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]

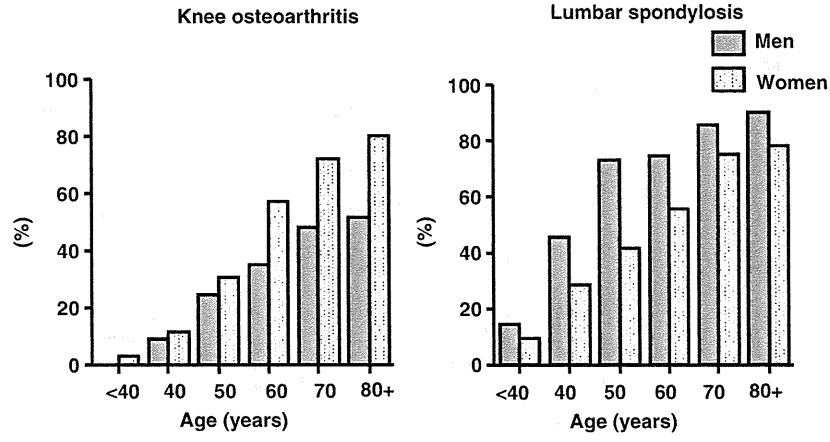

Figure 2 Prevalence of radiographic knee osteoarthritis and lumbar spondylosis, classified by age and gender

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,

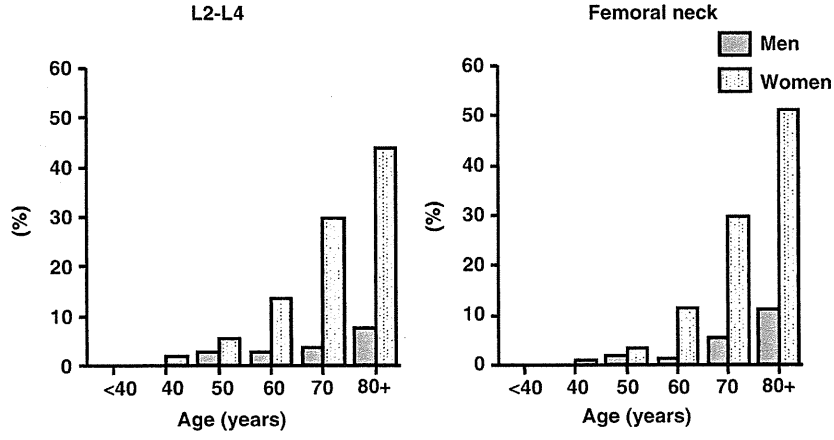

Figure 3 Prevalence of osteoporosis of the lumbar spine and femoral neck

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

	Men		Women	
Age strata (years)	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)

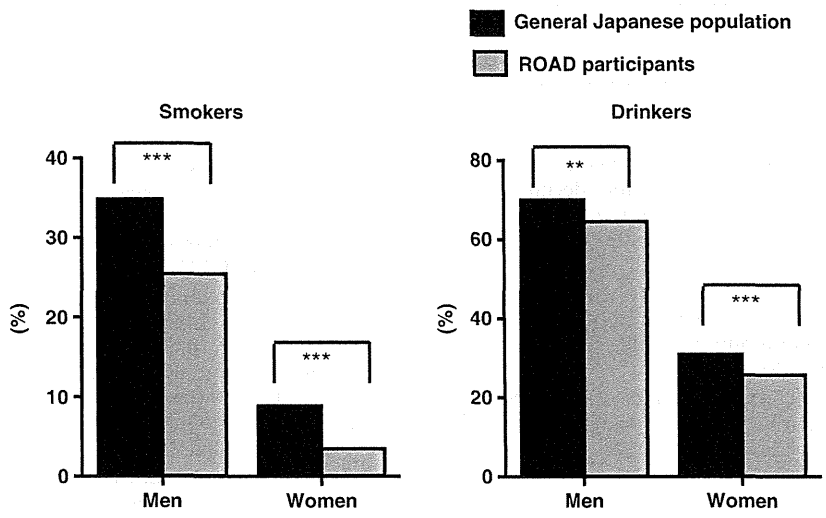

Figure 4 Comparison of the proportion of current smokers and drinkers between the participants of the ROAD study and the general Japanese population. $^{**}P < 0.01$, $^{***}P < 0.001$

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.

Arch Osteoporos (2010) 5:91–99
DOI 10.1007/s11657-010-0039-3

ORIGINAL ARTICLE

Health-related quality of life with vertebral fracture, lumbar spondylosis and knee osteoarthritis in Japanese men: the ROAD study

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: 30 July 2009 / Accepted: 15 February 2010 / Published online: 24 April 2010

Abstract

Summary This study examined associations of VFx, lumbar spondylosis and knee OA with QOL in 767 men over 40 years old from the ROAD study (mean, 69.7 years.). Multiple regression analysis showed VFx and knee OA as significantly associated with lower PCS scores, but lumbar spondylosis was not.

Purpose Little data have been accumulated regarding associations of vertebral fracture (VFx), lumbar spondylosis and knee osteoarthritis (OA) with quality of life (QOL) in men. The purpose of the present study is to clarify the impact of these diseases on QOL parameters such as the Medical Outcomes Study Short Form 8 (SF-8) and the EuroQOL (EQ-5D). In addition, to provide greater insight into the magnitude of QOL loss, a comparison was made with cerebral stroke.

Methods From the 3,040 participants in the ROAD study, this study analyzed 767 men over 40 years who had completed the questionnaires (mean, 69.7 years.). Vertebral fracture was assessed by lateral radiography of the lumbar spine. Lumbar spondylosis and knee OA were defined as Kellgren/Lawrence grade ≥3. Cerebral stroke was assessed by self-report.

Results Multiple regression analysis after adjustments for age, body mass index and presence of the above four diseases showed VFx was significantly associated with lower scores in physical function (PF), role physical (RP), bodily pain (BP) and vitality (VT) domains as well as physical component summary (PCS). Knee OA were significantly associated with lower scores in PF, RP, BP and PCS scores. Lumbar spondylosis was not associated with any domains of the SF-8. Lumbar spondylosis and knee OA were significantly associated with EQ-5D utility scores, but VFx was not. The impact for VFx on BP, VT and PCS scores was larger than cerebral stroke.

Conclusions This study revealed that VFx and knee OA impaired physical QOL in men, rather than lumbar spondylosis.

Keywords Quality of life · Vertebral fracture · Lumbar spondylosis · Knee osteoarthritis · Men

Electronic supplementary material The online version of this article (doi:10.1007/s11657-010-0039-3) contains supplementary material, which is available to authorized users.

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

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

Vertebral fracture (VFx) is reportedly associated with functional impairment [1], back pain, kyphosis [2, 3], esophageal reflux [4], depressive mood [5], respiratory dysfunctions [6] and mortality [7]. Lumbar spondylosis and knee osteoarthritis (OA), characterized by pathological features including disk or joint space narrowing and osteophytosis, are also major public health issues causing chronic pain and disability among the elderly [8–12]. In fact, prevalences of lumbar spondylosis and knee OA are quite high in the elderly in Japan [13–15], and 37,900,000 and 25,300,000 people ≥40 years old would be affected by radiographic lumbar spondylosis and knee OA, respectively [15]. Furthermore, according to the recent National Livelihood Survey of the Ministry of Health, Labour and Welfare in Japan, OA and fracture represent the fourth and fifth among diseases that cause disabilities, respectively, subsequently requiring support with regard to activities of daily living (ADL) [16].

Gender differences have been observed in these bone and joint diseases. The prevalence of knee OA is higher in women than men [14, 15], while that of lumbar spondylosis is higher in men [13, 15]. For VFx, prevalence is higher in women [17], while mortality is higher in men [18], so the impact of these diseases on quality of life (QOL) may also differ between genders. Although several studies have examined associations of VFx [19–27] and knee OA [28–32] with QOL, men and women were not separated [20, 21, 28, 29, 31, 32] or only women were focused [22, 23], and few large-scale population-based studies have examined bone and joint diseases in men [19, 24, 27, 30]. Furthermore, the association of VFx, lumbar spondylosis and knee OA with ADL and QOL may not be independent, but no studies have examined VFx, lumbar spondylosis and knee OA simultaneously in the same population using the same tools.

The objective of the present study is to clarify the impact of VFx, lumbar spondylosis and knee OA on QOL among 767 men using the cohorts of the ROAD study. In addition, to provide greater insight into the magnitude of QOL loss with VFx, lumbar spondylosis and knee OA, we made a comparison with cerebral stroke. Cerebral stroke is ranked first among diseases causing disabilities according to the recent National Livelihood Survey of the Ministry of Health, Labour and Welfare in Japan [16], and several studies have already reported that QOL is greatly affected after cerebral stroke [33]. Thus, such information can provide the health care physician with insights into the influence of VFx, lumbar spondylosis and knee OA on QOL.

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) constituting population-based cohorts established in several communities in Japan. As detailed profile of the ROAD study has already been described elsewhere [13–15, 34], the brief summary is provided here. To date, we have completed creation of a baseline database including clinical and genetic information for 3,040 inhabitants (1,061 men, 1,979 women) in the age range of 23 to 95 years (mean, 70.6 years), recruited from listings of resident registrations in three communities: an urban region in Itabashi, Tokyo, a mountainous region in Hidakagawa, Wakayama, and a 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, history, physical activity, reproductive variables and health-related QOL. Anthropometric measurements included height, weight, bilateral grip strength and body mass index (BMI) (weight [kg]/height^2 [m^2]). In the present study, to compare the magnitude of QOL loss in VFx, lumbar spondylosis and knee OA with another chronic disease, we assessed medical history of cerebral stroke by self-report. The following question was asked by an interviewer: "Have you ever experienced cerebral stroke?" Furthermore, to assess the impact of these bone and joint diseases according to symptoms, all participants were also interviewed regarding low back pain (LBP) by asking, "Have you experienced pain on most days in the past month, in addition to now?" Subjects who answered "yes" were defined as having LBP.

From the baseline data of the overall participants, the present study analyzed 767 men ≥40 years old who had completed questionnaires for 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 from L1/2 to L5/S with anteroposterior and lateral views and both knees using anteroposterior and lateral views with weight-bearing and foot map positioning. Vertebral fracture, lumbar

spondylosis and knee OA were determined by a single well-experienced orthopaedist blinded to participant clinical status (S.M.). Vertebral fracture 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 for Bone and Mineral Research (JSBMR) criteria [35]. The films were marked up, and morphometric measurements of anterior, middle and posterior heights on lateral radiography of the thoracic and lumbar spine were made. Wedge appearance was defined as a site where anterior height of the vertebra was ≤75% than posterior height. Biconcave appearance was where the height of the central part of the vertebra was ≤80% than that of the anterior or posterior parts of the vertebra. Crush appearance was where the height of the anterior, central and posterior parts of an axial vertebra was all reduced to ≤80% of the normal value (Fig. 1). Lumbar spondylosis and knee OA were assessed using the Kellgren/Lawrence (KL) radiographic atlas, and severity by KL grading was determined [36]. We have defined lumbar spondylosis and knee OA as KL ≥3 in at least one knee and in one intervertebral level, respectively. To evaluate intraobserver agreement of the JSBMR criteria for VFx and the KL grade (0–4) for the lumbar spine and knee, 100 randomly selected radiographs were scored by the same observer at >1 month after the first reading. Furthermore, 100 other radiographs were scored by two experienced orthopaedic surgeons (S.M. and H.O.) using the same radiographic atlas for interobserver agreement. Intra- and interobserver agreements were evaluated by kappa analysis. Intra- and interobserver agreements in JSBMR criteria for VFx and KL grade for lumbar spine and knee have been shown to be sufficient for assessment (0.93 and 0.91 for VFx, 0.84 and 0.76 for lumbar spine and 0.86 and 0.80 for knee, respectively).

Instruments

To carry out the QOL assessment, we used the SF-8 Health Survey (SF-8) scale. The SF-8 is an alternate form of the SF-36 Health Survey (SF-36) [37], the most widely used patient-based health status survey. The SF-8 was constructed to provide an even shorter alternative to the SF-36 for use in large population-based surveys of general and specific populations. The SF-8 uses one question to measure each of the eight SF-36 domains. Although none of the SF-8 items are identical to SF-36 items, the item pool including the SF-36 survey, SF-8 single-item scales and summary measures is scored on the same metric as the SF-36 scales and summary measures. The SF-8 and SF-36 measure 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). Each domain includes questions regarding overall health, limitations to usual physical activities due to physical health problems, difficulties in performing daily work due to physical health, severity of pain, energy levels, limitations to usual social activities due to physical health or emotional problems, severity of emotional problems and difficulties with usual work, school or other daily activities due to personal or emotional problems, respectively. 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 (PCS) and mental (MCS) summary scale measures. The SF-8 may be scored using a published algorithm for Japanese versions of the SF-8, which have been well validated [38]. We also used the EuroQOL (EQ-5D) questionnaire [39] translated into Japanese [40]. This five-dimensional health care classification included questions on the status of morbidity, self-care, usual activities, pain/discomfort and anxiety/depression. Participants were asked to indicate current health status by ticking the most appropriate of three statements about 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 [40].

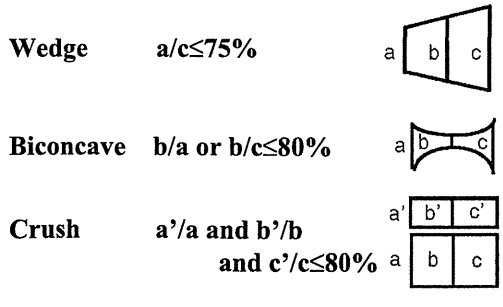

Fig. 1 Diagnostic criteria for VFxs accoding to the JSBMR

Statistical analysis

We performed nonpaired Student's *t* test to compare mean scores of QOL parameters between subjects with and without each chronic disease. Associations of VFx, lumbar spondylosis and knee OA with QOL parameters were determined by multiple regression analysis after adjustment for age and BMI. Next, to determine the independent impact of these bone and joint diseases, multiple regression analysis was used by age, BMI and presence of VFx, lumbar spondylosis and knee OA as independent variables. Furthermore, to compare the magnitude of QOL loss of the

three bone and joint diseases to cerebral stroke, multiple regression analysis was performed by age, BMI and presence of cerebral stroke in addition to VFx, lumbar spondylosis and knee OA as independent variables. Tukey honestly significant difference (HSD) test after adjustment for age and BMI was used to determine the differences of PCS values among VFx with LBP, VFx without LBP and no VFx and the differences among lumbar spondylosis with LBP, lumbar spondylosis without LBP and no lumbar spondylosis. Data analyses were performed using SAS version 9.0 (SAS Institute, Cary, NC).

Results

Impact of VFx, lumbar spondylosis and knee OA on QOL scores

Characteristics of the 767 men ≥40 years old in the ROAD study are shown in Table 1. Prevalence of lumbar spondylosis and knee OA were approximately 42% and 12%, respectively, compared to 12% for VFx. Six percent of all subjects had a medical history of cerebral stroke.

Table 1 Characteristics of participants

N	767
Age, years	69.7±10.5
Height, cm	162.8±6.7
Weight, kg	61.5±10.8
BMI, kg/m2	23.1±3.4
Medical history (%)	
Cerebral stroke	5.8
Prevalence (%)	
VFx	11.6
LS	41.6
KOA	12.0
LBP	15.4
SF-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 utility score	0.91±0.14

Except where indicated otherwise, values represent mean ±SD.

BMI body mass index; *VFx* vertebral fracture; *LS* lumbar spondylosis; *KOA* knee osteoarthritis; *LBP* low back pain; *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.

Table 2 shows scores for all domains in the SF-8 and the EQ-5D utility score according to the presence of chronic diseases. Scores for PF, RP BP, VT and PCS in the SF-8 were significantly lower in subjects with VFx compared to those in subjects without VFx, but GH, SF and RE were not. Physical function, RP, SF and PCS were significantly lower in subjects with lumbar spondylosis compared to subjects without lumbar spondylosis. For knee OA, scores of PF, RP, BP and PCS were significantly lower compared to subjects without knee OA. For MCS, the score was higher in subjects with VFx and knee OA compared to those in subjects without them. EQ-5D utility score was significantly lower in subjects with lumbar spondylosis and knee OA compared to those without them, respectively, while no significant difference was apparent in subjects with or without VFx.

We next performed further multiple regression analyses to examine the independent association of VFx, lumbar spondylosis and knee OA with QOL parameters after adjusting for age, BMI and all other bone and joint diseases. Beta values in each domain of SF-8 and EQ-5D utility score after adjusting for age, BMI and all other bone and joint diseases are shown in Table 3. Vertebral fracture was significantly associated with lower scores in PF, RP, BP, VT and PCS, while not in GH, SF and RE. Knee OA was significantly associated with lower PF, BP and PCS scores. For MCS, VFx and knee OA were associated with higher scores, but lumbar spondylosis was not associated. Lumbar spondylosis and knee OA were significantly associated with EQ-5D utility scores, while VFx was not. The Tukey HSD test after adjustment for age and BMI showed that PCS score was significantly lower in subjects having VFx with LBP than in subjects having VFx without LBP (Fig. 2). Vertebral fracture with or without LBP was significantly associated with lower PCS scores compared with no VFx. However, PCS scores were significantly lower in subjects having lumbar spondylosis with LBP than in subjects having lumbar spondylosis without LBP. There were no significant differences in PCS scores between subjects having lumbar spondylosis without LBP and those having no lumbar spondylosis.

Comparison of the magnitude of QOL loss in VFx, lumbar spondylosis and knee OA with that in cerebral stroke

To compare the magnitude of QOL loss in VFx, lumbar spondylosis and knee OA with another chronic disease, we analyzed the association of medical history of cerebral stroke with QOL (Supplementary Table). Multiple regression analysis showed that cerebral stroke was significantly associated with lower QOL scores measured by PF, RP, BP SF, MH and PCS in the SF-8, along with EQ-5D utility

Table 2 Mean scores of all domains, PCS and MCS in the SF-8 and EQ-5D by VFx, LS and KOA

	VFx		LS		KOA		Japanese general population*
	No	Yes	No	Yes	No	Yes	
SF-8							
GH	50.3 (5.5)	49.4 (5.4)	50.3 (5.4)	50.1 (5.6)	50.2 (5.4)	50.6 (6.2)	50.3 (6.6)
PF	50.2 (5.8)	48.1† (8.2)	50.5 (5.7)	49.2† (6.8)	50.3 (5.7)	47.7† (8.7)	49.8 (5.0)
RP	50.5 (6.2)	47.9† (9.1)	50.7 (6.3)	49.6† (7.2)	50.5 (6.3)	48.4† (8.6)	50.3 (5.0)
BP	50.8 (9.2)	47.0† (9.1)	50.7 (9.2)	49.9 (9.3)	50.7 (9.1)	48.3† (10.0)	50.8 (7.9)
VT	50.6 (6.2)	49.2† (6.4)	50.4 (6.1)	50.4 (6.4)	50.5 (6.2)	49.7 (6.4)	52.1 (5.6)
SF	52.4 (5.5)	52.4 (5.6)	52.8 (5.0)	51.9† (6.0)	52.3 (5.4)	53.0 (5.6)	50.3 (6.3)
MH	54.2 (5.4)	55.9† (3.7)	54.5 (5.2)	54.3 (5.3)	54.2 (5.2)	55.5† (5.4)	52.9 (5.9)
RE	51.9 (5.1)	52.6 (5.4)	52.2 (4.9)	51.7 (5.6)	52.0 (5.0)	52.4 (6.1)	51.3 (4.8)
PCS	47.9 (6.5)	43.9† (8.4)	47.8 (6.7)	46.8† (7.5)	47.8 (6.5)	44.7† (8.3)	48.3 (6.2)
MCS	53.1 (5.3)	55.6† (4.8)	53.4 (5.3)	53.4 (5.2)	53.1 (5.2)	55.3† (5.5)	51.9 (5.8)
EQ-5D	0.91 (0.14)	0.89 (0.16)	0.93 (0.13)	0.89† (0.16)	0.92 (0.14)	0.87† (0.17)	

Unless otherwise indicated, values represent mean (SD).

* Reference data derived from the 2002 general Japanese men at the age of 60 to 69 years [38]

† $p<0.05$ vs. subjects without the corresponding disease by non-paired Student's t test

score (Table 4). Adjusted beta values for PF and RP in VFx were lower than those in cerebral stroke, while these for BP, VT and PCS were higher in VFx. For knee OA, adjusted beta values for PF and RP were lower than those in cerebral stroke, while those for BP and PCS were higher. For EQ-5D utility score, lumbar spondylosis and knee OA was significantly associated with lower scores, but the adjusted beta values were lower than that in cerebral stroke.

Discussion

This is the first population-based study to examine the effects of a variety of bone and joint diseases including VFx, lumbar spondylosis and knee OA on QOL as measured by both SF-8 and EQ-5D in Japanese men. In the present study, we performed multiple regression analysis to determine independent associations of QOL parameters with each bone and joint disease after adjustment for age, BMI and all other bone and joint diseases. Vertebral fracture and knee OA were significantly associated with lower PCS scores, while they were associated with higher MCS. Lumbar spondylosis was associated with the EQ-5D utility scores, while not with any domains in the SF-8. The impact of diseases on PCS was largest in VFx among the three bone and joint diseases in men. Furthermore, to provide greater insight into the magnitude of QOL loss with the bone and joint diseases, we compared the

Table 3 Beta values for VFx, LS and KOA in all domains, PCS and MCS in the SF-8 and EQ-5D

	VFx		LS		KOA	
	Beta[a]	Adjusted beta[b]	Beta[a]	Adjusted beta[b]	Beta[a]	Adjusted beta[b]
SF-8						
GH	−0.054	−0.053	−0.015	−0.009	0.018	0.020
PF	−0.094*	−0.088*	−0.051	−0.032	−0.087*	−0.082*
RP	−0.113*	−0.109*	−0.038	−0.016	−0.073*	−0.069
BP	−0.133*	−0.131*	−0.035	−0.010	−0.081*	−0.078*
VT	−0.074*	−0.074*	−0.003	0.011	−0.056	−0.055
SF	0.011	0.018	−0.051	0.060	0.066	0.071
MH	0.106*	0.109*	−0.013	−0.035	0.076*	0.076*
RE	0.038	0.046	-0.052	−0.062	0.032	0.035
PCS	−0.181*	−0.178*	−0.042	−0.007	−0.118*	−0.113*
MCS	0.149*	0.153*	−0.015	−0.047	0.121*	0.122*
EQ-5D	−0.050	−0.035	−0.107*	−0.096*	−0.081*	−0.073*

[a] Beta values are shown using multiple regression analysis after adjustment for age and BMI

[b] Adjusted beta values are shown using multiple regression analysis after adjustment for age, BMI and all other diseases

* $p<0.05$

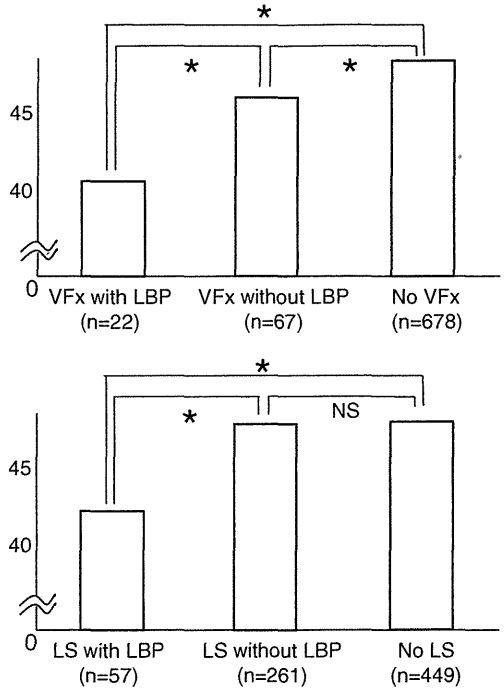

Fig. 2 Physical component summary values among subjects having VFx with LBP, VFx without LBP and no VFx, and those having lumbar spondylosis (LS) with LBP, LS without LBP and no LS. The number of subjects in each group is shown in parentheses. *$p<0.05$ by Tukey HSD test adjustment for age and BMI

impact of these bone and joint diseases on QOL loss with that of cerebral stroke. The impact of VFx and knee OA on BP and PCS loss was larger than that of cerebral stroke.

Few population-based studies have examined relationships between radiographic VFx and QOL [19–21, 24, 27], and genders were only adjusted, not separated in almost all these studies, although the impact of vertebral deformities on QOL may differ between genders. In the Canadian Multicentre Osteoporosis Study [27], no strong fracture-related associations of subclinical vertebral deformity with QOL were found in men as measured by the Health Utilities Index (HUI) Mark II and III Systems [41]. In the present study, radiographic VFx showed a significant association with lower PCS scores in men, with the largest impact among the three bone and joint diseases. Furthermore, multiple regression analysis showed that the magnitude of PCS loss was stronger than that of cerebral stroke, which is ranked first among the diseases causing disabilities according to the recent National Livelihood Survey of the Ministry of Health, Labour and Welfare in Japan [16]. Furthermore, VFx with LBP had a strong effect on PCS, while VFx without LBP had a moderate but significant effect. Reasons for the discrepancy between the present study and the Camos study can be partly attributed to differences in QOL measurements. In HUI scores, multi-attribute utility score reflects global health, but PCS reflects only physical QOL. In fact, for pain domains, subclinical vertebral deformities tend to be associated with lower HUI scores as seen for the SF-8 in the present study. Another reason may be racial differences. Racial variations exist in the prevalence of vertebral deformities [42, 43], so differences may also exist in the impact of QOL. For GH, SF and RE in the SF-8, VFx was not associated with the scores by multiple regression analysis. In this study, VFx was diagnosed according to lumbar radiographs, so many fractures in men may have occurred years previously and may have been related to trauma, which must be one reason why some domains of QOL were not impaired.

The significant effect of knee OA on QOL is shown by poorer scores in PF, BP and PCS domains in the SF-8 in multiple regression analysis. A previous survey in Chinese using a GH-related QOL measure also showed that OA has comparable impact compared with stroke, asthma and chronic obstructive pulmonary disease [32], but men and women were not separated in that analysis. The present study is the first population-based study to clarify that knee OA is significantly associated with lower PCS scores in men. Although multiple regression analysis showed that the magnitude of the impact on PCS is lower than VFx, prevalence is much higher for knee OA than for VFx, so the total burdens of these diseases might be similar.

Likewise, for lumbar spondylosis, few population-based studies have examined QOL [20]. Unlike VFx or knee OA, multiple regression analysis in the present study showed that lumbar spondylosis was not associated with PCS in men, supporting previous findings [20], although gender was only adjusted in that analysis. These results may be

Table 4 Comparison of adjusted beta values for the three bone and joint diseases such as VFx, LS and KOA with that for cerebral stroke in the SF-8 and EQ-5D

	VFx	LS	KOA	Stroke
SF-8				
GH	−0.054	0.007	0.004	−0.070
PF	−0.092*	−0.031	−0.097*	−0.107*
RP	−0.115*	−0.015	−0.083*	−0.125*
BP	−0.136*	−0.008	−0.086*	−0.079*
VT	−0.078*	0.004	−0.063	−0.029
SF	0.013	−0.061	0.061	−0.100*
MH	0.106*	−0.033	0.066	−0.096*
RE	0.042	−0.065	0.028	−0.053
PCS	−0.183*	0.007	−0.128*	−0.107*
MCS	0.151*	−0.049	0.118*	−0.036
EQ-5D	−0.039	−0.090*	−0.081*	−0.122*

Adjusted beta values are shown using multiple regression analysis after adjustment for age, BMI and all other diseases

*$p<0.05$

explained by the fact that associations between lumbar spondylosis and LBP are not so strong [13, 44, 45]. In fact, the domain of BP score in SF-8 was not associated with lumbar spondylosis in this study.

In the present study, VFx and knee OA were significantly associated with lower PCS, while they were associated with higher MCS. Past literatures also showed the dissociation between PCS and MCS in VFx and knee OA [20, 46]. Several factors may contribute to the dissociation between MCS and PCS for VFx and knee OA. 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 MH issues than disease-specific scales such as the Kessler psychological distress scale [47]. In fact, Hill et al. [48] showed that psychological distress has been shown to be significantly more frequent in those with arthritis than those without, although scores on the MCS were not significantly different between these two groups. Second, the dissociation may be due to a disability paradox [49], which suggests that people with chronic disabilities report serious limitations in ADL, problems in performing social roles, yet state that they have excellent or good QOL. Many subjects with VFx and knee OA had LBP or knee pain, which leads to functional impairment. This may be associated with lower scores of PCS, but the individual may not feel that the impairment of social activity or ADL was due to mental factors. Particularly in elderly individuals, pain or functional impairment may be considered a natural consequence of being elderly. Vertebral fracture and knee OA were thus not associated with lower scores for SF or RE domains in the SF-8 and, thus, showed no associations with MCS. Conversely, elderly individuals may think that having cerebral stroke is not a natural consequence of being elderly, potentially contributing to the differences between VFx, knee OA and cerebral stroke.

The present study showed that the association of chronic diseases with QOL differed between the SF-8 and EQ-5D. For VFx, PCS of the SF-8 was reduced, while EQ-5D utility score was not, while for lumbar spondylosis, both PCS and MCS of the SF-8 was not associated, but the EQ-5D utility scores were significantly reduced. The reason may be explained by the fact that in the EQ-5D, all five domains are combined together to analyze the association with chronic diseases, while PCS and MCS are analyzed separately in the SF-8. In fact, associations of VFx differed between PCS and MCS of the SF-8, so when all domains were combined together, the results may differ. Lumbar spondylosis reduced both the PCS and MCS scores, although they were not significant, so when combined, the association may be significant. For VFx and knee OA, the SF-8 may be more useful to examine associations with QOL than the EQ-5D.

There are several limitations in the present study. First, this was a large-scale, population-based study, but a cross-sectional study of baseline data. Causal relationships could therefore not be determined. The ROAD study is a longitudinal survey, so further progress may help to elucidate any causal relationships. Second, among the 1,047 men ≥40 years old in the ROAD 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 only used semi-quantitative methods to assess VFx. Furthermore, we used the KL system for lumbar spondylosis and knee OA. Since the KL system emphasizes osteophytosis, it is unclear how to handle lumbar spondylosis or knee OA with disc or joint space narrowing but no osteophytosis. We are currently developing a computer-aided diagnostic program to enable fully automatic measurement of the major features of VFx, lumbar spondylosis and knee OA, including joint and disc space narrowing and osteophytosis on plain radiography [50]. Fourth, cerebral stroke was assessed by self-report, so severity could not be examined. Furthermore, cerebral stroke is a serious disease, so participants are considered highly likely to know if they have been diagnosed with cerebral stroke, although some participants may not; thus, strict comparison with bone and joint diseases was limited.

Conclusions

The present cross-sectional study using a large-scale population from the ROAD study revealed that VFx and knee OA were significantly associated with lower PCS scores of the SF-8 in men, while lumbar spondylosis was not. The impact of diseases on PCS was the largest for VFx in men. Further progress, along with continued longitudinal survey in the ROAD study, will elucidate the environmental and genetic backgrounds of VFx, lumbar spondylosis and knee OA and the relationship with QOL.

Acknowledgements This work was supported by Grants-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 (JOA-Subsidized Science Project Research 2006-1), and grant no. 166 from the Japan Orthopaedics and Traumatology Foundation.

The authors thank Dr. Anamizu, members of the department of orthopaedics, Mr. Kutsuma, other members of the department of

radiology at Tokyo Metropolitan Geriatric Medical Center, Mrs. Tomoko Takijiri, other members of the Public Office in Hidakagawa Town, Mrs. Tamako Tsutsumi, Mrs. Kanami Maeda, and other members of the Public Office in Taiji Town for their assistance in the location and scheduling of participants for examinations.

Conflict of Interest All authors have no conflicts of interest.

References

1. Burger H, Van Daele PL, Grashuis K, Hofman A, Grobbee DE, Schutte HE, Birkenhager JC, Pols HA (1997) Vertebral deformities and functional impairment in men and women. J Bone Miner Res 12:152–157
2. Ross PD (1997) Clinical consequences of vertebral fractures. Am J Med 103:30S–42S, discussion 42S–43S
3. Nevitt MC, Ettinger B, Black DM, Stone K, Jamal SA, Ensrud K, Segal M, Genant HK, Cummings SR (1998) The association of radiographically detected vertebral fractures with back pain and function: a prospective study. Ann Intern Med 128:793–800
4. Yamaguchi T, Sugimoto T, Yamada H, Kanzawa M, Yano S, Yamauchi M, Chihara K (2002) The presence and severity of vertebral fractures is associated with the presence of esophageal hiatal hernia in postmenopausal women. Osteoporos Int 13:331–336
5. Gold DT, Lyles KW, Shipp KM, Drezner MK (2001) Osteoporosis and its nonskeletal consequences: their impact on treatment decisions. In: Marcus R, Feldman D, Kelsey J (eds) Osteoporosis, 2nd edn. Academic Press, San Diego, pp 819–829
6. Leech JA, Dulberg C, Kellie S, Pattee L, Gay J (1990) Relationship of lung function to severity of osteoporosis in women. Am Rev Respir Dis 141:68–71
7. Johnell O, Kanis JA, Oden A, Sernbo I, Redlund-Johnell I, Petterson C, De Laet C, Jonsson B (2004) Mortality after osteoporotic fractures. Osteoporos Int 15:38–42
8. Sharma L, Kapoor D (2007) Epidemiology of osteoarthritis. In: Moskowitz RW, Altman RD, Hochberg MC, Buckwalter JA, Goldberg VM (eds) Osteoarthritis: diagnosis and medical/surgical management, 4th edn. Lippincott Williams & Wilkins, Philadelphia, pp 3–26
9. Guccione AA, Felson DT, Anderson JJ, Anthony JM, Zhang Y, Wilson PW, Kelly-Hayes M, Wolf PA, Kreger BE, Kannel WB (1994) The effects of specific medical conditions on the functional limitations of elders in the Framingham Study. Am J Public Health 84:351–358
10. Felson DT, Zhang Y (1998) An update on the epidemiology of knee and hip osteoarthritis with a view to prevention. Arthritis Rheum 41:1343–1355
11. Hadjipavlou AG, Simmons JW, Pope MH, Necessary JT, Goel VK (1999) Pathomechanics and clinical relevance of disc degeneration and annular tear: a point-of-view review. Am J Orthop 28:561–571
12. Emery SE, Ringus VM (2007) Osteoarthritis of the spine. In: Moskowitz RW, Altman RD, Hochberg MC, Buckwalter JA, Goldberg VM (eds) Osteoarthritis: diagnosis and medical/surgical management, 4th edn. Lippincott Williams & Wilkins, Philadelphia, pp 427–452
13. Muraki S, Oka H, Akune T, Mabuchi A, En-Yo Y, Yoshida M, Saika A, Suzuki T, Yoshida H, Ishibashi H, Yamamoto S, Nakamura K, Kawaguchi H, Yoshimura N (2008) 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 68:1401–1406
14. Muraki S, Oka H, Akune T, Mabuchi A, En-Yo Y, Yoshida M, Saika A, Suzuki T, Yoshida H, Ishibashi H, Yamamoto S, Nakamura K, Kawaguchi H, Yoshimura N (2009) Prevalence of radiographic knee osteoarthritis and its association with knee pain in the elderly of Japanese population-based cohorts: the ROAD study. Osteoarthritis Cartilage 17:1137–1143
15. Yoshimura N, Muraki S, Oka H, Mabuch A, En-yo Y, Yoshida M, Saika A, Yoshida H, Suzuki T, Kawaguchi H, Nakamura K, Akune T. 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 27:620–628
16. Ministry of Health, Labour and Welfare (2007) The outline of the results of National Livelihood Survey 2007 available online at http://www.mhlw.go.jp/toukei/list/20-19-1.html.
17. Yoshimura N, Kinoshita H, Oka H, Muraki S, Mabuchi A, Kawaguchi H, Nakamura K (2006) Cumulative incidence and changes in the prevalence of vertebral fractures in a rural Japanese community: a 10-year follow-up of the Miyama cohort. Arch Osteoporos 1:43–49
18. Bliuc D, Nguyen ND, Milch VE, Nguyen TV, Eisman JA, Center JR (2009) Mortality risk associated with low-trauma osteoporotic fracture and subsequent fracture in men and women. JAMA 301:513–521
19. Masunari N, Fujiwara S, Nakata Y, Nakashima E, Nakamura T (2007) Historical height loss, vertebral deformity, and health-related quality of life in Hiroshima cohort study. Osteoporos Int 18:1493–1499
20. van Schoor NM, Smit JH, Twisk JW, Lips P (2005) Impact of vertebral deformities, osteoarthritis, and other chronic diseases on quality of life: a population-based study. Osteoporos Int 16:749–756
21. Cockerill W, Lunt M, Silman AJ, Cooper C, Lips P, Bhalla AK, Cannata JB, Eastell R, Felsenberg D, Gennari C, Johnell O, Kanis JA, Kiss C, Masaryk P, Naves M, Poor G, Raspe H, Reid DM, Reeve J, Stepan J, Todd C, Woolf AD, O'Neill TW (2004) Health-related quality of life and radiographic vertebral fracture. Osteoporos Int 15:113–119
22. Badia X, Diez-Perez A, Alvarez-Sanz C, Diaz-Lopez B, Diaz-Curiel M, Guillen F, Gonzalez-Macias J (2001) Measuring quality of life in women with vertebral fractures due to osteoporosis: a comparison of the OQLQ and QUALEFFO. Qual Life Res 10:307–317
23. Oleksik A, Lips P, Dawson A, Minshall ME, Shen W, Cooper C, Kanis J (2000) Health-related quality of life in postmenopausal women with low BMD with or without prevalent vertebral fractures. J Bone Miner Res 15:1384–1392
24. Adachi JD, Loannidis G, Berger C, Joseph L, Papaioannou A, Pickard L, Papadimitropoulos EA, Hopman W, Poliquin S, Prior JC, Hanley DA, Olszynski WP, Anastassiades T, Brown JP, Murray T, Jackson SA, Tenenhouse A (2001) The influence of osteoporotic fractures on health-related quality of life in community-dwelling men and women across Canada. Osteoporos Int 12:903–908
25. Lips P, Cooper C, Agnusdei D, Caulin F, Egger P, Johnell O, Kanis JA, Kellingray S, Leplege A, Liberman UA, McCloskey E, Minne H, Reeve J, Reginster JY, Scholz M, Todd C, de Vernejoul MC, Wiklund I (1999) Quality of life in patients with vertebral fractures: validation of the Quality of Life Questionnaire of the European Foundation for Osteoporosis (QUALEFFO). Working party for quality of life of the European Foundation for Osteoporosis. Osteoporos Int 10:150–160
26. Tosteson AN, Gabriel SE, Grove MR, Moncur MM, Kneeland TS, Melton LJ 3rd (2001) Impact of hip and vertebral fractures on quality-adjusted life years. Osteoporos Int 12:1042–1049
27. Adachi JD, Ioannidis G, Pickard L, Berger C, Prior JC, Joseph L, Hanley DA, Olszynski WP, Murray TM, Anastassiades T, Hopman

W, Brown JP, Kirkland S, Joyce C, Papaioannou A, Poliquin S, Tenenhouse A, Papadimitropoulos EA (2003) The association between osteoporotic fractures and health-related quality of life as measured by the Health Utilities Index in the Canadian Multicentre Osteoporosis Study (CaMos). Osteoporos Int 14:895–904
28. Brazier JE, Harper R, Munro J, Walters SJ, Snaith ML (1999) Generic and condition-specific outcome measures for people with osteoarthritis of the knee. Rheumatology (Oxford) 38:870–877
29. Xie F, Li SC, Luo N, Lo NN, Yeo SJ, Yang KY, Fong KY, Thumboo J (2007) Comparison of the EuroQol and short form 6D in Singapore multiethnic Asian knee osteoarthritis patients scheduled for total knee replacement. Arthritis Rheum 57:1043–1049
30. Woo J, Lau E, Lee P, Kwok T, Lau WC, Chan C, Chiu P, Li E, Sham A, Lam D (2004) Impact of osteoarthritis on quality of life in a Hong Kong Chinese population. J Rheumatol 31:2433–2438
31. Bachmeier CJ, March LM, Cross MJ, Lapsley HM, Tribe KL, Courtenay BG, Brooks PM (2001) A comparison of outcomes in osteoarthritis patients undergoing total hip and knee replacement surgery. Osteoarthritis Cartilage 9:137–146
32. Lam CL, Lauder IJ (2000) The impact of chronic diseases on the health-related quality of life (HRQOL) of Chinese patients in primary care. Fam Pract 17:159–166
33. Carod-Artal FJ, Egido JA (2009) Quality of life after stroke: the importance of a good recovery. Cerebrovasc Dis 27(Suppl 1):204–214
34. Yoshimura N, Muraki S, Oka H, Kawaguchi H, Nakamura K, Akune T. Cohort profile: Research on Osteoarthritis/osteoporosis Against Disability (ROAD) study Int J Epidemiol (in press)
35. Inoue T (1990) Clinical features and findings: osteoporosis. Bone 4:39–47 (in Japanese)
36. Kellgren JH, Lawrence JS (eds) (1963) The epidemiology of chronic rheumatism: atlas of standard radiographs of arthritis. Blackwell Scientific, Oxford, England
37. Ware JE, Snow KK, Kolinski M, Gandeck B (1993) SF-36 health survey manual and interpretation guide. The Health Institute, New England Medical Centre, Boston, USA
38. Fukuhara S, Suzukamo Y (2004) Manual of the SF-8 Japanese version. Institute for Health Outcome and Process Evaluation Research, Kyoto, Japan (in Japanese)
39. Dolan P (1997) Modeling valuations for EuroQol health states. Med Care 35:1095–1108
40. Japanese EuroQol Translation Team (1997) The development of the Japanese EuroQol instrument. J Health Care Soc 8:109–123 (in Japanese)
41. Feeny DH, Torrance GW, Furlong WJ (1996) Health utilities index. In: Spilker B (ed) Quality of life and pharmacoeconomics in clinical trials, 2nd edn. Lippincott, Philadelphia, pp 239–252
42. Duan Y, Wang XF, Evans A, Seeman E (2005) Structural and biomechanical basis of racial and sex differences in vertebral fragility in Chinese and Caucasians. Bone 36:987–998
43. Tracy JK, Meyer WA, Grigoryan M, Fan B, Flores RH, Genant HK, Resnik C, Hochberg MC (2006) Racial differences in the prevalence of vertebral fractures in older men: the Baltimore Men's Osteoporosis Study. Osteoporos Int 17:99–104
44. Symmons DP, van Hemert AM, Vandenbroucke JP, Valkenburg HA (1991) A longitudinal study of back pain and radiological changes in the lumbar spines of middle aged women. II. Radiographic findings. Ann Rheum Dis 50:162–166
45. O'Neill TW, McCloskey EV, Kanis JA, Bhalla AK, Reeve J, Reid DM, Todd C, Woolf AD, Silman AJ (1999) The distribution, determinants, and clinical correlates of vertebral osteophytosis: a population based survey. J Rheumatol 26:842–848
46. Boutron I, Rannou F, Jardinaud-Lopez M, Meric G, Revel M, Poiraudeau S (2008) 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 16:1024–1031
47. Kessler RC, Andrews G, Colpe LJ, Hiripi E, Mroczek DK, Normand SL, Walters EE, Zaslavsky AM (2002) Short screening scales to monitor population prevalences and trends in non-specific psychological distress. Psychol Med 32:959–976
48. Hill CL, Gill T, Taylor AW, Daly A, Grande ED, Adams RJ (2007) Psychological factors and quality of life in arthritis: a population-based study. Clin Rheumatol 26:1049–1054
49. Albrecht G, Devlieger P (1999) The disability paradox: high quality of life against all odds. Soc 48:977–988
50. Oka H, Muraki S, Akune T, Mabuchi A, Suzuki T, Yoshida H, Yamamoto S, Nakamura K, Yoshimura N, Kawaguchi H (2008) Fully automatic quantification of knee osteoarthritis severity on plain radiographs. Osteoarthritis Cartilage 16:1300–1306

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 $\geq$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

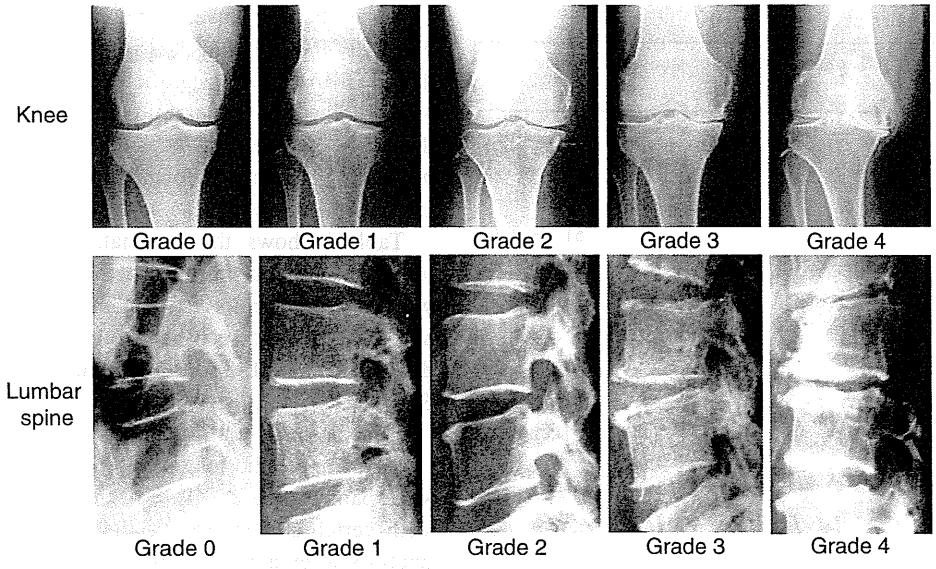

Fig. 1 Kellgren–Lawrence (KL) grade at knee and lumbar spine. *Knee*: *Grade 1* Doubtful narrowing of the joint space and possible osteophytic lipping, *Grade 2* definite osteophytes and possible narrowing of the joint space, *Grade 3* multiple moderate osteophytes, definite narrowing of the joint space, 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