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ORIGINAL ARTICLE

Capacity of endogenous sex steroids to predict bone loss in Japanese men: 10-year follow-up of the Taiji Cohort Study

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Abstract This prospective cohort study aimed to evaluate the capacity of endogenous sex steroids to predict male osteoporosis (OP) among community-dwelling inhabitants. Among 1,028 male residents aged 40–79 years, 50 men belonging to each age stratum (200 in total) were randomly selected from a resident registration list. In the years 1993, 1996, 2000, and 2003, bone mineral density (BMD) of the lumbar spine and proximal femur was measured by dual-energy X-ray absorptiometry. Serum total estradiol (E_2) and free testosterone (FT) were measured using samples extracted in 1993. Among the 200 participants at baseline, 153 subjects completed 10-year follow-ups. Mean values of serum E_2 and FT were 22.4 and 9.4 pg/ml, respectively. Rates of change for BMD at the lumbar spine and femoral neck were 0.8% and 0.5% during the first 3 years, 0.0% and 0.5% during 7 years, and 0.8% and –0.3% over 10 years, respectively. According to multivariate regression analysis after adjusting for age and body mass index, mean values of FT were significantly related to the rate of change of BMD at the femoral neck at 3 years (beta = 0.21; $r^2 = 0.05$; $P < 0.01$), but not at 7 or 10 years. Serum FT level could offer a useful predictor of bone loss within 3 years.

Keywords Testosterone · Estrogen · Bone loss · Male osteoporosis · Population-based cohort study

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Introduction

Osteoporosis (OP) is associated with impairment of activities of daily living (ADL) and quality of life (QOL), leading to increased morbidity and mortality in the elderly [1, 2]. As the proportion of the elderly population is rapidly increasing, an urgent need exists for the development of methods to prevent OP. The estimated number of patients with OP in Japan is about 10 million [3], and cases of hip fracture, as the most severe complication of OP and a key cause of bedridden status, are increasing annually, according to the results of a national survey [4].

Although OP is widely considered as a disorder that mainly affects women, 13% of cases of lumbar spine OP and 24% of cases of femoral neck OP involve men [3]. Up to 20% of hip fractures occur in men, and the number of men with fractures has been rising in Japan [3, 4]. In addition, several studies have shown higher mortality rates after hip fracture in men than in women [5–8], suggesting that male OP warrants urgent attention.

Estrogen is a well-known determinant of low bone mass, bone loss, and osteoporotic fracture in women [9–12]. Reports from the study of osteoporotic fracture suggest that in elderly women, undetectable levels of estradiol, which occur in about one-third of the population, are strongly associated with low bone mineral density (BMD), rapid

bone loss, and increased fracture risk [13–15]. In addition, lower androgen concentrations are reportedly weakly associated with lower BMD and rapid bone loss at some skeletal sites [13].

By contrast, less epidemiological evidence has been gathered regarding the influence of serum sex hormone levels on bone loss, OP, and osteoporotic fracture in men. Some studies of BMD in men have reported positive associations with endogenous androgen levels [16–19], but others have found no significant association [20, 21]. The influence of endogenous sex hormone concentrations on bone loss in men thus remains controversial.

In the present study, to clarify the age distribution of serum levels of endogenous sex steroids and to explore the predictive capacity of these levels for bone loss in men for the early detection of male OP, we measured baseline concentrations of endogenous sex steroids in male subjects randomly selected from a rural population in Japan and conducted follow-up for 10 years.

Materials and methods

Establishment of baseline cohort

This survey was performed in the Japanese town of Taiji. The Taiji cohort has been profiled in detail elsewhere [22–24] and so is summarized here only briefly. Taiji is located in the southern coastal area of Wakayama Prefecture. A list of all inhabitants born in 1913–1952, and therefore aged between 40 and 79 years old in 1993, was compiled based on resident registrations as of the end of 1992. A cohort of 2,261 inhabitants (1,028 men, 1,233 women) was identified, and all members of the cohort completed a self-administered, 125-item questionnaire addressing topics such as dietary habits, smoking habits, alcohol consumption, and physical exercise (whole cohort).

From the whole cohort, 50 men in each of four age groups between 40 and 79 years by decade of birth year (1913–1922, 1923–1932, 1933–1942, and 1943–1952), for a total of 200 participants, were randomly selected. BMD was measured for these 200 participants in 1993. At this time, blood samples of all participants were taken. An interviewer administered a second questionnaire to these 200 participants covering items of past medical history, including questions related to osteoporotic fractures and falls, family history, calcium intake, dietary habits, physical exercise, occupational activities, sun exposure, and, for women, additional questions about reproductive variables (baseline study).

Measurements of endogenous sex steroids

At the baseline study in 1993, blood samples were taken from all participants. After centrifugation of blood samples, sera were immediately placed in dry ice, transferred to a freezer within 24 h, and kept at –80°C until assayed. Serum levels of total estradiol (E_2) and free testosterone (FT) were measured using an immunoradiometric assay (DPC-free estradiol kit and DPC-free testosterone kit, respectively; Mitsubishi Kagaku, Tokyo, Japan). The lowest measurable levels of E_2 and FT were 10 and 0.4 pg/ml, respectively, and percent of coefficient of variation (CV%) for E2 and FT were both less than 15% (unpublished data).

BMD measurements

Baseline BMD was measured in 1993 using dual-energy X-ray absorptiometry (DXA) (QDR 1000; Hologic, Bedford, MA, USA), providing anteroposterior images of lumbar vertebrae L2–L4 and the proximal femur (femoral neck, Ward's triangle, trochanter). These measurements were repeated on the same participants after 3, 7, and 10 years (1996, 2000, and 2003).

To control for the precision of DXA, the equipment was checked at every examination in 1993, 1996, 2000, and 2003 using the same phantom, and BMD of the phantom was regulated to 1.030 ± 0.016 g/cm^2 (1.5%) during all examinations. All BMD measurements were performed by the same medical doctor (N.Y.). Intraobserver variability for DXA scans by this investigator was 0.35% using the phantom, as reported previously [25].

Annual rates of change for BMD during 3-, 7-, and 10-year observations were calculated as follows:

$$\text{Annual rate (\%/year)} = [(\text{BMD follow-up} - \text{BMD baseline})/\text{BMD baseline/follow-up years}] \times 100$$

All examinations were performed with the full consent of the participants. These studies were approved by the ethics committees of both Wakayama Medical University and the University of Tokyo.

Statistical analysis

All statistical analyses were performed using STATA statistical software (STATA, College Station, TX, USA). Differences were tested for significance using analysis of variance for comparisons among multiple groups, and Scheffe's least significant difference (LSD) test for pairs of groups. Significant items were selected, and multiple regression analysis was performed with adjustment of suitable variables.

Results

Eligible participants and baseline characteristics

Background data including physical characteristics for all male participants at baseline are shown in Table 1. Mean weight and height in their fifties, sixties, and seventies, and mean body mass index (BMI) in their seventies were significantly lower than those in their forties ($P < 0.05$).

Among the 200 male participants at baseline, 1 man in his sixties declined to undergo blood and urinary examinations for endogenous hormones. Examinations at baseline were thus performed on 199 men. The second visit, aimed at evaluating changes in BMDs over 3 years, obtained measurements for 181 of the 200 initially recruited participants (90.5%). The following reasons were given for the loss of 19 participants at the 3-year follow-up: 8 men had died, 1 man had moved, 1 man was ill, 4 men declined to participate, and 2 men were away from the area at the time of follow-up. The third visit, aimed at evaluating changes in BMDs over 7 years, evaluated 170 of the 200 initially recruited participants (85%). Loss of 30 participants at the 7-year follow-up was explained as follows: 14 men had died, 3 men had moved, 6 men were ill, 5 men declined to participate, and 2 men were away from the area at the time of follow-up. Among the 200 male participants initially recruited, 153 men participated in the fourth visit held in 2003 (76.5%). Loss of 47 participants at the 10-year follow-up was explained as follows: 33 men had died, 6 men had moved, 4 men were ill, 2 men declined to participate, and 2 men were away from the area at the time of follow-up.

Mean levels of serum concentration of sex steroids at baseline

Age distributions of mean E_2 and FT levels at the initial survey are also shown in Table 1. Because data below the measurable range were excluded from analysis, E_2 and FT data could be obtained for 178 and 198 participants, respectively. Mean serum levels of E_2 and FT were 22.4 and 9.4 pg/ml, respectively. Although no significant age-related trends were seen for E_2, a significant trend toward low values of FT was noted according to age ($P < 0.001$). In addition, mean serum FT was significantly higher for men in their forties than for men in their sixties and seventies ($P < 0.05$).

Predictive capacity of endogenous sex steroids for bone change

Initial mean values and rates of change in L2–L4 BMD over the 3-, 7-, and 10-year periods, classified by age stratum, are shown in Table 2. BMD values at L2–L4 for men had increased slightly by the 10-year follow-up in their fifties and sixties but had decreased a little in the forties and seventies. BMD values at the femoral neck over 10 years had decreased for men in their forties and fifties and had increased considerably in their seventies.

According to multivariate regression analysis using each rate of change for BMD at the lumbar spine over 3, 7, and 10 years as an objective factor and serum levels of E_2 as an explanatory factor after adjusting for age and BMI, beta values for the rate of change for BMD for the first 3, 7, and 10 years were 0.02, 0.04, and –0.02, respectively. Similarly, on multivariate regression analysis using each rate of change for BMD at the femoral neck over 3, 7, and 10 years as an objective factor and serum levels of E_2 as an explanatory factor after adjusting for age and BMI, beta values for the rate of change for BMD for the first 3, 7, and 10 years were –0.07, 0.09, and –0.01, respectively. Total E_2 values could not predict bone change at the lumbar spine or femoral neck at 3, 7, or 10 years.

Again, using the results of multivariate regression analysis to clarify associations between serum FT and

Table 1 Summary characteristics for male participants at baseline classified by age

Birth cohort	Age-group (years)	*n*	Age (years)	Height (cm)	Weight (kg)	BMI (kg/m^2)	E2 (pg/mL)		FT (pg/mL)	
			Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	*n*	Mean (SD)	*n*	Mean (SD)
1943–1952	40–49	50	44.2 (2.6)	168.8 (5.2)	69.0 (10.4)	24.2 (3.2)	46	22.1 (7.4)	50	10.9 (2.8)
1933–1942	50–59	50	54.8 (2.7)	165.6 (5.0)[a]	63.5 (9.4)[a]	23.1 (2.9)	43	22.2 (7.0)	50	9.8 (2.6)
1923–1932	60–69	50	64.6 (2.5)	163.0 (4.8)[a]	62.9 (9.6)[a]	23.6 (3.2)	46	23.1 (8.5)	49	8.8 (2.6)[a]
1913–1922	70–79	50	74.0 (2.7)	160.7 (5.4)[a,b]	57.5 (8.3)[a,b,c]	22.2 (2.8)[a]	43	22.3 (7.7)	49	8.2 (3.1)[a]
1913–1952	40–79	200	59.4 (11.4)	164.5 (5.9)	63.2 (10.2)	23.3 (3.1)	178	22.4 (7.6)	198	9.4 (2.9)

BMI body mass index, *E2* total estradiol, *FT* free testosterone, *n* number of participants, *SD* standard deviation

[a] Significantly different ($P < 0.05$) from values of participants in their forties

[b] Significantly different ($P < 0.05$) from values of participants in their fifties

[c] Significantly different ($P < 0.05$) from values of participants in their sixties

Table 2 Mean values (SD) of bone mineral density (g/cm^2) and change rate (%) at lumbar spine L2–L4 and femoral neck over 3, 7, and 10 years, classified by age and gender

Birth cohort	Age-group (years)	L2–L4								Femoral neck			
		Baseline		2nd visit (3-year follow-up)		3rd visit (7-year follow-up)		4th visit (10-year follow-up)		Baseline	2nd visit	3rd visit	4th visit
		n	BMD (g/cm^2)	*n*	Change rate (%/3 years)	*n*	Change rate (%/7 years)	*n*	Change rate (%/10 years)	BMD (g/cm^2)	Change rate (%/3 years)	Change rate (%/7 years)	Change rate (%/10 years)
1943–1952	40–49	50	1.05 (0.15)	48	0.6 (3.8)	46	−0.6 (5.1)	43	−0.2 (5.8)	0.86 (0.09)	0.3 (4.6)	−1.8 (4.8)	−1.5 (10.9)
1933–1942	50–59	50	0.98 (0.17)	47	1.0 (3.3)	46	−0.0 (6.3)	46	1.6 (8.0)	0.80 (0.13)[a]	−0.2 (4.9)	0.7 (10.0)	−3.0 (6.8)
1923–1932	60–69	50	1.04 (0.21)	49	1.3 (3.6)	47	1.4 (7.1)	41	2.3 (9.4)	0.77 (0.11)[a]	1.0 (7.0)	−0.1 (9.3)	0.3 (12.5)
1913–1922	70–79	50	0.97 (0.19)	37	0.1 (5.3)	31	−1.2 (7.9)	23	−1.5 (9.2)	0.71 (0.08)[a,b,c]	0.9 (6.3)	4.6 (10.2)[a]	6.6 (16.2)[b]
1913–1952	40–79	200	1.01 (0.18)	181	0.8 (4.0)	170	0.0 (6.6)	153	0.8 (8.1)	0.79 (0.12)	0.5 (5.7)	0.5 (8.9)	−0.3 (11.7)

SD standard deviation, *BMD* bone mineral density, *n* number of participants

[a] Significantly different ($P < 0.05$) from values of subjects in their forties

[b] Significantly different ($P < 0.05$) from values of subjects in their fifties

[c] Significantly different ($P < 0.05$) from values of subjects in their sixties

BMD changes at the lumbar spine and femoral neck, beta values of FT for the rate of change for BMD at the lumbar spine at the first 3, 7, and 10 years were 0.08, 0.08, and 0.03, respectively, and those at the femoral neck were 0.21, 0.14, and 0.06, respectively. Mean FT levels were significantly related to the rate of change for BMD at the femoral neck during the first 3 years ($R^2 = 0.05$, $P < 0.01$), but could not predict bone change at any site at 7 or 10 years.

Discussion

The present study examined endogenous hormone levels among men in Japan, measuring changes in BMD over spans of 3, 7, and 10 years. The present study clarified the age distribution of endogenous sex steroids, and a significant trend was seen toward low FT levels with age. FT tended to be significantly lower in the sixties and older when compared with levels in the forties in the present study. Our results support the findings of other reports. Orwoll et al. [26] showed that testosterone levels, particularly FT levels, for 2,623 men 65 years or older were associated with increasing age. Similar findings have been described in other cross-sectional and longitudinal studies [27–29]. Based on these results, we concluded that older men tended to show lower testosterone levels than younger men, similar to the situation with E_2 in women. Some men might display testosterone insufficiency, as seen in women with E_2 insufficiency. However, we do not yet have enough evidence regarding normal ranges in young men and thresholds for testosterone insufficiency. In addition, levels of testosterone may vary among individuals and be influenced by body composition such as adipose tissue, muscle, and bone.

In contrast to testosterone, no significant age-related trend in E_2 was found in the present study. Little information is available regarding E_2 levels in older men. Orwoll et al. [26] reported that E_2 concentrations decreased as age increased, and similar findings have been described in various reports [30–33]. However, other studies have noted stable [34–36] or rising [37] E_2 levels with increasing age. Although the reasons for these discrepancies are unclear, E_2 levels may vary among individuals and may be influenced by body composition such as adipose tissue, muscle, and bone, as well as testosterone.

Regarding the ethnic variations in serum sex steroid levels, as most previous reports have been based on studies of Caucasian men, ethnic variations in FT levels among men remain unclear. To the best of our knowledge, the Osteoporotic Fractures in Men Study (MrOS) is the only study in which a sufficient number of Asian men have participated [26]. For reasons of differences in measurement methods, direct comparison of the present results and

those from the MrOS study is inappropriate, but FT levels among Japanese men tended to be lower than those in MrOS participants, although no significant difference in E_2 levels was apparent. Orwoll et al. [26] analyzed ethnic differences in the MrOS study and stated that FT levels were lower in Asian men than in other races such as Caucasian, African-American, and Hispanic subjects, but no such differences were seen for E_2. The present results support these findings.

The present study found that serum levels of FT could offer a useful predictor of bone loss at the femoral neck within 3 years, but this effect was diluted with longer observation. Regarding the effects of testosterone on bone loss at the hip, Cauley et al. [38] reported, in an epidemiological study of 1,327 men ≥65 years old, that men in the lowest FT category experienced greater hip bone loss over 1.8 years. In addition, Ensrud et al. [39] reported that among men with weight loss, the rate of decline in total hip BMD showed a stepwise increase in magnitude with greater decreases in bioavailable testosterone from baseline. In the present study, the effect of FT levels on bone loss within the relatively short term up to 3 years was observed at the femoral neck, independent of age and BMI, supporting previous reports. Although reasons for site-specific differences in the predictive capacity of FT remain uncertain, we have already reported that bone loss rate differs depending on the site involved in another cohort study [40]. We have also reported that characteristics differ between fast bone losers at the lumbar spine and femoral neck [41]. One reason for site-specific differences might be because degenerative changes that increase BMD, such as osteophytosis or sclerotic change, are observed more frequently at the lumbar spine than at the femoral neck. These results suggest that the predictive capacity of FT might differ according to the sites involved.

A recent study showed that older men with total testosterone or E_2 deficiency were more likely to be osteoporotic [19], but no report evaluated the capacity of serum sex steroids to predict occurrence of OP. Regarding the relationship between testosterone and fracture risk, Mellstrom et al. [42] reported that FT within the normal range was independently associated with the presence, but not occurrence, of osteoporotic fracture in elderly men. In contrast, an analysis from the Rotterdam Study failed to confirm any association between testosterone and fracture risk [43]. Data from the Framingham study indicated that men with low serum testosterone and E_2 levels were at increased risk for incident hip fractures [44]. A recent report from the Dubbo osteoporosis epidemiology study revealed that in men older than 60 years, serum testosterone is independently associated with the risk of osteoporotic fracture [45]. We also tried to evaluate the predictive capacity of serum levels of sex steroids and occurrence of OP based on WHO criteria [46] and osteoporotic fractures, but only identified 7 cases of OP and 10 cases of osteoporotic fractures including 1 vertebral fracture, 1 hip fracture, 2 wrist fractures, 3 costal fractures, 2 ankle fractures, and 1 finger fracture. After analysis using Cox proportional hazards models adjusted for age and BMI, serum levels of FT were significantly related to incidence of OP (hazard ratio, 0.42; 95% confidence interval, 0.19–0.90), but not to incidence of osteoporotic fractures. This analysis suggests the possibility of serum FT as a predictor for OP occurrence over 10 years. However, the number of occurrences of OP seems to be too small to reach any conclusion regarding the presence or absence of associations between sex steroids and OP or osteoporotic fractures.

There are several limitations in the present study. First, the small sample size seemed to be the most severe weakness. In fact, as already noted, only 7 cases of OP and 10 cases of osteoporotic fractures were accumulated during the 10 years of the study. Longer observation in the present cohort might be required to confirm the association between sex steroids and OP or osteoporotic fracture. Second, the dropout rate over 10 years for patients in their seventies was considerably high (54.0%). This high dropout rate might cause bias. In fact, the tendency toward an increase in BMD at the femoral neck for patients in their seventies was skewed by withdrawal bias. On the basis of this hypothesis, we reanalyzed the multivariate regression analysis to assess the change rate of BMD at the femoral neck and serum FT with exclusion of subjects in their seventies. However, the results were similar, with serum levels of FT predicting bone loss at the femoral neck within 3 years (beta = 0.17, $P = 0.05$), but diluted effects with longer observation (7 years: beta = 0.8, $P = 0.38$; 10 years: beta = 0.03, $P = 0.77$). Third, all serum samples were extracted between 0900 and 1500, not at a fixed time in the morning, although samples for measurement of FT are recommended to be collected in the morning. Serum levels of testosterone tend to increase toward night, peaking in the early morning, then decreasing rapidly and reaching a nadir between 1300 and 2300. We collected samples when FT levels would probably have been decreasing toward the nadir. The present study might thus have underestimated FT values compared to collection at a fixed time in the morning.

Conversely, the study design shows several notable strengths. In this population-based cohort study, subjects were selected randomly from the resident registration list. BMD was carefully measured by a single observer (N.Y.), and measurements were repeated 3, 7, and 10 years later with high participation rate by the same device and same observer. Another strength was that the effect of serum levels of sex steroids on changes in BMD could be estimated directly.

In conclusion, we clarified that serum levels of FT could predict bone loss within 3 years, but not longer. Further observations are required to confirm the relationship between FT, E_2, and spinal OP and osteoporotic fractures. Other environmental and genetic factors should also be evaluated to develop strategies for the early prevention of OP.

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Conflict of interest statement The authors have no conflicts/disclosures to declare regarding the present manuscript.

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EPIDEMIOLOGY

Health-Related Quality of Life in Subjects With Low Back Pain and Knee Pain in a Population-Based Cohort Study of Japanese Men

The Research on Osteoarthritis Against Disability Study

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Study Design. Cross-sectional surveys of health-related quality of life (QOL) in subjects with low back pain and knee pain using a population-based cohort.

Objective. The purpose of the present study was to clarify the impact of low back pain and knee pain on QOL in men. In addition, we analyzed the impacts of vertebral fracture (VFx), lumbar spondylosis, and knee osteoarthritis (OA) on the magnitude of QOL loss in men with low back pain and knee pain.

Summary of Background Data. Low back pain and knee pain are major public health issues causing disability among the elderly men, but there were no population-based studies to compare the impact of low back pain on QOL with that of knee pain in Japanese men.

Methods. From 3040 participants in the Research on Osteoarthritis Against Disability study, data from 767 men older than 40 years who completed questionnaires (mean age = 69.7 years) were examined. To carry out the QOL assessment, the Medical Outcomes Study Short Form 8 (SF-8) and EuroQol (EQ-5D) were used. We examined the association of low back pain and knee pain with QOL. Furthermore, we also examined the presence of VFx and the severity of lumbar spondylosis and knee OA with the magnitude of QOL loss in men with low back pain and knee pain, respectively.

Results. The impact of low back pain on QOL was larger than that of knee pain. In men with low back pain, there were few associations between Kellgren-Lawrence grade and QOL, whereas VFx was associated with physical QOL. For men with knee pain, Kellgren-Lawrence grade equal to 4 knee OA was associated with QOL.

Conclusion. This study revealed that low back pain has a larger impact than knee pain on QOL. Furthermore, low back pain with VFx is strongly associated with physical QOL loss.

Key words: knee pain, low back pain, osteoarthritis, quality of life, vertebral fracture. **Spine 2011;36:1312–1319**

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The present study was conducted with the approval of ethical committees of the University of Tokyo and the Tokyo Metropolitan Institute of Gerontology.

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Low back pain and knee pain are major public health issues causing disability among the elderly in most developed countries.[1–3] The prevalence of low back pain and knee pain is high in the elderly in Japan, ranging from 25% to 30%.[2,3] According to the recent National Livelihood Survey of the Ministry of Health, Labour, and Welfare in Japan, low back pain is rated first among symptoms that send men to the hospital.[4] Thus, it is important to clarify the impact of low back pain and knee pain on quality of life (QOL). Several studies have focused on the association of low back pain with

QOL in whites,[5–8] but for knee pain, there are few studies regarding its association with QOL.[9] Furthermore, to the best of our knowledge, there are no population-based studies that examine the impact of low back pain and knee pain on QOL in the same population using the same tool, although low back pain and knee pain may not be independent. Furthermore, the presence of pain at both sites may have more impact on QOL than pain at a single site. One of the main causes of low back pain in the elderly is vertebral fracture (VFx).[10] Low back pain is also believed to be one of the principal clinical symptoms of lumbar spondylosis, although the magnitude of the impact of lumbar spondylosis on low back pain is not as strong as one would expect.[2,11,12] A significant part of knee pain is caused by knee osteoarthritis (OA),[13,14] and the prevalence of knee pain increases as knee OA becomes more severe.[3] Thus, the impact of pain on QOL may differ on the basis of the cause and severity of the underlying disease. However, to the best of our knowledge, there are no population-based studies that examine the association of pain with QOL according to the cause or severity of the underlying disease.

Furthermore, sex differences have been observed in low back pain and knee pain. The prevalence of low back pain and knee pain differs between men and women,[2,3] and low back pain is rated as the first symptom that sends men to the hospital, although it is rated as the second symptom for women.[4] Thus, the impact of this pain on QOL may be stronger in men than in women. Although studies have examined the association of low back pain[5–8] or knee pain[9] with QOL, neither men nor women were analyzed separately[5,6,9] or the studies focused only on women.[7,8] There are no large-scale population-based studies examining the impact of low back pain or knee pain on QOL in men alone.

The objective of the present study was to clarify the independent association of low back pain and knee pain with QOL among 767 men using cohorts from Research on Osteoarthritis Against Disability (ROAD). We also examined whether the presence of both low back pain and knee pain had a larger impact on QOL than pain at only one site. Furthermore, we analyzed the impact of VFx, lumbar spondylosis, and knee OA on the magnitude of loss of QOL in men with low back pain and knee pain.

MATERIALS AND METHODS

Subjects

The ROAD study is a nationwide prospective study for bone and joint diseases (with OA and osteoporosis as the representative bone and joint diseases) consisting of population-based cohorts established in several communities in Japan. As detailed profile of the ROAD study has been described elsewhere,[15,16] and only a brief summary is provided here. To date, we have completed the creation of a baseline database including clinical and genetic information of 3040 inhabitants (1061 men and 1979 women) aged 23 to 95 years (mean = 70.6 years), who were recruited from listings of resident registrations 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 ethical committees of the University of Tokyo and the Tokyo Metropolitan Institute of Gerontology. Participants completed an interviewer-administered questionnaire of 400 items that included lifestyle information such as smoking habits, alcohol consumption, family history, and health-related QOL. We also examined the presence of cerebral stroke, diabetes mellitus, cardiac disease, and hypertension using an interviewer-administered questionnaire, as QOL may be affected by these comorbidities. Furthermore, because a lower level of physical activity may affect the association of pain with QOL, we obtained a history of leisure physical activity, including information on participation in sports and the frequency and duration of other leisure activities such as walking, jogging, swimming, playing tennis, playing baseball, playing golf, and muscle strength training. Anthropometric measurements included height and weight, and body mass index (BMI; weight [kg]/height^2 [m^2]) was calculated. All subjects were interviewed by experienced orthopedists regarding low back pain and knee pain and were asked, "Have you experienced low back pain on most days in the past month, in addition to now?" and "Have you experienced knee pain on most days in the past month, in addition to now?," respectively. Those who answered yes were defined as having pain. From the baseline data of the overall participants, the present study analyzed 767 men aged 40 years or older who completed a questionnaire of the Medical Outcomes Study Short Form 8 (SF-8) and the EuroQol (EQ-5D).

Radiographic Assessment

All participants underwent radiographic examination of the lumbar spine including intervertebral levels L1–L2 to L5–S with anteroposterior and lateral views, and both knees using anteroposterior and lateral views with weight-bearing and foot map positioning. Lumbar spine and knee radiographs were read without knowledge of participant clinical status by a single experienced orthopedist (S. M.). VFx was assessed by lateral radiographs of the lumbar spine (L1–L5) in terms of a wedge, biconcave, or crush appearance according to the Japanese Society of Bone and Mineral Research criteria[17] (Figure 1). Lumbar spondylosis and knee OA were assessed using the Kellgren-Lawrence (KL) radiographic atlas, and the

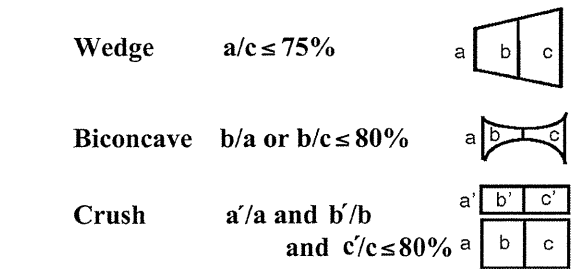

Figure 1. Diagnostic criteria for vertebral fractures according to the Japanese Society for Bone and Mineral Research.

severity was determined by KL grading.[18] We defined lumbar spondylosis and knee OA as KL 2 or more in at least one knee and one intervertebral level, respectively.

Instruments

The SF-8 scale was used for the QOL assessment. The SF-8 was constructed to provide a shorter alternative to the SF-36,[19] the most widely used patient-based health status survey, for use in large population-based surveys of general and specific populations. The SF-8 measures eight concepts: general health (GH), physical function (PF), role physical (RP), bodily pain (BP), vitality (VT), social function (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 scores (PCS) and mental component scores (MCS) summary scale measures. The SF-8 can be scored using a published algorithm for Japanese versions of the SF-8, which have been well-validated.[20] We also used the EuroQol (EQ-5D) questionnaire,[21] which was translated into Japanese.[22] The five-dimensional health care 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 choosing the most appropriate of the three statements about each of the five QOL dimensions. Each statement represents an increasing degree of severity. These results were coded and converted to a score of utility using a table of values.[22]

Statistical Analysis

We used the nonpaired student *t* test to examine differences between subjects with and without low back pain and knee pain. To determine the independent impact of low back pain and knee pain on QOL, multiple regression analysis was used with age, BMI, low back pain, and knee pain as independent variables. Furthermore, to examine the impact of the presence of both low back pain and knee pain on QOL, QOL scores in subjects with both low back pain and knee pain, with low back pain only, with knee pain only, and without these conditions were compared using the Tukey Honestly Significant Difference (HSD) test after adjustment for age and BMI. We further examined the association of KL grade at the lumbar spine and knee with the magnitude of QOL loss in subjects with low back pain and knee pain, respectively, using the Tukey HSD test after adjustment for age and BMI. If a subject had pain in both knees, the more severe KL grade was used for that subject. For the lumbar spine, the most severe KL grade among all intervertebral spaces was used. We also examined the association of the presence of VFx with the magnitude of QOL loss in subjects with low back pain using multiple regression analysis after adjustment for age, BMI, cerebral stroke, diabetes mellitus, cardiac disease, and hypertension. The association of physical activity with the magnitude of QOL loss in subjects with low back pain and in those with knee pain was determined using multiple regression analysis after adjustment for age, BMI, cerebral stroke, diabetes mellitus, cardiac disease, and hypertension. Data analyses were performed using SAS version 9.0 (SAS Institute Inc., Cary, NC).

RESULTS

Characteristics of the 767 participants aged 40 years and older in the ROAD study are shown in Table 1. The prevalence of low back pain and knee pain was approximately 15% and 21%, respectively. The prevalence of lumbar spondylosis and knee OA was 80% and 42%, respectively, which was high compared with that of VFx.

TABLE 1. Characteristics of Participants

N	767
Age, yr	69.7 ± 10.5
Height, cm	162.8 ± 6.7
Weight, kg	61.5 ± 10.8
BMI, kg/m^2	23.1 ± 3.4
Low back pain, %	15.4
Knee pain, %	20.6
Vertebral fracture, %	11.6
Lumbar spondylosis, %	80.0
Knee osteoarthritis, %	42.1
Comorbidities, %	
Cerebral stroke	5.8
Diabetes mellitus	13.8
Cardiac disease	13.4
Hypertension	41.1
Medical Outcomes Study Short Form 8	
GH	50.2 ± 5.5
PF	49.9 ± 6.2
RP	50.2 ± 6.7
BP	50.4 ± 9.2
VT	50.4 ± 6.3
SF	52.4 ± 5.5
MH	54.4 ± 5.3
RE	52.0 ± 5.2
PCS	47.4 ± 6.8
MCS	53.4 ± 5.3
EQ-5D	0.91 ± 0.14

Values are mean ± SD unless otherwise indicated.

BMI indicates body mass index; BP, bodily pain; EQ-5D, EuroQol; GH, general health; MCS, mental component summary; MH, mental health; PCS, physical component summary; PF, physical function; RE, role emotional; RP, role physical; SF, social function; VT, vitality;

TABLE 2. Mean (SD) Scores of All Domains, PCS, and MCS in the SF-8 and EQ-5D in Men with and Without Low Back Pain and Knee Pain

	Low Back Pain			Knee Pain		
	No	Yes	Adjusted Beta*	No	Yes	Adjusted Beta*
Medical Outcomes Study Short Form 8						
GH	50.5 (5.4)	48.3† (5.6)	−0.105‡	50.5 (5.4)	49.1† (5.5)	−0.100‡
PF	50.5 (5.8)	47.0† (7.5)	−0.135‡	50.4 (5.7)	48.2† (7.6)	−0.085‡
RP	50.7 (6.4)	47.4† (7.7)	−0.102‡	50.7 (6.2)	48.7† (7.9)	−0.073‡
BP	51.4 (9.2)	44.6† (7.2)	−0.235‡	51.1 (9.2)	47.6† (8.7)	−0.119‡
VT	50.8 (6.3)	48.4† (5.8)	−0.110‡	50.8 (6.1)	49.0† 6.5)	−0.109‡
SF	52.8 (5.0)	50.5† (7.5)	−0.100‡	52.5 (5.3)	52.4 (5.8)	0.028
MH	54.6 (5.1)	53.1† (6.0)	−0.078‡	54.4 (5.2)	54.6 (5.3)	0.034
RE	52.3 (4.9)	50.6† (5.5)	−0.087‡	52.1 (4.9)	51.9 6.2)	−0.0001
PCS	48.2 (6.5)	43.3† (7.2)	−0.191‡	48.1 (6.5)	44.8† (7.2)	−0.147‡
MCS	53.4 (5.1)	53.1 (6.3)	−0.010	53.2 (5.2)	54.2 (5.6)	0.076‡
EQ-5D	0.93 (0.13)	0.83† (0.17)	−0.180‡	0.92 (0.13)	0.87† (0.16)	−0.099‡

Values are mean (SD) unless otherwise indicated.

**The adjusted beta values are shown using multiple regression analysis after adjustment for age, body mass index, the other pain, cerebral stroke, diabetes mellitus, cardiac disease, and hypertension.*

†P < 0.05 versus subjects without the corresponding pain by nonpaired student t test.

‡P < 0.05 by multiple regression analysis.

BP indicates bodily pain; EQ-5D, EuroQol; GH, general health; MCS, mental component summary; MH, mental health; PCS, physical component summary; PF, physical function; RE, role emotional; RP, role physical; SF, social function; SF-8, 8-Item Short Form Health Survey; VT, vitality.

Table 2 shows the scores for all domains in the SF-8 and the EQ-5D utility score by the presence of low back pain and knee pain. We further examined the independent association of low back pain and knee pain with QOL using multiple regression analysis after adjustment for age, BMI, cerebral stroke, diabetes mellitus, cardiac disease, hypertension, and the other pain. Low back pain was significantly associated with lower QOL scores in all the domains of the SF-8 except for MCS, and in the EQ-5D utility scores, whereas knee pain was associated with lower scores of GH, PF, RP, BP, VT, and PCS in the SF-8 and the EQ-5D utility score, but not with SF, MH, and RE. For the MCS, knee pain was associated with higher scores. The adjusted beta values of low back pain were larger than those of knee pain in almost all QOL domains.

To examine the impact of the presence of both low back pain and knee pain on QOL, we next compared the QOL scores in the subjects with both low back pain and knee pain, only low back pain, only knee pain, and without any pain (Table 3). The Tukey HSD test after adjustment for age, BMI, cerebral stroke, diabetes mellitus, cardiac disease, and hypertension showed that the scores for almost all physical domains in the SF-8 were significantly lower in subjects with both low back pain and knee pain, only low back pain, and only knee pain than in those without pain. The EQ-5D utility score was also significantly lower in subjects with both low back pain and knee pain, those with only low back pain, and those with only knee pain than in those without pain. There were no significant differences in any domains between subjects with both low back pain and knee pain and those with only low back pain. Some domains tended to be lower in subjects with pain in both sites than in those with only knee pain, but differences were not significant.

Next, to clarify the impact of VFx and lumbar spondylosis on the magnitude of QOL loss in men with low back pain, we examined the association of KL grade of lumbar spine and the presence of VFx with QOL in the subjects with low back pain (Table 4). In men with low back pain, there were no associations of KL grade with any domain of the SF-8 and the EQ-5D utility scores, whereas the RP and PCS scores were significantly lower in subjects with VFx than in those without fracture.

Likewise, we examined the association of KL grade of knee with QOL in the subjects with knee pain (Table 5). After adjustment for age and BMI, the Tukey HSD test showed that the PCS in the SF-8 was significantly lower in men with KL 4 knee OA than in those with KL 0 or 1.

We next analyzed the association of physical activity with QOL in subjects with low back pain and in those with knee pain (see Table, Supplemental Digital Content 1, http://links.lww.com/BRS/A519). Multiple regression analysis

TABLE 3. Mean (SD) Scores of All Domains, PCS, and MCS in the SF-8 and EQ-5D in Men by the Combination of Low Back Pain and Knee Pain

	Low Back Pain and Knee Pain	Only Low Back Pain	Only Knee Pain	No Low Back Pain or Knee Pain
Prevalence, %	**5.2**	**9.8**	**15.5**	**69.6**
Medical Outcomes Study Short Form 8				
GH	48.2* (5.4)	48.7* (5.7)	49.3* (5.5)	50.8 (5.3)
PF	47.7* (6.2)	46.8* (8.2)	48.4* (8.1)	50.9 (5.0)
RP	48.0 (6.9)	47.6* (8.0)	49.0* (8.3)	51.1 (5.8)
BP	45.3* (7.7)	44.6* (6.9)	48.4* (8.9)	52.1 (9.1)
VT	47.9* (6.1)	48.8* (5.7)	49.3* (6.6)	51.1 (6.1)
SF	51.1 (6.5)	50.7 (7.9)	52.8 (5.5)	52.8 (4.8)
MH	54.4 (4.8)	52.7* (6.4)	54.7 (5.4)	54.6 (5.0)
RE	51.6 (5.0)	50.4* (7.2)	52.0 (6.5)	52.3 (4.4)
PCS	43.4* (6.5)	43.5* (7.5)	45.3* (7.4)	48.8 (6.1)
MCS	54.1 (5.6)	53.0 (6.7)	54.3 (5.5)	53.2 (5.0)
EQ-5D	0.82* (0.17)	0.84* (0.16)	0.88* (0.15)	0.94 (0.12)

Values are mean (SD) unless otherwise indicated.

**Significantly lower than that of subjects with no low back pain or knee pain by the Tukey Honestly Significant Difference test after adjustment for age, body mass index, cerebral stroke, diabetes mellitus, cardiac disease, and hypertension.*

BP indicates bodily pain; EQ-5D, EuroQol; GH, general health; MCS, mental component summary; MH, mental health; PCS, physical component summary; PF, physical function; RE, role emotional; RP, role physical; SF, social function; SF-8, 8-Item Short Form Health Survey; VT, vitality.

after adjustment for age, BMI, cerebral stroke, diabetes mellitus, cardiac disease, and hypertension showed that physical activity was not associated with any QOL parameter in subjects with low back pain or in those with knee pain.

DISCUSSION

This is the first large-scale, population-based cohort study in Japanese men that examined the impact of low back pain and knee pain on QOL measured by the SF-8 as well as the EQ-5D. In the present study, low back pain and knee pain were significantly associated with QOL in men, and multiple regression analysis showed that the adjusted beta values of low back pain were larger than that of knee pain in almost all QOL domains. Furthermore, in men with low back pain, VFx was significantly associated with QOL loss. For men with knee pain, KL 4 knee OA was strongly associated with magnitude of QOL loss compared with KL 0 or 1.

Previous studies showed that low back pain was associated with QOL,[5–8] but no studies focused on men, although sex differences were found in low back pain.[2,4] In addition, although low back pain and knee pain may not be independent, and the presence of pain at both sites may have more impact on QOL loss than pain at one site, no studies have examined the impact of low back pain and knee pain on QOL simultaneously in the same population. In the present study, low back pain and knee pain were significantly associated with lower QOL scores in men. The adjusted beta values of low back pain were higher than that of knee pain in almost all QOL domains, suggesting that low back pain had more impact on QOL loss than knee pain, although we did not evaluate the pain severity of low back pain and knee pain. Furthermore, the pain thresholds and pain onset in daily living in low back pain are not the same as in knee pain, so strict comparisons between low back pain and knee pain are limited, even though we examined the association of low back pain and knee pain with QOL in the same populations using the same method. The presence of both low back pain and knee pain was also significantly associated with QOL loss compared with no low back pain or knee pain, whereas there were no differences in QOL parameters between subjects with both low back pain and knee pain and those with only low back pain. These findings suggest that when both low back pain and knee pain exist, the combination may not result in any additional impact on QOL than pain in single site; it is possible that the impact of knee pain on QOL may be obscured by low back pain, because the impact of low back pain on QOL was larger than that of knee pain.

Previous clinical studies showed that strong impacts of clinical VFx on QOL were observed.[23,24] The present study also clarified that VFx had significant associations with the magnitude of QOL loss measured by RP and PCS of the SF-8 in subjects with low back pain, indicating that low back pain with VFx has a more severe impact on physical QOL than low back pain without VFx in men. This means that VFx may not

TABLE 4. Mean (SD) Scores on the SF-8 and EQ-5D by Vertebral Fracture and Kellgren-Lawrence Grade in Subjects with Low Back Pain

	Vertebral Fracture			Lumbar Spondylosis		
	No	Yes	KL 0,1	KL 2	KL 3	KL 4
Prevalence, %	**18.6**	**81.4**	**16.2**	**35.0**	**28.2**	**20.5**
Medical Outcomes Study Short Form 8						
GH	48.6 (5.6)	47.2 (5.9)	46.8 (6.8)	49.9 (5.3)	47.8 (5.4)	47.4 (5.3)
PF	47.5 (7.6)	44.8 (7.0)	48.6 (5.7)	49.4 (5.7)	43.6 (9.6)	46.3 (6.7)
RP	48.1 (7.3)	44.3* (8.7)	49.1 (6.9)	49.3 (6.9)	45.5 (8.5)	45.5 (8.2)
BP	44.9 (7.4)	43.2 (6.2)	42.3 (4.9)	46.2 (7.6)	45.2 (6.8)	43.2 (8.2)
VT	48.7 (6.0)	47.0 (5.0)	47.6 (7.7)	48.8 (5.3)	47.9 (5.5)	48.9 (5.6)
SF	50.4 (7.8)	51.2 (6.2)	49.4 (8.8)	52.6 (4.9)	49.6 (8.4)	49.0 (8.4)
MH	52.5 (6.1)	55.4 (4.5)	51.7 (7.6)	55.3 (4.0)	51.6 (6.1)	52.0 (6.4)
RE	50.2 (6.9)	52.2 (3.6)	49.0 (8.3)	52.6 (3.3)	49.1 (8.3)	50.5 (5.6)
PCS	44.2 (6.6)	39.4* (8.2)	44.0 (5.0)	44.9 (7.1)	41.9 (8.0)	42.0 (7.5)
MCS	52.4 (6.2)	56.4 (5.8)	51.0 (8.5)	54.9 (4.5)	52.2 (6.1)	52.8 (6.7)
EQ-5D	0.82 (0.17)	0.85 (0.16)	0.86 (0.15)	0.87 (0.14)	0.78 (0.17)	0.80 (0.19)

Values are mean (SD) unless otherwise indicated.

**P < 0.05 versus no vertebral fracture by the Tukey Honestly Significant Difference test after adjustment for age, body mass index, cerebral stroke, diabetes mellitus, cardiac disease, and hypertension.*

BP indicates bodily pain; EQ-5D, EuroQOL; GH, general health; MCS, mental component summary; MH, mental health; PCS, physical component summary; PF, physical function; RE, role emotional; RP, role physical; SF, social function; SF-8, 8-Item Short Form Health Survey; VT, vitality.

only be a cause of low back pain but also worsen the severity of low back pain. Meanwhile, the severity of lumbar spondylosis was not significantly associated with magnitude of QOL loss in subjects with low back pain. This finding may be partly explained by the weak association between lumbar spondylosis and low back pain reported by us and others.[2,11,12] Indeed, disc degeneration was reported to be detected by magnetic resonance imaging in at least one lumbar level in all but one asymptomatic volunteer in a group with volunteers aged 60 to 80 years.[25] Regarding the knee, the adjusted beta values of knee pain on QOL were weak compared with low back pain, whereas the KL 4 knee OA was significantly associated with magnitude of PCS loss in subjects with knee pain compared with KL 0 or 1. The PCS in subjects with KL 2 knee OA were similar to those with KL 0 or 1. Considering the definition of the KL grade, this may also mean that osteophytosis and joint space narrowing, which are representative features of knee OA, have a different impact on QOL; that is, osteophytosis may have a weak impact on QOL, whereas joint space narrowing may have a strong impact.

As measured by MCS of the SF-8, low back pain was not significantly associated with lower scores in the present study, whereas knee pain was significantly associated with higher scores on MCS, and significantly lower PCS scores. Several factors may contribute to the dissociation between MCS and PCS for low back pain and knee pain. First, 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.[26] In fact, Hill et al[27] showed that psychological distress has been shown to be significantly more frequent in those with arthritis than those without, although scores on MCS were not significantly different between these two groups. Second, the dissociation may be due to a disability paradox,[28] which suggests that people with chronic disabilities report serious limitations in Activities of Daily Living (ADL) and problems in performing social roles, yet state that they have excellent or good QOL. Low back pain and knee pain lead to functional impairment. This may be associated with lower PCS scores, but the individual may not feel that the impairment of social activity or ADL was due to mental factors. Particularly in elderly individuals, pain may be considered a natural consequence of being elderly and thus may not lead to lower MCS.

There are several limitations to the present study. First, this is a large-scale population-based study, but a cross-sectional study of baseline data, so a causal relationship could not be determined. The ROAD study is a longitudinal survey, so further progress will elucidate any causal relationships. Second, among the 1047 men 40 years or older in the ROAD

TABLE 5. Mean (SD) Scores of the SF-8 and EQ-5D by KL Grade in Subjects with Knee Pain

	KL 0,1	KL 2	KL 3	KL 4
Prevalence, %	**57.9**	**30.1**	**7.8**	**4.2**
Medical Outcomes Study Short Form 8				
GH	48.8 (5.2)	50.0 (4.8)	49.2 (6.5)	47.3 (6.9)
PF	49.4 (6.1)	48.9 (7.2)	47.0 (10.1)	43.6 (9.3)
RP	49.6 (7.5)	49.5 (6.9)	46.2 (12.0)	46.2 (6.7)
BP	47.5 (8.2)	50.1 (8.6)	43.8 (8.2)	44.8 (9.5)
VT	49.8 (5.7)	49.6 (7.1)	47.1 (7.4)	46.2 (6.3)
SF	53.5 (4.2)	51.2 (6.8)	51.9 (7.2)	52.3 (6.0)
MH	54.9 (5.1)	54.2 (5.0)	54.2 (6.6)	55.4 (5.5)
RE	52.7 (3.9)	51.3 (6.6)	50.9 (9.9)	51.6 (7.0)
PCS	45.4 (6.6)	46.7 (6.3)	42.2 (9.6)	40.3* (6.8)
MCS	54.8 (4.7)	52.9 (5.2)	54.4 (7.3)	55.8 (6.8)
EQ-5D	0.90 (0.15)	0.88 (0.16)	0.81 (0.20)	0.80 (0.17)

Values are mean (SD) unless otherwise indicated.

**P < 0.05 versus KL 0,1 by the Tukey Honestly Significant Difference test after adjustment for age, body mass index, cerebral stroke, diabetes mellitus, cardiac disease, and hypertension.*

BP indicates bodily pain; EQ-5D, EuroQol; GH, general health; KL, Kellgren-Lawrence; MCS, mental component summary; MH, mental health; PCS, physical component summary; PF, physical function; RE, role emotional; RP, role physical; SF, social function; SF-8, 8-Item Short Form Health Survey; VT, vitality.

study, 767 men had completed questionnaires for both the SF-8 and the EQ-5D, so the response rate was 73.7%. Subjects who completed questionnaires may have had better QOL than those who did not, so our results regarding QOL may have represented overestimations. 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 onset of VFx. In terms of clinical fractures, we examined the history of fracture, including VFx, in the ROAD study by self-report, and no clinical VFx occurred within the 1 month before baseline examination. However, we could not compare radiographs of the lumbar spine at baseline examination with those before the examination, as subjects had not undergone radiography of the lumbar spine before that examination. We were therefore unable to assess the incidence of subclinical fracture within the 1 month before baseline examination, although clinical and subclinical fractures are associated with lower QOL in women.[29] However, the association between severity of low back pain and the interval from onset of subclinical VFx may be weaker than that for clinical VFx, so the absence of data on the incidence of subclinical VFx may not strongly affect the present results.

In conclusion, the present study revealed that the impact of low back pain was larger than that of knee pain in almost all QOL domains. In men with low back pain, VFx had some association with physical QOL loss. In men with knee pain, KL 4 knee OA was strongly associated with QOL loss. Further progress will elucidate the backgrounds of low back pain and knee pain.

➢ Key Points

- ❑ Low back pain and knee pain are major public health issues causing disability among the elderly men, but there were no population-based studies to compare the impact of low back pain on QOL with that of knee pain in Japanese men.
- ❑ The objective of the present study was to clarify the independent association of low back pain and knee pain with QOL among 767 men using cohorts from ROAD.
- ❑ The impact of low back pain on QOL was larger than that of knee pain. In men with low back pain, there were few associations between KL grade and QOL, whereas VFx was associated with physical QOL, indicating that low back pain with VFx is strongly associated with physical QOL loss.

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