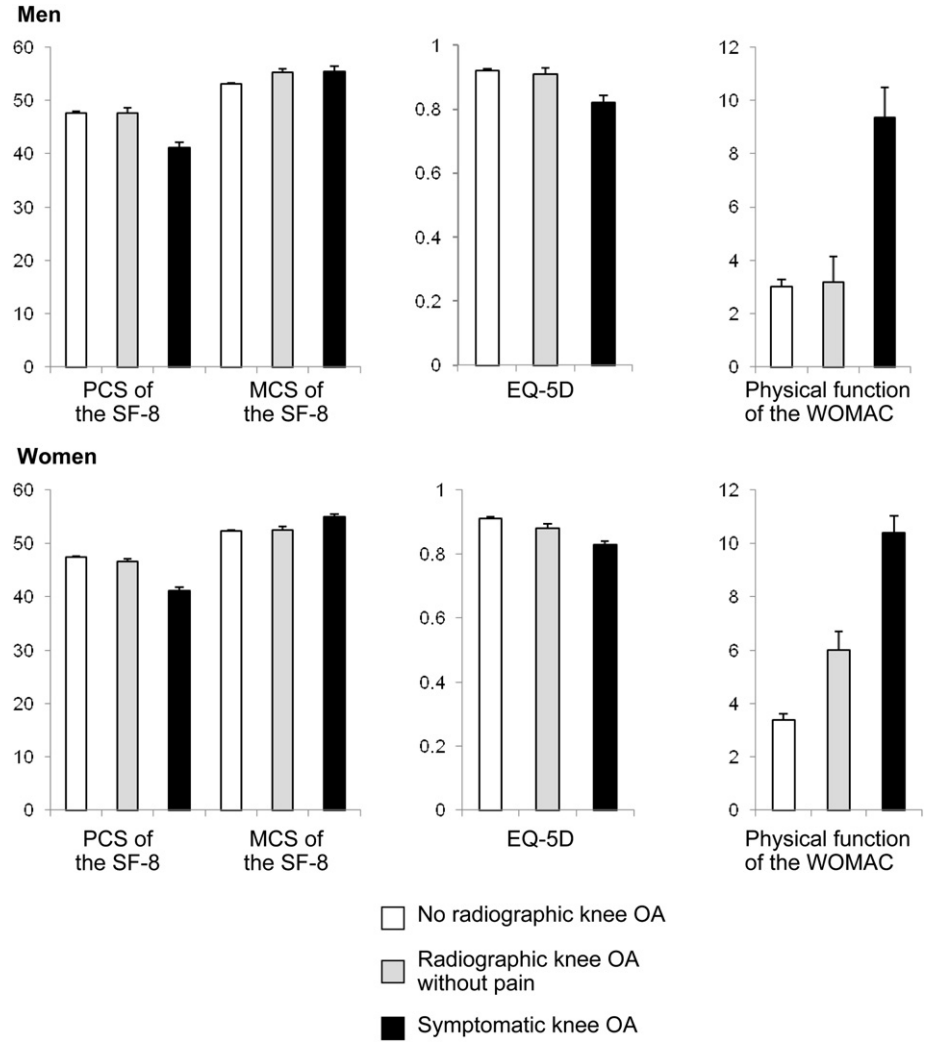

Fig. 1. Mean scores and SE of the SF-8, EQ-5D, and WOMAC scales in men and women with symptomatic knee OA ($N = 38$ and 154, respectively), radiographic knee OA without pain ($N = 53$ and 140, respectively), and no radiographic knee OA ($N = 676$ and 1065, respectively). Symptomatic knee OA was defined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

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