

IV. 研究成果の刊行物・別刷

COHORT PROFILE

Cohort Profile: Research on Osteoarthritis/ Osteoporosis Against Disability study

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Accepted 15 July 2009

How did the study come about?

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

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

What does the ROAD study cover?

The ROAD study is a multi-centre prospective observational study that aims to elucidate the environmental and genetic background of bone and joint diseases (with OA and OP as the representative bone and joint diseases). It is designed to examine the extent to which risk factors for these diseases are related to

the clinical features of the diseases, laboratory and radiographic findings, bone mass, bone geometry, lifestyle, nutritional factors, anthropometric and neuromuscular measures and fall propensity. It also aims to determine how these diseases affect the ADL and QOL of Japanese men and women.

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

Who are in the sample?

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

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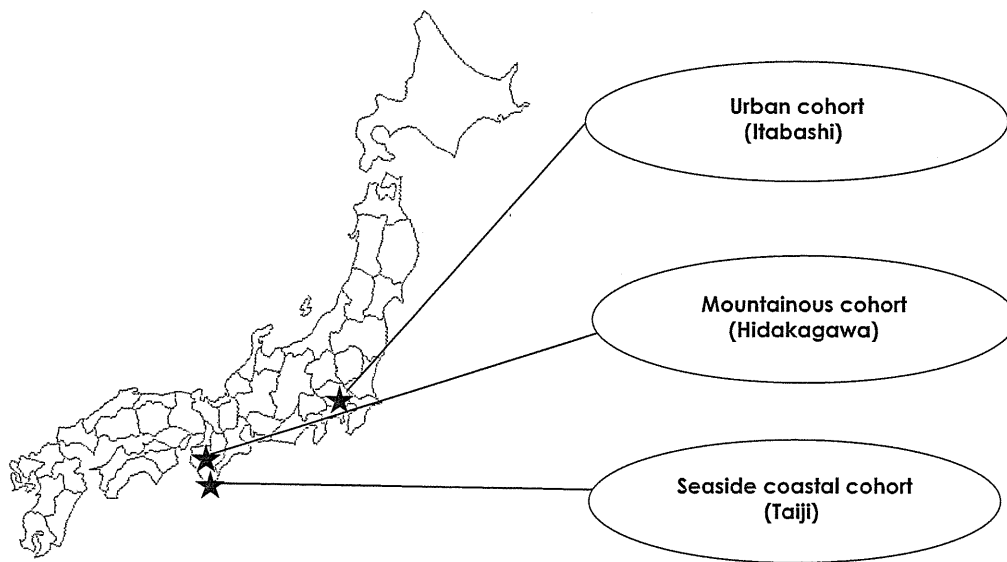


Figure 1 Locations of the three regions from which the study cohort was derived

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

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

BMI = body mass index.

two regions was ≥40 years. In the urban region, invitation letters were distributed only to the inhabitants whose name was on a list of community-dwelling people that was prepared in 2002.¹¹

Subjects from each area who were willing to attend the study were invited to participate. Despite being younger (58 years) than the age limit defined in the inclusion criteria, 2 inhabitants from the urban area, 9 from the mountainous area and 36 from the coastal area were included in the study because they were very keen to participate. Over the 1.5-year

period from October 2005 to March 2007, 3040 of 5785 candidates were enrolled from the three regions (participation rate, 52.5%).

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

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

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

How often have they been followed up?

We intend to follow-up the three population-based cohorts of the ROAD study for at least 10 years. In October 2008, after a follow-up period of 3 years, a second comprehensive clinical examination

was started and is ongoing. We will repeat the baseline measurements during the second examination. A third and fourth examination will be performed at 6 and 10 years, respectively, after the baseline examination.

What has been measured?

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

Interviewer-administered questionnaire

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

Table 2 Summary of data collected in the ROAD study

Interviewer-administrated questionnaire

Cigarette smoking, alcohol consumption
 Medical history, medications
 Reproductive variables, lactation
 Dietary history, history of falls and fractures
 Physical activity using PASE
 Family history
 Evaluation of knee symptoms using WOMAC
 Health-related QOL (EQ5D, SF-8)

Dietary assessment

Nutrient intake calculated using BDHQ

Anthropometric measurements

Height, weight, arm span, grip strengths
 Circumference of both wrists, circumference of waist
 Heart rate, systolic and diastolic blood pressure

Visual and neuromuscular function

Visual acuity
 Walking speed with tandem walking 6 m x 20 cm
 Rise from a chair

Biochemical measurements

Blood samples Blood counts, haemoglobin, haemoglobin A1C, blood sugar
 Sera Total protein, AST, ALT, GGT, total cholesterol, HDL-cholesterol, triglyceride
 BUN, uric acid, creatinine

DNA samples extracted

Urine samples Urinary protein, occult blood, sugar, urobilinogen

Medical information

Pain in back, lumbar, knee and hip
 Swelling and range of motion of the joints
 Tendon reflexes
 Cognitive function used by Mini-Mental Status Examination

Radiographic assessment

Anteroposterior and lateral views of lumbar spine
 Anteroposterior view of both knees
 Anteroposterior view of both hips

BMD measurements

Lumbar spine and proximal femur (mountainous and coastal areas)

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

evaluated using the WOMAC.¹³ The health-related QOL was evaluated using the EuroQOL, EQ5D¹⁴ 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 follows¹⁹: 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 $1.032 \pm 0.016 \text{ g/cm}^2$ ($\pm 1.5\%$) 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

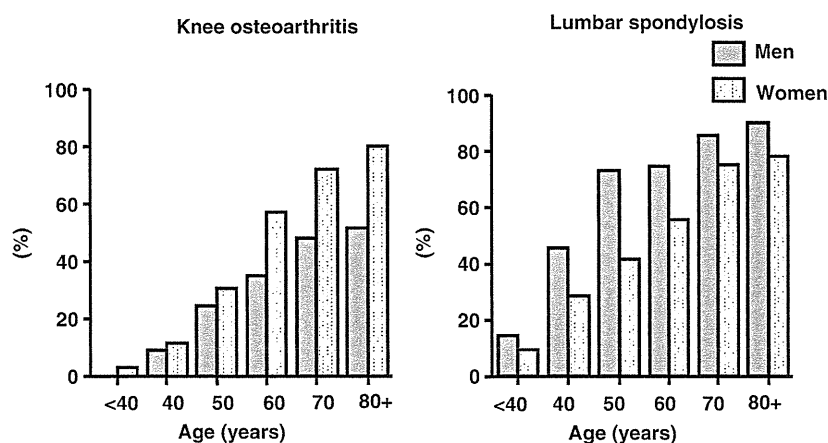


Figure 2 Prevalence of radiographic knee osteoarthritis and lumbar spondylosis, classified by age and gender

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 $<0.714 \text{ g/cm}^2$ (in case of both men and women), and femoral neck BMD $<0.546 \text{ g/cm}^2$ (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 ≥ 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,

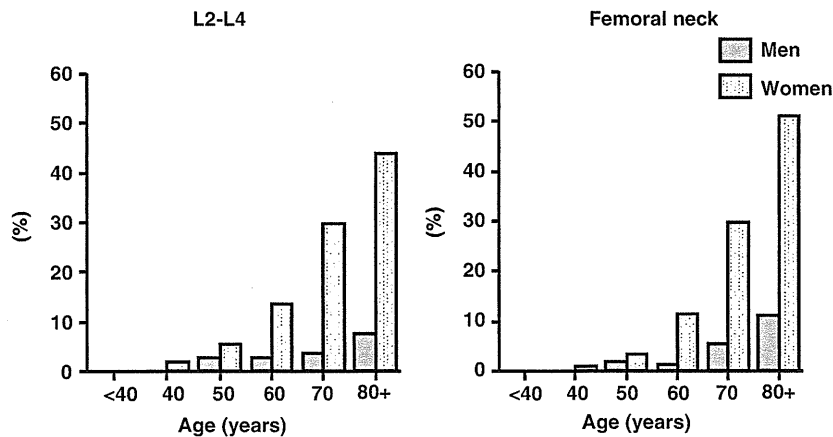


Figure 3 Prevalence of osteoporosis of the lumbar spine and femoral neck

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 men²⁵ 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.

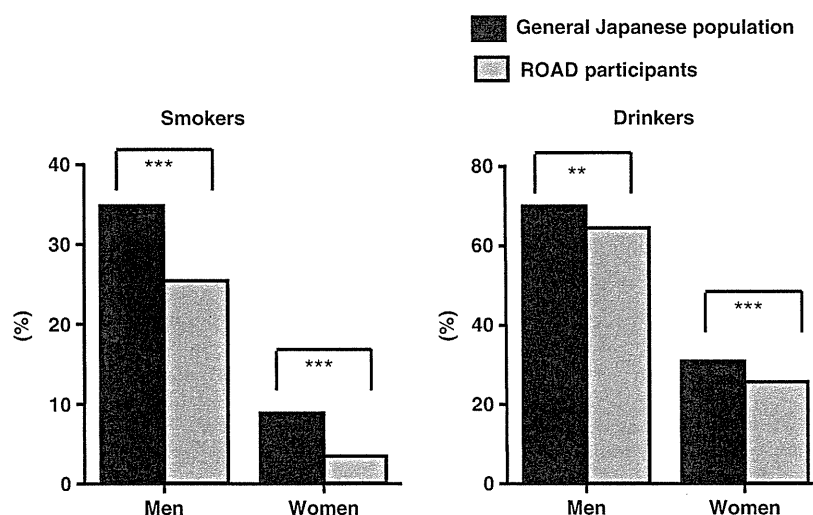
Further, BMD was measured only in the participants from the mountainous and coastal areas. The total number of participants from these two areas (1690) may be large enough to accurately estimate the incidence and evaluate risk factors. Nevertheless, regional bias should be taken into account while generalizing 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/m²) of the participants with general Japanese population

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

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

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

Funding

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

Acknowledgements

The authors wish to thank Mrs Tomoko Takijiri, Mrs Kumiko Shinou and other staff of the public office

in Hidakagawa town, and Mrs Tamako Tsutsumi, Mrs Kanami Maeda and other staff of the public office in Taiji town for their assistance in locating participants and scheduling examinations.

Conflict of interest: None declared.

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

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

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.

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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

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]/height² [m²]). 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 $\leq 75\%$ than posterior height. Biconcave appearance was where the height of the central part of the vertebra was $\leq 80\%$ 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 $\leq 80\%$ 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 $KL \geq 3$ 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].

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

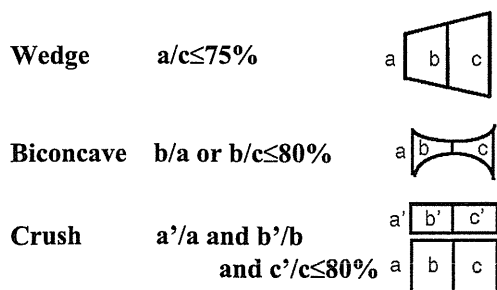


Fig. 1 Diagnostic criteria for VFXs according to the JSBMR

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

Table 1 Characteristics of participants

N	767
Age, years	69.7 \pm 10.5
Height, cm	162.8 \pm 6.7
Weight, kg	61.5 \pm 10.8
BMI, kg/m ²	23.1 \pm 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 \pm 5.5
PF	49.9 \pm 6.2
RP	50.2 \pm 6.7
BP	50.4 \pm 9.2
VT	50.4 \pm 6.3
SF	52.4 \pm 5.5
MH	54.4 \pm 5.3
RE	52.0 \pm 5.2
PCS	47.4 \pm 6.8
MCS	53.4 \pm 5.3
EQ-5D utility score	0.91 \pm 0.14

Except where indicated otherwise, values represent mean \pm 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.

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 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

* $p < 0.05$

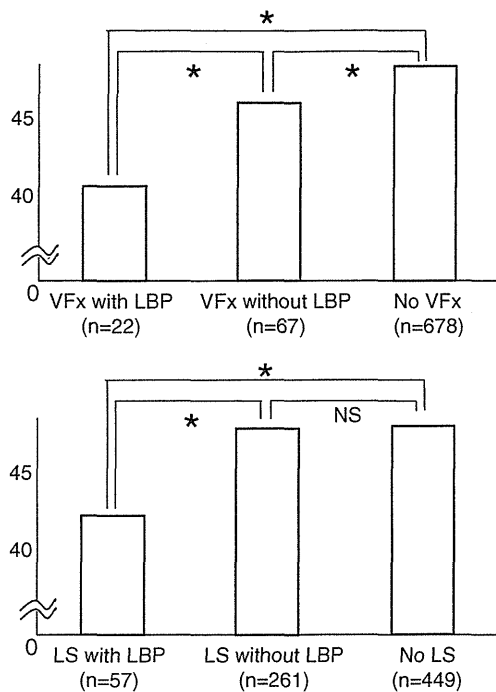


Fig. 2 Physical component summary values among subjects having VFX with LBP, VFX without LBP and no VFX, and those having lumbar spondylosis (LS) with LBP, LS without LBP and no LS. The number of subjects in each group is shown in parentheses. * $p < 0.05$ by Tukey HSD test adjustment for age and BMI

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.

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

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

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.

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

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

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

Materials and methods

Materials

Recruitment for the ROAD study has been described in detail elsewhere [13, 14]. To date, we have completed the creation of a baseline database that includes clinical and genetic information on 3,040 Japanese inhabitants (1,061 men, 1,979 women) in the age range of 23–95 years (mean 70.6 years), who were recruited from listings of resident registration in three communities. All participants provided written informed consent, and the study was conducted with the approval of the ethics committees of the University of Tokyo and the Tokyo Metropolitan Institute of

Gerontology. Participants completed an interviewer-administered questionnaire consisting of 400 items, which included questions on lifestyle, such as smoking habits, alcohol consumption, family history, past history, physical activity, reproductive variables, and health-related QOL. Anthropometric measurements included height, weight, bilateral grip strength, and body mass index (BMI), which was calculated as weight in kilograms divided by the square of height in meters. All subjects were interviewed by well-experienced orthopedists on aspects related to knee pain and low back pain, who asked, “In the past month, have you experienced knee pain on most days?” and “In the past month, have you experienced low back pain on most days?”, respectively. Those respondents who answered “yes” were defined as having pain. From the baseline data compiled on all ROAD participants, we extracted data on 1,369 Japanese women ≥ 40 years old who had completed the questionnaire comprising the Medical Outcomes Study Short Form-8 (SF-8) health survey [15], the EuroQOL (EQ-5D) [16], and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) [17, 18].

Radiographic assessment

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

Assessment instruments

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