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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)

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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

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Introduction

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

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

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

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

Materials and methods

Materials

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

Radiographic assessment

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

Assessment instruments

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

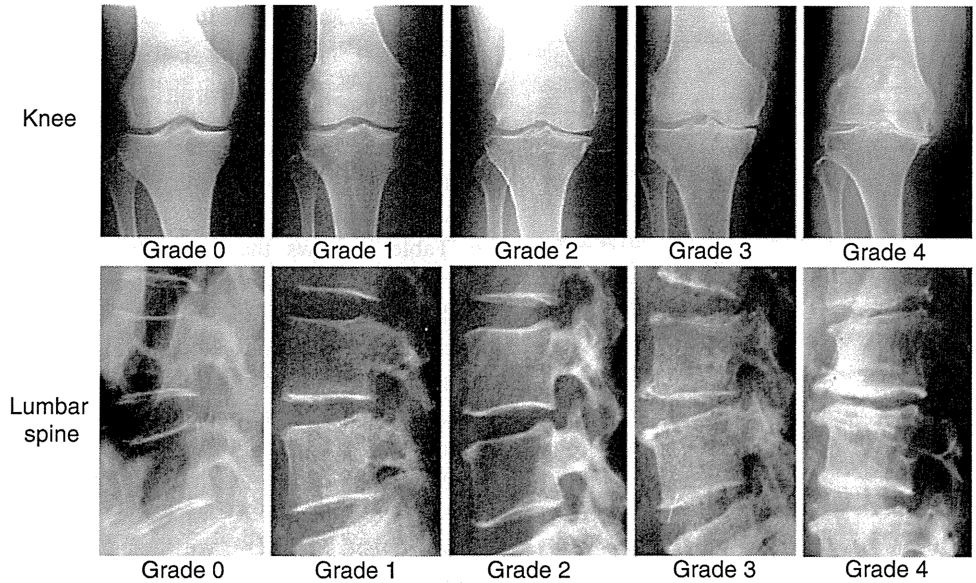

Fig. 1 Kellgren–Lawrence (KL) grade at knee and lumbar spine. *Knee*: *Grade 1* Doubtful narrowing of the joint space and possible osteophytic lipping, *Grade 2* definite osteophytes and possible narrowing of the joint space, *Grade 3* multiple moderate osteophytes, definite narrowing of the joint space,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

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

Statistical analysis

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

Results

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

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

Table 1 Characteristics of the participants

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

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

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

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

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

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

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

Discussion

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

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

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

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

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

[c] $p < 0.05$

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

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

Except where indicated otherwise, values represent the mean ± SD

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

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

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

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

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

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

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

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

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

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

This study has several limitations. First, it was a large-scaled population-based study, but the baseline data were cross-sectional, so causal relationships could not be determined. The ROAD study is a longitudinal survey that will eventually shed light on the causal relationships. Second, we only used a semi-quantitative method to assess VFx. In addition, the KL system was used for knee OA and lumbar spondylosis. The KL system is the most conventional grading system to detect the radiographic severity of knee OA, but joint space narrowing and osteophyte formation cannot be assessed separately in this categorical system. In addition, since the KL system emphasizes osteophytosis, the handling of data on lumbar spondylosis with disc space narrowing but no osteophytosis is unclear. In addition, in terms of the lumbar spine, we did not include lumbar spinal canal stenosis (LSCS), scoliosis, spondylolisthesis, or narrowing of the nerve canal in our analysis, although these changes are also associated with QOL. To determine the associations of these changes of the lumbar spine and knee with QOL, we are currently developing a computer-aided diagnostic program to enable automatic measurement of the major features of VFx, disc space narrowing, osteophytosis, LSCS, scoliosis, spondylosis, and narrowing of the nerve canal in the lumbar spine, and of joint space narrowing and osteophytosis at the knee on plain radiographs [43]. Third, we did not include the onset of VFx in the analysis, although the severity of low back pain often appears to be associated with the interval from the onset of VFx. With respect to clinical fractures, we examined the history of fracture, including vertebral fracture, in the ROAD study by self-report, and no clinical vertebral fractures occurred within 1 month prior to baseline examination. However, we could not compare radiographs of the lumbar spine at baseline examination with those before the examination as the subjects had not undergone radiography of the lumbar spine prior to that examination. We were therefore unable to assess the incidence of subclinical fracture within the month prior to the baseline examination. Both clinical and subclinical vertebral fractures are associated with lower QOL in women [44], but the association between the severity of low back pain and the interval from onset of subclinical VFx may be weaker than that for clinical VFx; consequently, the absence of data on the incidence of subclinical VFx may not strongly affect the present results.

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

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Conflict of interest statement None.

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Original article

Normal and threshold values of radiographic parameters for knee osteoarthritis using a computer-assisted measuring system (KOACAD): the ROAD study

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Abstract
Background. Although radiographic severity of the knee is commonly determined by the Kellgren-Lawrence (KL) grading scale, it does not separately assess joint space narrowing or osteophyte formation. The present study aimed to establish normal and threshold values of radiographic parameters for knee osteoarthritis (OA) using the knee osteoarthritis computer-aided diagnosis (KOACAD) measuring system on a large-scale population-based cohort of the Research on Osteoarthritis/Osteoporosis Against Disability (ROAD) population.
Methods. From a total of 3040 participants in the ROAD study, standing anteroposterior radiographs of the knee were obtained from 2975 subjects (1041 men, 1934 women) in the ROAD cohort, and 5950 knees were evaluated using the KOACAD system to obtain the medial and lateral minimum joint space width (mJSW), medial and lateral joint space area (JSA), osteophyte area (OPA), and femorotibial angle (FTA). These indices were compared with the KL scores, and cutoff values for radiographic knee OA were determined by receiver operating characteristic (ROC) curve analysis.
Results. The mean KOACAD parameters for KL = 0 were as follows: medial mJSW 3.70 mm; lateral mJSW 4.77 mm, medial JSA 125.0 mm^2, lateral JSA 140.0 mm^2, OPA 0, and FTA 176.1° in men; for women they were medial mJSW 3.26 mm, lateral mJSW 4.22 mm, medial JSA 100.9 mm^2, lateral JSA 111.0 mm^2, OPA 0, and FTA 174.9°. Threshold values for KL ≥ 2 provided by ROC curve analysis with area under the curve (AUC) > 0.7 were medial mJSW 2.8 mm and medial JSA 107.3 mm^2 in men and medial mJSW 2.7 mm in women. Those for KL ≥ 3 were medial mJSW 2.1 mm, medial JSA 81.1 mm^2, OPA 2.4 mm^2, and FTA 179.6° in men; and medial mJSW 2.1 mm, medial JSA 66.6 mm^2, OPA 2.5 mm^2, and FTA 178.1° in women. We then determined the cutoff values for medial knee OA and lateral knee OA.
Conclusions. The present study established normal and threshold values of parameters for knee OA using an automated computer-assisted program on plain radiographs.

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Introduction

Osteoarthritis (OA) is a major public health problem among the elderly that affects activities of daily living (ADL) and quality of life (QOL), leading to increased morbidity and mortality. According to the recent National Livelihood Survey by the Ministry of Health, Labor, and Welfare in Japan, OA is ranked first and fourth among the diseases that cause disabilities requiring support and long-term care, respectively.[1]

Given the increasing proportion of the elderly among the Japanese population, a comprehensive, evidence-based prevention strategy for OA is urgently needed. However, few indices have been identified that can predict the future occurrence and progression of OA. Risk factors for knee OA are known to include age, heavy weight, previous knee injury, and history of work involving overloading the knees.[2–4]

One of the reasons for the scarcity of epidemiological studies on OA might be the diagnostic criteria. Most cases of OA are radiographically determined based on a rating of grade 2 or more on the Kellgren-Lawrence (KL) grading scale.[5] The KL scale is the most conventional grading system for determining the radiographic severity of knee OA, but this categorical scale does not assess joint space narrowing or osteophyte formation separately. Accumulating evidence has shown that osteophytosis and joint space narrowing display distinct etiological mechanisms, and their progression is neither constant nor proportional.[6–8] When examining factors associated with knee OA, these two features should thus be assessed separately. In addition, other indices of knee OA on plain radiographs, such as the femorotibial angle (FTA) and joint space area, should be determined for evaluation of the severity of knee OA. However, reference values of these indices have yet to be established for a general population.

In the present study, we obtained values for medial and lateral minimum joint space width (mJSW), medial and lateral joint space area (JSA), osteophyte area (OPA), and FTA using the knee osteoarthritis computer-aided diagnosis (KOACAD) measuring system, which we developed and reported elsewhere.[9] We used it in a large-scale population-based cohort study called the Research on Osteoarthritis/Osteoporosis Against Disability (ROAD)[10,11] to establish normal reference and threshold values of radiographic parameters for knee OA.

Participants and methods

Participants

Reference values were obtained based on the results of measurements from the participants of the ROAD study, a nationwide prospective study comprising population-based cohorts established in several communities in Japan. Recruitment methods for this study have been described in detail elsewhere.[9,10] To date, we have completed creation of a baseline database that includes clinical and genetic information of 3040 inhabitants (1061 men, 1979 women) in the age range of 23–95 years (mean 70.6 years), recruited from resident registrations in three communities. All participants provided written informed consent, and the study was conducted with the approval of the ethics committees of the participating institutions.

In the present study, from among a total cohort of 3040 participants, 2975 individuals (1041 men, 1934 women) with knee radiographs that could be evaluated by the KOACAD system were selected as subjects for analysis. Among 65 dropouts in the present analysis, 29 underwent total knee arthroplasty (TKA), and 1 had unilateral knee arthroplasty (UKA). The radiographic conditions for the remaining 35 subjects were insufficient for automated analysis due to severe flexion contracture, so we excluded them from the overall analysis.

A summary of the characteristics of subjects are shown in Table 1. No significant differences in baseline characteristics were seen between the 3040 participants in the whole cohort and the 2975 subjects in the present analysis.

Table 1. Summary characteristics of participants

Characteristic	Men	Women
No. of participants	1041	1934
Age (yrs)	71.0 (10.7)	69.8 (11.3)
Height (cm)	162.5 (6.7)	149.8 (6.5)
Weight (kg)	61.3 (10.0)	51.5 (8.6)
Body mass index (kg/m^2)	23.2 (3.0)	22.9 (3.5)
Current smokers	25.7%	3.5%
Current drinkers	64.2%	25.9%

Results are the mean (SD) unless otherwise specified

Radiographic assessment

All participants underwent radiographic examination of both knees using an anteroposterior (AP) view with weight-bearing and foot-map positioning. Fluoroscopic guidance with a horizontal AP X-ray beam was used to visualize the joint space properly, and images were downloaded into digital imaging and communication in medicine (DICOM) format files. The KOACAD system has been described in detail elsewhere[9] and is only briefly summarized here. The KOACAD was programmed to measure mJSW and JSA in the medial and lateral compartments, OPA at the medial tibia, and FTA using digitized knee radiographs. Initially, correction for radiographic magnification was performed based on the image size of a rectangular metal plate.

Next, to determine the region of interest (ROI) including the tibiofemoral joint space, a vertical neighborhood difference filter was applied to identify points with high absolute values for difference of scales. The center of all points was then calculated, and the ROI was chosen. Within the ROI, the outline of the femoral condyle was designated as the upper rim of the joint space. The two ends were determined, and vertical lines from the ends were designated as the outside rims of the joint space. Outlines of anterior and posterior margins of the tibial plateau were drawn similarly to that of the femoral condyle, and the middle line between the two outlines was designated as the lower rim of the joint space (Fig. 1A). A straight regression line for the lower rim outline was then drawn, and the intersections of the lower rim outline and the regression line were designated as the inside rims.

Medial and lateral JSAs were determined as areas surrounded by the upper, lower, inside, and outside rims, as defined above. Medial and lateral mJSWs were further determined as the minimum vertical distances in the respective JSA (Fig. 1B).

To measure the osteophyte area and FTA, medial and lateral outlines of the femur and tibia were drawn. Inflection points for these outlines were then calculated. The medial outline of the tibia from the inflection point was drawn upward to the joint level, and the area that was medially prominent over the smoothly extended outline was designated the osteophyte area (Fig. 1C).

For FTA, a middle line between the medial and lateral outlines of the femur from the top of the image

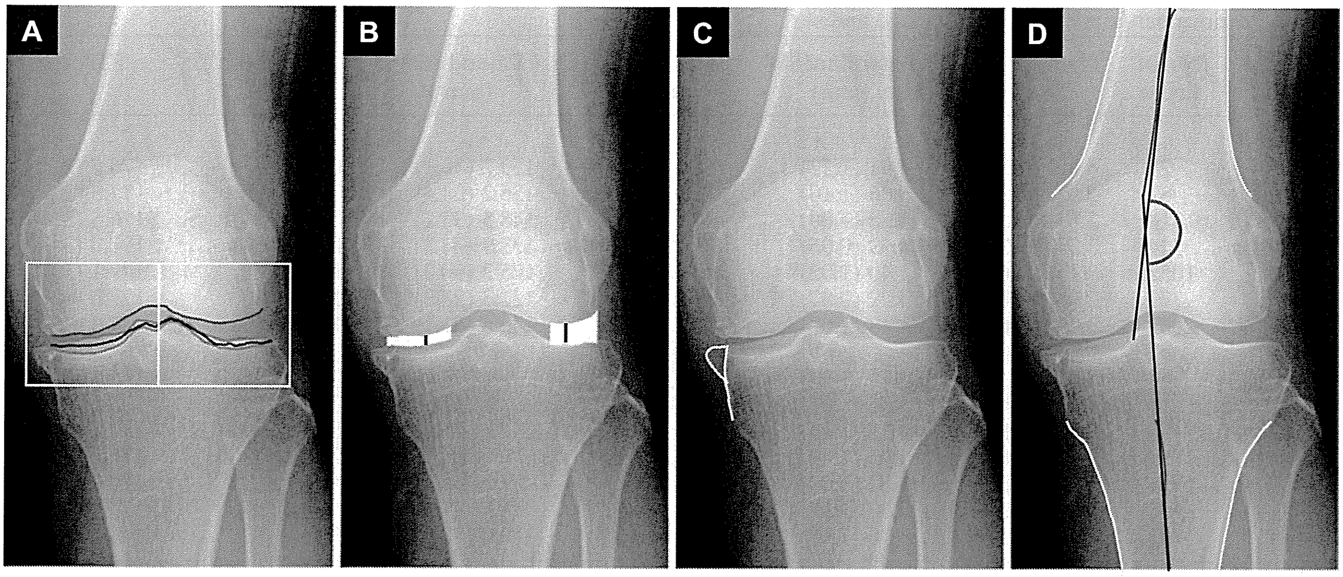

Fig. 1. Schema of image processing by the knee osteoarthritis computer-aided diagnosis (KOACAD) measuring system. **A** Outlines of anterior and posterior margins of the tibial plateau. The *middle line* between these two outlines represents the lower rim of the joint space. **B** Medial and lateral minimum joint space widths (mJSWs) as minimum vertical distances in joint space areas (JSAs). **C** Osteophyte area (area surrounded by *white lines*) determined as the medial prominence over the smoothly extended outline of the tibia. **D** Tibiofemoral angle as the lateral angle between straight regression lines (*black lines*) of the *middle lines* above in the femur and tibia. (From Oka et al.[9], with permission)

to the inflection points was drawn, and the straight regression line was determined as the axis of the femur. Similarly, the straight regression line of the middle line of the tibia from the bottom to the inflection points was designated as the axis of the tibia. The lateral angle between the two axis lines was calculated as the FTA (Fig. 1D).

This system can thus quantify the major features of knee OA on standard radiographs. Moreover, it allows objective, accurate, simple, easy assessment of the structural severity of knee OA without any manual operation in general clinical practice.

The severity of OA was radiographically determined according to the KL grading scale as follows[5]: KL0, normal joint; KL1, slight osteophytes; KL2, definite osteophytes; KL3, disc-space narrowing and large osteophytes; and KL4, bone sclerosis, joint space narrowing, and large osteophytes. In the ROAD study, joints that exhibited only joint space narrowing and no large osteophytes were graded as KL3. All radiographs were examined by a single, experienced orthopedic surgeon (S.M.) who was blinded to the clinical status of the participants.

Establishment of normal values and threshold values for parameters for knee OA

Each index determined using the KOACAD system — medial mJSW, lateral mJSW, medial JSA, lateral JSA, OPA, FTA — was compared with KL scores. First, we established normal values of these parameters using mean values for knees with KL grade 0. Cutoff values for radiographic knee OA for KL ≥ 2 and KL ≥ 3 were then determined using receiver operating characteristic (ROC) curve analysis. The present study adopted cutoff points that maximized the area under the ROC curve (AUC) as threshold values. Threshold values were determined for total OA including medial and lateral OA, and then separate threshold values were determined for medial and lateral OA. Although parameters for medial OA could be obtained separately for each sex, those for lateral OA were evaluated for the combined number of men and women, given the small number of cases with lateral OA.

Statistical analysis

All statistical analyses were performed using STATA statistical software (STATA, College Station, TX, USA). First, the Kolmogrov-Smirnov Lilliefors test was used to evaluate the normality of distribution of each variable. All parameters were confirmed to fit normal distributions (P values after Kolmogrov-Smirnov Lilliefors test: medial mJSW 0.40; lateral mJSW 0.6; medial JSA 0.37; lateral JSA 0.76; OPA 0.10; FTA 0.49). Differences in values of the parameters were tested for significance using analysis of variance (ANOVA) for comparisons among multiple groups. Trends of values

Table 2. Various parameters classified by age and sex

Age strata (years)	No. of knees	Medial mJSW (mm)	Lateral mJSW (mm)	Medial JSA (mm^2)	Lateral JSA (mm^2)	OPA (mm^2)	FTA (°)
Men							
<40	28	4.12 (0.92)	4.91 (1.22)	141.6 (27.3)	153.2 (30.1)	0	176.5 (2.2)
40–49	82	3.67 (0.75)	5.06 (1.10)	132.9 (27.9)	156.2 (34.4)	0.40 (1.98)	177.5 (2.4)
50–59	214	3.63 (0.75)	4.88 (1.06)	124.1 (26.9)	148.5 (33.1)	0.30 (1.51)	176.5 (3.2)
60–69	334	3.37 (0.93)[a]	4.59 (0.96)[bc]	113.9 (28.4)[abc]	138.9 (28.8)[bc]	0.96 (3.60)	177.0 (3.0)
70–79	1052	3.13 (0.96)[abcd]	4.40 (1.02)[bc]	102.5 (26.7)[abcd]	125.7 (30.3)[abcd]	1.35 (4.68)[c]	177.1 (3.3)
80+	372	2.94 (0.98)[abcd]	4.22 (0.87)[abcd]	97.2 (27.4)[abcd]	121.3 (28.0)[abcd]	1.31 (4.06)	177.0 (4.0)
Total	2082	3.22 (0.96)	4.48 (1.02)	107.3 (29.0)	130.6 (31.7)	1.12 (4.07)	177.0 (3.3)
Women							
<40	62	3.37 (0.61)	4.31 (1.23)	106.3 (24.0)	116.8 (32.6)	0.18 (1.25)	175.6 (3.0)
40–49	210	3.22 (0.64)	4.36 (1.01)	104.0 (22.2)	116.9 (25.8)	0.46 (2.09)	175.5 (2.7)
50–59	418	3.03 (0.78)	4.23 (1.15)	97.5 (26.2)	112.3 (28.3)	0.96 (2.87)	175.8 (4.0)
60–69	762	2.80 (0.98)[abc]	4.03 (1.09)[b]	89.8 (28.7)[abc]	106.6 (28.7)[bc]	2.33 (6.39)	176.4 (3.8)
70–79	1764	2.52 (0.92)[abcd]	3.87 (1.00)[bcd]	79.5 (26.3)[abcd]	99.4 (26.8)[abcd]	4.60 (11.2)[abcd]	176.9 (4.2)[bc]
80+	652	2.32 (0.95)[abcde]	3.80 (1.08)[abcd]	77.4 (26.9)[abcd]	97.9 (28.0)[abcd]	6.39 (12.70)[abcde]	177.1 (4.6)[bc]
Total	3868	2.65 (0.95)[#]	3.96 (1.07)[#]	84.9 (28.0)[#]	103.2 (28.2)[#]	3.76 (9.87)[#]	176.6 (4.1)[#]

Results are the mean (SD)
mJSW, minimal joint space width; JSA, joint space area; OPA, osteophyte area; FTA, femoro-tibial angle; KL grade: Kellgren-Lawrence grade
[a] Significantly different from those of the group <40 years ($P < 0.05$)
[b] Significantly different from those of the group in their 40s ($P < 0.05$)
[c] Significantly different from those of the group in their 50s ($P < 0.05$)
[d] Significantly different from those of the group in their 60s ($P < 0.05$)
[e] Significantly different from those of the group in their 70s ($P < 0.05$)
[#] Significantly different from those of men ($P < 0.001$)

according to the KL grade were tested using the Jonckheere-Terpstra trend test. Scheffe's least significant difference test was then used for pairs of groups.

Results

The mean values for mJSW, JSA, OPA, and FTA, classified by sex, are shown in Table 2. The values for medial and lateral mJSW, medial and lateral JSA, OPA, and FTA all differed significantly between the sexes ($P < 0.001$). The mean values for medial mJSW, JSA, and FTA were significantly greater in men than in women ($P < 0.001$). By contrast, the OPA values in both knees were significantly lower in men than in women ($P < 0.001$).

The mean values for mJSW, JSA, OPA, and FTA classified by age are also shown in Table 2. The medial mJSW for men in their sixties was significantly smaller than that for men <40 years; and that for men ≥70 years was significantly smaller than that of men <70 years ($P < 0.05$). Lateral mJSW for subjects in their sixties and seventies was significantly smaller than that for subjects in their forties and fifties ($P < 0.05$). Medial JSA for subjects in their sixties was significantly smaller than that for subjects <60 years old ($P < 0.05$); and that for subjects ≥70 years was significantly smaller than that for subjects <70 years ($P < 0.05$). Lateral JSA for subjects in their sixties was significantly smaller than that for subjects in their forties and fifties ($P < 0.05$); and that for subjects ≥70 years was significantly smaller than that for subjects <70 years ($P < 0.05$). No significant differences in OPA or FTA were seen according to age in men except for OPA in subjects between their fifties and seventies. In women, the medial mJSW for subjects in their sixties was significantly smaller than that for subjects <60 years ($P <0.05$); that for women in their seventies was significantly smaller than that for subjects <70 years ($P < 0.05$); and that for women ≥80 years was significantly smaller than that of subjects <80 years ($P < 0.05$). The lateral mJSW for subjects in their sixties was significantly smaller than that for subjects in their forties ($P < 0.05$); that for subjects in their seventies was significantly smaller than that for subjects in their forties, fifties, and sixties ($P < 0.05$); and that for subjects ≥80 years was significantly smaller than that for subjects <70 years ($P < 0.05$). The medial JSA and lateral JSA showed trends with age similar to those of men. However, the mean OPA was significantly larger in women ≥70 years than in younger women ($P < 0.05$), and the FTA was significantly larger for subjects ≥70 years than for women in their forties and fifties ($P < 0.05$).

Table 3 shows mean values for mJSW, JSA, OPA, and FTA classified by KL grade. All values increased significantly according to the severity of the KL grade (P for trends < 0.0001). Regarding differences in the above-mentioned indices, values for medial mJSW and

Table 3. Various parameters classified by Kellgren-Lawrence grade

KL grade	Proportion of knees (%)	Medial mJSW (mm)	Lateral mJSW (mm)	Medial JSA (mm^2)	Lateral JSA (mm^2)	OPA (mm^2)	FTA (°)
Men							
KL0	24.4	3.70 (0.77)	4.77 (1.01)	125.0 (27.1)	140.0 (33.6)	0	176.1 (2.6)
KL1	38.4	3.40 (0.76)[a]	4.50 (0.93)[a]	109.8 (23.5)[a]	128.9 (29.0)[a]	0.48 (2.24)	176.6 (2.7)
KL2	28.5	3.02 (0.78)[ab]	4.38 (1.02)[a]	99.3 (22.5)[ab]	125.1 (29.8)[a]	1.08 (3.25)[ab]	177.5 (3.1)[ab]
KL3	6.3	2.10 (1.00)[abc]	4.06 (1.40)[abc]	84.1 (31.3)[abc]	129.5 (38.2)[a]	5.37 (8.70)[abc]	178.1 (4.5)[ab]
KL4	2.4	0.79 (0.84)[abcd]	4.04 (1.12)[ab]	44.7 (32.7)[abcd]	137.3 (39.5)	12.05 (10.36)[abcd]	184.2 (6.2)[abcd]
Total	100.0	3.22 (0.96)	4.48 (1.02)	107.3 (29.1)	130.8 (31.8)	1.12 (4.08)	177.0 (3.3)
Women							
KL0	13.9	3.26 (0.65)	4.22 (1.08)	100.9 (23.7)	111.0 (29.4)	0	174.9 (2.9)
KL1	30.6	2.95 (0.73)[a]	3.95 (0.99)[a]	89.7 (24.3)[a]	101.3 (26.0)[a]	0.68 (2.26)	175.6 (3.0)[a]
KL2	38.3	2.66 (0.73)[ab]	3.93 (0.96)[a]	84.5 (23.5)[ab]	100.3 (25.5)[a]	3.39 (6.67)[ab]	176.6 (3.3)[ab]
KL3	13.1	1.85 (0.92)[abc]	3.91 (1.20)[a]	73.3 (27.4)[abc]	106.5 (30.2)[bc]	11.15 (17.54)[abc]	178.7 (4.8)[abc]
KL4	4.1	0.67 (1.02)[abcd]	3.83 (1.68)[a]	34.6 (34.8)[abcd]	112.1 (43.7)[bc]	19.70 (20.65)[abcd]	183.8 (7.1)[abcd]
Total	100.0	2.65 (0.94)[#]	3.97 (1.06)[#]	84.9 (27.9)[#]	103.4 (28.1)[#]	3.76 (9.90)[#]	176.6 (4.1)[#]

Results are the mean (SD)
[a]Significantly different from those of KL0 ($P < 0.05$)
[b]Significantly different from those of KL1 ($P < 0.05$)
[c]Significantly different from those of KL2 ($P < 0.05$)
[d]Significantly different from those of KL3 ($P < 0.05$)
[#]Significantly different from those of men ($P < 0.05$)

medial JSA in both sexes tended to be smaller with increasing KL grade ($p < 0.05$). Values for OPA and FTA in both sexes were significantly larger in the KL 2–4 group than in the KL 0–1 group ($P < 0.05$). Age differences in values of lateral mJSW and JSA were smaller than those for medial mJSW and JSA.

We performed ROC curve analysis to identify threshold values of these indices to determine the knee OA defined by KL ≥ 2 and KL ≥ 3. ROC curve analysis provided threshold values of KL ≥ 2 and KL ≥ 3 in OA parameters for the two knees (Table 4). Threshold values of KOACAD parameters for KL ≥ 2 with AUC > 0.7 were medial mJSW 2.8 mm and medial JSA 107.3 mm^2 in men and medial mJSW 2.7 mm in women. Those for KL ≥ 3 were medial mJSW 2.1 mm, medial JSA 81.1 mm^2, OPA 2.4 mm^2, and FTA 179.6° in men; and they were medial mJSW 2.1 mm, medial JSA 66.6 mm^2, OPA 2.5 mm^2, and FTA 178.1° in women. In contrast, the AUC of the lateral mJSW and lateral JSA for KL ≥ 2 and KL ≥ 3 in OA parameters was near 0.5, meaning that the capacity of these parameters to distinguish diseased knees from normal knees was low.

In addition, we provided threshold values for parameters for both the medial and lateral knee OA using ROC curve analysis (Table 4). Medial OA comprised 97.8% of total OA cases, with the lateral type making up the remaining 2.2%. Although most threshold values for medial OA were similar to those for total OA, the AUC values for parameters of medial OA (e.g., medial mJSW, medial JSA) were higher than for total OA. In contrast, for lateral OA, the AUC values for lateral mJSW and lateral JSA for KL ≥ 2 and KL ≥ 3 in OA parameters were higher than those for total OA, which were near 0.99, meaning that the capacity of these parameters to distinguish disease states from the normal population was high.

Discussion

We have reported elsewhere the automated computer-assisted program KOACAD, which can accurately measure values of mJSW, JSA, OPA, and FTA.[9] In the previous report,[9] we clarified that KOACAD allows accurate, easy assessment of the structural severity of knee OA without any manual operation. The present study applied this system to baseline data from the ROAD study, obtaining normal and threshold values of the above-mentioned indices for objective diagnosis of knee OA.

In the present study, we first established normal values for mJSW, JSA, OPA, and FTA using mean values of these parameters for knees with KL grade 0. The mean values were medial mJSW 3.70 mm, lateral mJSW 4.77 mm, medial JSA 125.0 mm^2, lateral JSA 140.0 mm^2, OPA 0, and FTA 176.1° in men; and medial mJSW 3.26 mm, lateral mJSW 4.22 mm, medial JSA 100.9 mm^2, lateral JSA 111.0 mm^2, OPA 0, and FTA 174.9° in women. All these indices except OPA were significantly lower in women than in men, suggesting that the values are influenced by differences in stature. We concluded that normal and threshold values for knee OA should be established for each sex.

The JSW has been recommended as a candidate index for progression of knee OA,[12] but few data

Table 4. Threshold values of various parameters, by Kellgren-Lawrence grades 2 and 3

Parameter	Threshold value	AUC	Sensitivity	Specificity (%)
Total				
KL ≥ 2				
Men				
Medial mJSW (mm)	2.8	0.726	58.4	76.8
Lateral mJSW(mm)	4.3	0.566	52.3	59.0
Medial JSA (mm^2)	107.3	0.715	71.0	60.3
Lateral JSA (mm^2)	115.5	0.551	39.5	68.2
OPA (mm^2)	1.0	0.599	23.9	95.5
FTA (°)	178.5	0.633	42.7	79.3
Women				
Medial mJSW (mm)	2.7	0.730	63.7	72.5
Lateral mJSW(mm)	4.3	0.521	66.4	38.5
Medial JSA (mm^2)	85.9	0.654	64.5	59.9
Lateral JSA (mm^2)	79.2	0.509	19.8	83.4
OPA (mm^2)	1.0	0.691	44.3	92.4
FTA (°)	177.4	0.664	48.6	77.0
KL ≥ 3				
Men				
Medial mJSW (mm)	2.1	0.875	73.6	92.1
Lateral mJSW(mm)	4.3	0.608	65.2	54.3
Medial JSA (mm^2)	81.1	0.800	58.4	88.9
Lateral JSA (mm^2)	135.7	0.522	50.0	60.1
OPA (mm^2)	2.4	0.739	52.8	93.5
FTA (°)	179.6	0.702	52.5	85.5
Women				
Medial mJSW (mm)	2.1	0.842	65.3	92.0
Lateral mJSW(mm)	2.5	0.507	15.7	93.0
Medial JSA (mm^2)	66.6	0.717	48.7	83.2
Lateral JSA (mm^2)	116.4	0.562	38.8	73.0
OPA (mm^2)	2.5	0.768	66.1	82.2
FTA (°)	178.1	0.744	64.6	76.3
Medial OA				
KL ≥ 2				
Men				
Medial mJSW (mm)	2.8	0.728	58.5	76.8
Lateral mJSW(mm)	4.3	0.560	51.7	59.0
Medial JSA (mm^2)	107.3	0.717	71.3	60.3
Lateral JSA (mm^2)	115.5	0.545	38.8	68.2
OPA (mm^2)	1.2	0.599	23.9	95.5
FTA (°)	178.5	0.639	43.2	79.3
Women				
Medial mJSW (mm)	2.7	0.732	63.9	72.5
Lateral mJSW(mm)	5.4	0.505	92.9	10.9
Medial JSA (mm^2)	85.9	0.655	64.7	59.9
Lateral JSA (mm^2)	97.9	0.505	56.1	46.3
OPA (mm^2)	1.0	0.693	44.7	92.4
FTA (°)	177.4	0.677	49.9	77.0
KL ≥ 3				
Men				
Medial mJSW (mm)	2.1	0.888	76.3	90.4
Lateral mJSW(mm)	4.3	0.598	64.2	54.4
Medial JSA (mm^2)	81.1	0.809	59.0	89.0
Lateral JSA (mm^2)	135.3	0.536	52.6	59.7
OPA (mm^2)	2.4	0.741	53.2	93.4
FTA (°)	179.6	0.719	54.0	85.5
Women				
Medial mJSW (mm)	2.1	0.854	66.6	92.2
Lateral mJSW(mm)	4.6	0.512	29.7	75.8
Medial JSA (mm^2)	66.6	0.727	49.4	83.4
Lateral JSA (mm^2)	116.5	0.587	40.8	72.8
OPA (mm^2)	2.5	0.774	67.3	82.1
FTA (°)	178.1	0.771	67.9	76.0

Table 4. *Continued*

Parameter	Threshold value	AUC	Sensitivity	Specificity (%)
Lateral OA				
KL ≥ 2				
Men and women				
Medial mJSW (mm)	2.1	0.683	43.1	92.4
Lateral mJSW(mm)	2.2	0.995	100.0	98.1
Medial JSA (mm^2)	75.7	0.664	50.0	84.2
Lateral JSA (mm^2)	69.7	0.990	100.0	95.4
OPA (mm^2)	1.2	0.626	30.6	93.8
FTA (°)	173.3	0.795	65.3	81.5
KL ≥ 3				
Men and women				
Medial mJSW (mm)	2.1	0.680	46.0	92.0
Lateral mJSW(mm)	2.2	0.992	100.0	97.0
Medial JSA (mm^2)	75.1	0.638	48.7	84.5
Lateral JSA (mm^2)	69.1	0.987	100.0	95.6
OPA (mm^2)	4.8	0.706	43.2	96.5
FTA (°)	173.3	0.805	64.9	80.8

AUC, area under the curve

regarding normal values have been accumulated.[13] Gensburger et al. showed that the mean medial and lateral JSW in women were 5.1 mm and 6.0 mm, respectively,[13] suggesting that those values in Caucasian populations may be larger than our results in women; no normal values for men were available. In addition, although evaluations of knee alignment are known to be useful for diagnosing arthritic conditions affecting the knee joint and also serve as a guide for conservative management and surgical planning,[14,15] few reports have shown normal values of FTA along with JSA and OPA.

Koshino measured the FTA of 85 knees in men and 97 knees in women aged 25–35 years and reported normal FTA values of 178° in men and 176° in women.[16] These results seem broadly consistent with our results, although no sex differences were apparent in our study, with values of 176° for both men and women. In any case, this represents the first report of reference values for the above-mentioned parameters using a population-based cohort. The results may thus be useful for diagnosing knee OA. Furthermore, by a longitudinal follow-up of the present cohort, these parameters would be expected to predict the progress of knee OA.

We then determined the threshold values for knee OA using ROC curve analysis. In this analysis, we regarded parameters with AUC > 0.7 as good indices for features of knee OA according to a previous report.[17] For KL ≥ 2, threshold values of KOACAD parameters with AUC > 0.7 were only the mJSW in men and women and the medial JSA in men. AUCs > 0.7 on ROC curve analysis means that the threshold of parameters might show good capacity for accurate diagnosis of the disorder in question. In contrast, AUCs of threshold values of parameters regarding the lateral region (i.e., KL ≥ 2; 0.566 for lateral mJSW 4.3 mm, 0.551 for lateral JSA 115.5 mm^2 in men; 0.521 for lateral mJSW 4.3 mm, 0.509 for lateral JSA 79.2 mm^2 in women) seem insufficient as indicators for knee OA. In contrast, for KL ≥ 3, OPA and FTA seem to represent good predictors with satisfactory AUCs. These results suggest that such parameters are more useful in severe knee OA than in mild knee OA.

We also tried to determine threshold values for medial knee OA and lateral knee OA. Because most cases of knee OA were medial knee OA (97.8%), the above-mentioned threshold values were considered applicable for medial OA. Conversely, in the diagnosis for lateral OA, for both KL ≥ 2 and KL ≥ 3, threshold values for medial mJSW and medial JSA were no longer parameters with good predictive capacity. By contrast, AUCs of threshold values for parameters of the lateral region (KL ≥ 2: 0.995 for lateral mJSW 2.2 mm, 0.990 for lateral JSA 69.7 mm^2; KL ≥ 3: 0.992 for lateral mJSW 2.2 mm, 0.987 for lateral JSA 69.1 mm^2) were preferable as good predictors. Similar to medial knee OA, for KL ≥ 3 the OPA and FTA seem to represent good predictors with satisfactory AUC. These results suggest that parameters at the medial side are useful in medial knee OA, and parameters at the lateral side are useful in lateral knee OA. However, evaluation of lateral OA was performed in only 65 participants (2.2%), so we could not analyze data for men and women separately. Regarding lateral OA and threshold KOACAD parameters, further investigation is warranted.

On the other hand, discrepancies between continuous values obtained from the KOACAD system and categorical scales such as the KL scale might add to the limitations of the KL grading scale. Most previous studies have been performed in patients with knee OA defined by a KL score; but utilizing this categorical scale at the diagnosis of OA seems to result in the loss of a considerable amount of information, as the contribution of joint space narrowing and osteophytes is relatively small. Even though these indices are linear and constant in number, joint space narrowing is simply categorized as mild or severe and osteophytes as slight, definite, or large. In addition, the optimal method for handling joints with severe joint space narrowing but no osteophyte formation is unclear.

One solution to such problems might be found in a radiographic atlas of individual features published by the Osteoarthritis Research Society International (OARSI).[18] OARSI proposed a new grading scale in which joint space narrowing and osteophyte formation at the medial and lateral tibiofemoral compartments on radiographs should be evaluated separately. Several studies have evaluated the severity of joint space narrowing and osteophytes in the osteoarthritic knee utilizing the OARSI scale,[19] although these studies did not assess distinct features of knee OA such as joint space narrowing, osteophyte formation, or joint angulation in one sitting. To the best of our knowledge, no quantitative assessment systems for osteophytes have been described other than in the KOACAD,[9] so the present study is the first to assess threshold values for knee OA in a population-based cohort.

Unlike categorical methods for grading the severity of knee OA (e.g., KL or OARSI scales), KOACAD enables measurement of independent parameters for knee OA. We have already confirmed that low medial mJSW and high FTA are associated with the presence of knee pain, unlike lateral mJSW or an osteophyte area.[9] These accurate and continuous parameters obtained by KOACAD might be candidates for predictors of rapid progress from mild knee OA. These parameters might also be helpful for assessing risk factors for the occurrence of OA. We assumed that 25.3 million people (8.6 million men, 16.7 million women) ≥40 years would be affected by radiographic knee OA, and 7.8 million people (2.2 million men, 5.6 million women) ≥40 years would be affected by knee OA with knee pain.[10] Preventive strategies for OA are certainly in urgent demand. At the planning stage for the strategies against knee OA, the provision of accurate, objective, quantitative indices to measure outcomes seems highly important.

However, some limitation might apply to automated systems for all knee OA. First, as we stated, the number of cases with lateral knee OA was small for accurate determination of thresholds. Second, with radiographs of cases showing severe flexion contracture of the knee (>20°), the KOACAD system failed to measure parameters automatically. However, the system includes a manual mode, and in such cases orthopedic specialists can obtain values by manual measurement.

We believe this system may not only be useful for objective evaluation of knee OA in daily clinical practice or population-based epidemiological studies, it also acts as a proper surrogate measure for the development of disease-modifying drugs for OA. We hope in the future that this system will be applied worldwide to develop international criteria and for the diagnosis and treatment of knee OA.

Conclusion

We have established normal and threshold values of parameters for knee OA using an automated computer-assisted program, KOACAD, on plain radiographs.

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ORIGINAL ARTICLE

Predictors of residual symptoms in lower extremities after decompression surgery on lumbar spinal stenosis

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Abstract Leg pain/numbness and gait disturbance, two major symptoms in the lower extremities of lumbar spinal stenosis (LSS), are generally expected to be alleviated by decompression surgery. However, the paucity of information available to patients before surgery about specific predictors has resulted in some of them being dissatisfied with the surgical outcome when the major symptoms remain after the procedure. This prospective, observational study sought to identify the predictors of the outcome of a decompression surgery: modified fenestration with restorative spinoplasty. Of 109 consecutive LSS patients who underwent the decompression surgery, 89 (56 males and 33 females) completed the 2 year follow-up. Both leg pain/numbness and gait disturbance determined by the Japanese Orthopedic Association scoring system were significantly improved at 2 years after surgery compared to those preoperative, regardless of potential predictors including gender, preoperative presence of resting numbness in the leg, drop foot, cauda equina syndrome, degenerative spinal deformity or myelographic filling defect, or the number of decompressed levels. However, 27 (30.3%) and 13 (14.6%) patients showed residual leg pain/numbness and gait disturbance, respectively. Among the variables examined, the preoperative resting numbness was associated with residual leg pain/numbness and gait disturbance, and the preoperative drop foot was associated with residual gait disturbance, which was confirmed by logistic regression analysis after adjustment for age and gender. This is the first study to identify specific predictors for these two remaining major symptoms of LSS after decompression surgery, and consideration could be given to including this in the informed consent.

Keywords Lumbar spinal stenosis · Decompression surgery · Outcome · Predictor

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Introduction

Lumbar spinal stenosis (LSS) is a degenerative disorder causing neurological symptoms in the lower extremities such as leg pain/numbness and gait disturbance, both of which dramatically deteriorate the patients' quality of life [3, 4, 17]. With elderly populations growing worldwide, degenerative LSS has become the most frequent indication for spine surgery [12]. The most common surgery is decompression of the lumbar spine, which is performed mainly to reduce the above symptoms in the lower extremities. In fact, a prospective study revealed that the surgery generally resulted in a more preferable greater outcome than non-surgical treatments in the LSS patients [20]. However, about 20–40% of patients have been reported to be dissatisfied with the result due to residual symptoms [1, 8, 9]. To avoid the discrepancy between a patient's expectations and actual surgical outcome, a surgeon should preoperatively inform the patient in detail of the possible post-surgery outcome of the major symptoms such as leg pain/numbness and gait disturbance.

There have been several reports on the factors that could predict the outcome of LSS surgeries [7–9, 15, 19]; however, some of the surgeries included arthrodesis in addition to decompression. Furthermore, the outcomes were evaluated using several validated measures, so that they covered a broad range including low back pain, psychological status, patients' satisfaction, quality of life, etc. other than symptoms in the lower extremities. Hence, the predictors identified are rather ambiguous such as the presence of other comorbidities, patient's assessment of his/her health, subclinical vascular factors and illness behavior. Since little has been known about the specific predictors of outcomes in the lower extremities after decompression surgery, this study sought to identify the factors associated with two major symptoms in the lower extremities of LSS patients: leg pain/numbness and gait disturbance, after a minimally invasive decompression surgery.

Materials and methods

Patients

Consecutive patients, who were blinded to the study, were entered into this prospective observational study from January 2000 through December 2002. Symptoms of leg pain/numbness and/or gait disturbance in LSS patients, which did not respond to conservative therapies for more than 3 months, were considered to be indications for the decompression surgery [10]. The LSS was confirmed by plain radiographs, magnetic resonance imaging and myelography followed by contrast-enhanced computed tomography scan. The patients with severe spinal deformity (spondylolisthesis with Meyerding grades ≥II or lumbar scoliosis with Cobb angle >20 degrees), spondylolysis, post-traumatic stenosis or re-stenosis after prior decompression surgery were excluded, because they were indicated for an additional arthrodesis surgery. A total of 109 patients who met the criteria underwent our original decompression surgery called modified fenestration with restorative spinoplasty [11]. They were allowed to sit up and walk on the 1st or 2nd postoperative day with a soft lumbar support. Examinations were performed preoperatively and at 2 years after surgery. The study was conducted with the approval of the institutional review board (IRB) and all participants (blinded) provided written informed consent.

Data elements

The severity of leg pain/numbness or gait disturbance was evaluated as four grades according to the Japanese Orthopedic Association (JOA) scoring system [5]: 0 (none), 1 (occasionally mild), 2 (always present or sometimes severe) and 3 (always severe) for leg pain/numbness; and 0 (none), 1 (able to walk >500 m with pain/numbness/weakness), 2 (unable to walk 500 m due to pain/numbness/weakness) and 3 (unable to walk 100 m due to pain/numbness/weakness) for gait disturbance. The presence of a residual symptom was defined as a JOA score of 0 or 1 at 2 years after surgery, regardless of the preoperative score. In addition, a score of 2 after 2 years and of 2 or 3 preoperatively were also regarded as the presence of a residual symptom. Potential predictors of outcome included age, gender, preoperative presence of resting numbness in the leg, drop foot [manual muscle test (MMT) score below 3 out of 5 in the tibialis anterior and/or peroneal muscle], cauda equina syndrome (urinary retention, perineal anesthesia or symptoms in bilateral lower extremities), degenerative spinal deformity (spondylolisthesis with more than 5% anterior slippage by the Taillard method [16] and/or lumbar scoliosis with more than 10 degrees of Cobb angle) on plain radiographs, a complete filling defect on myelography in the standing position and the number of decompressed levels. Radiographic findings were independently evaluated by three spine surgeons and were determined with the agreement of at least two of them.

Analyses

Statistical analyses were performed using the SPSS 16.0J for Windows. A P value of <0.05 was considered to be statistically significant and all reported P values were two sided. Paired t test was used to examine the difference between the preoperative and postoperative JOA scores. Association of age, gender, preoperative presence of the above findings or the number of decompressed levels with residual leg pain/numbness or gait disturbance was evaluated by chi-square test in the stratified subgroups. Logistic regression analysis was performed to estimate odds ratio (OR) and the associated 95% confidence interval (CI) after adjustment for age and gender.

Results

Comparison of preoperative and postoperative scores

Of the 109 patients enrolled, 101 (93%) could be followed postoperatively for 2 years. The reasons for the eight dropouts were two deaths from lung cancer and heart