evaluated using the WOMAC.[13] The health-related QOL was evaluated using the EuroQOL, EQ5D[14] and the SF-8.[15] The study staff recorded all the medications administered and their doses. Physical activity was quantified using the PASE.[16]

Dietary assessment

Dietary assessment was made using a BDHQ, and the dietary intakes of nutrients during the previous month were determined. Each participant received a questionnaire that included detailed explanations. Well-trained interviewers clarified any unclear sections in the questionnaire, which was to be completed by the participants at their leisure. The BDHQ is a four-page structured questionnaire that includes questions about the frequency of consumption of 80 principal foods. The serving sizes of the foods are described as normal portions, i.e. the standard weight and volume of servings commonly consumed by the general Japanese population. The BDHQ was modified from a comprehensive, 16-page version of a validated self-administered diet history questionnaire.[17] A total of 141 components, including dietary energy and nutrient intakes, were calculated using an *ad hoc* computer algorithm for the BDHQ.

Anthropometric measurements

Anthropometric factors were measured by well-trained medical nurses. The height and weight of the participants at age 25 years were also noted. BMI [weight in kilograms/(height in metres)^2] was calculated on the basis of the current height and weight.

Visual and neuromuscular function

Visual acuity was assessed by the Landolt ring test. Walking speed was determined by recording the time taken by a subject to walk 6 m at the fastest possible speed. The time required for tandem walking across a 6-m long and 20-cm wide path was used to determine balance. The ability to rise from a chair without using the arms (chair stand) and the ability to perform five chair stands was evaluated; the time required to complete the tasks was noted.

Biochemical measurements

Blood and urine samples were obtained from each participant for biochemical and genomic examinations. Urinary protein, occult blood, sugar and urobilinogen were tested using disposable reagent strips (uro-hema-combi sticks; Siemens Medical Solutions Diagnostics, Tokyo, Japan). Residual blood, plasma, serum and urine specimens were processed and stored in a deep freezer (–80°C). DNA was extracted from stored whole-blood specimens, and biochemical markers of bone turnover and cartilage will be measured using these stored serum and urine samples.

Medical history

Medical history was obtained by experienced orthopaedic surgeons (S.M. and H.O.). To quantify cognitive function, the participants were instructed to complete the modified Mini-Mental Status Examination—Japanese version.[18] Physicians explained any unclear sections of this questionnaire to the participants and assessed the participants' cognitive status on the basis of the completed questionnaire.

Radiographic assessment

The severity of OA was radiographically determined according to the Kellgren–Lawrence (KL) grading system as follows[19]: KL0—normal joint; KL1—slight osteophytes; KL2—definite osteophytes; KL3—disc-space narrowing and large osteophytes; and KL4—bone sclerosis, disc-space narrowing and large osteophytes. In the ROAD study, joints that exhibited only disc-space narrowing and no large osteophytes were graded as KL3. The radiographs were examined by a single, experienced orthopaedic surgeon (S.M.), who was blinded to the clinical status of the participants. If at least one knee joint was graded as KL2 or higher, the participant was diagnosed with radiographic knee OA. Similarly, if at least one intervertebral joint of the lumbar spine was graded as KL2 or higher, the participant was diagnosed with radiographic lumbar spondylosis.

BMD measurement

In the mountainous and coastal areas, the BMD of the lumbar spine and proximal femur was measured using dual energy X-ray absorptiometry (DXA) (Hologic Discovery; Hologic, Waltham, MA, USA) during the baseline examination. Another BMD measurement was scheduled for the second examination.

To maintain the quality of measurement, the same DXA equipment was used, and the same spine phantom was scanned daily to monitor the machine's performance in study populations from different regions. The BMD of the phantom was adjusted to $1.032 \pm 0.016\,g/cm^2$ ($\pm 1.5\%$) during all examinations. In addition, to exclude inter-observer variability, the same physician (N.Y.) examined all participants. In another study, N.Y. had measured the intra-observer variability in both *in vitro* and *in vivo* experiments using Lunar DPX.[20] In the case of the *in vitro* experiment, the coefficient of variance (CV) for the BMD of the L2–L4 vertebrae was 0.35%. In the case of the *in vivo* experiments, which were performed on five male volunteers, the CVs for the BMDs of the L2–L4 vertebrae, the proximal femur, Ward's triangle and the trochanter were 0.61–0.90, 1.02–2.57, 1.97–5.45 and 1.77–4.17%, respectively.

OP was defined on the basis of the World Health Organization (WHO) criteria; specifically, it was diagnosed when the BMD T-scores were lower than the mean lumbar peak bone mass minus 2.5 SDs.[21]

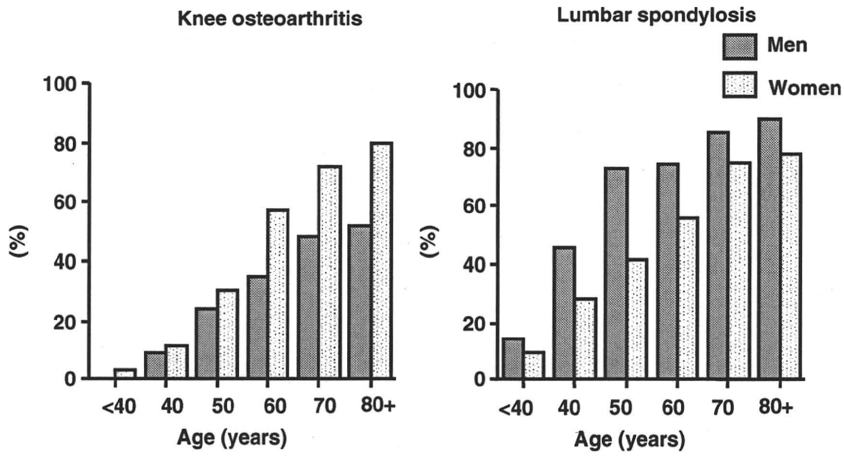

Figure 2 Prevalence of radiographic knee osteoarthritis and lumbar spondylosis, classified by age and gender

In Japan, the mean BMD of the L2–L4 vertebrae among both young male and female adults has been measured using Hologic DXA.[22] These indices were used in the present study; lumbar spine BMD <0.714 g/cm^2 (in case of both men and women), and femoral neck BMD <0.546 g/cm^2 (men) or 0.515 g/cm^2 (women) were considered to indicate OP.

All assessments performed in the baseline study will be repeated at the first, second and third follow-ups.

What is attrition like?

The first follow-up (second examination) commenced on October 2008, 3 years from baseline assessment. By the end of 2008, follow-up was completed in Hidakagawa, the mountainous region. Of the 864 participants (319 men and 545 women) in the baseline study, 635 subjects (224 men and 411 women) attended the second examination. The response rate for the second examination in the mountainous area was 73.5%. The most common reasons for non-participation were illness and difficulty in visiting the clinic (43% of the dropouts). Further, 26 people (12% of the dropouts) who participated in the baseline study died during the 3-year period following the initial assessment. In other two areas, the follow-ups are on going. The total attrition will be determined at the end of March 2010.

What has the ROAD study found?

By analysing the data from the baseline study, we have determined the prevalence of OA and OP.

OA

The age–sex distribution of radiographic knee OA and lumbar spondylosis was calculated (Figure 2); both conditions were diagnosed at KL grades of $\geqslant 2$. In the overall population, the prevalence of radiographic knee OA and lumbar spondylosis was 54.6% (42.0% in men and 61.5% in women) and 70.2% (80.6% in men and 64.6% in women), respectively. Thus, both the overall and sex-specific prevalence of lumbar spondylosis were higher than those of knee OA.[23]

OP

The prevalence of OP was calculated for the participants from mountainous and coastal regions in the ROAD study (Figure 3). The prevalence of OP of the lumbar spine and femoral neck in women was 6- and 5-fold, respectively, than in men. The differences were significant ($P < 0.001$).[23]

What are the main strengths and weaknesses of the ROAD study?

Strengths

In Japan, little epidemiological information is available of musculoskeletal diseases such as OA and OP. The ROAD study is the first large population-based prospective study conducted on the Japanese population and is designed to supply essential information, chiefly of OA and OP.

We confirmed the high prevalence of OA and OP among the ROAD study participants, and we will conduct follow-up examinations for at least 10 years in order to clarify the relationships of OA, OP and osteoporotic fractures with the following parameters: lifestyle, anthropometric and neuromuscular measurements, bone mass, bone geometry and fall propensity. Further, we will determine how these impairments affect QOL and mortality. We also expect to assess the similarities and differences in the risk factors of OA and OP. In addition, we will clarify the incident morbidity of other lifestyle-related disorders,

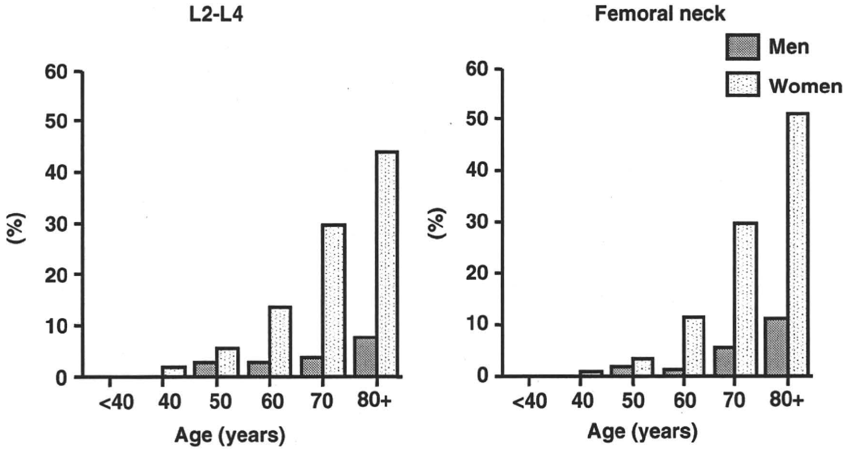

Figure 3 Prevalence of osteoporosis of the lumbar spine and femoral neck

such as obesity, hypertension, diabetes mellitus, cardiovascular and metabolic diseases and dementia.

The ROAD study data will facilitate the development of clinical guidelines for the detection and prevention of osteoporotic fractures in other countries. This study was designed such that it would be similar to the Study of Osteoporotic Fractures, a large observational study on the determinants of fractures in older women,[24] and to MrOS, a large observational study on the determinants of fractures in older men[25] in the USA.

Finally, the completion of the ROAD study will provide unique opportunities for the study of other conditions that are common among older men and women, such as obesity, diabetes, cardiovascular disease, cognitive disorders and frailty. The blood, plasma, serum and urine specimens stored during the ROAD study will enable the clarification of a variety of new biochemical and genetic factors associated with musculoskeletal disorders and the aforementioned diseases.

Weaknesses

Although the ROAD study includes a large number of subjects (more than 3000), these subjects are voluntary participants and have been recruited from only three areas; hence, they do not truly represent the general population. The 'healthy' and 'regional' selection biases should be confirmed.[26] We could not directly compare the baseline characteristics between the responders and non-responders owing to lack of data regarding the non-responders. Hence, to determine whether a selection bias existed in the ROAD study, we compared the anthropometric measurements and frequencies of smoking and alcohol drinking between the participants and the general Japanese population. The values for the general population were obtained from the 2005 National Health and Nutrition Survey conducted by the Ministry of Health, Labour and Welfare, Japan, which is an annual survey to clarify the health status of the Japanese population and is conducted on approximately 18 000 inhabitants from 6000 randomly selected families.[27]

The BMIs of ROAD study participants and the Japanese population were compared (Table 3). No significant differences were identified, except that the male participants aged 70–74 years were significantly smaller in build than men of this age group in the overall Japanese population ($P < 0.05$).

The proportion of current smokers and current drinkers (those who regularly smoked or drank more than once a month) in the general Japanese population was compared with that in the study population (Figure 4). Both proportions were significantly higher in the general Japanese population than in the study population (smokers: men, $P < 0.001$ and women, $P < 0.001$; drinkers: men, $P < 0.01$ and women, $P < 0.001$), suggesting that participants of the ROAD study had healthier lifestyles than the general Japanese population. This bias due to the selection of 'healthy' individuals should be taken into consideration while generalizing the results of the ROAD study.

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

Can I get hold of the data? Where can I find out more?

The ROAD study group welcomes specific and detailed proposals for new collaborations. Initial enquiries should be addressed to N.Y. Some information about the ROAD study is available on the website of the Department of Joint Disease Research, 22nd Century Medical and Research Centre,

Table 3 Comparison of BMI (SD) (kg/m^2) of the participants with general Japanese population

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)

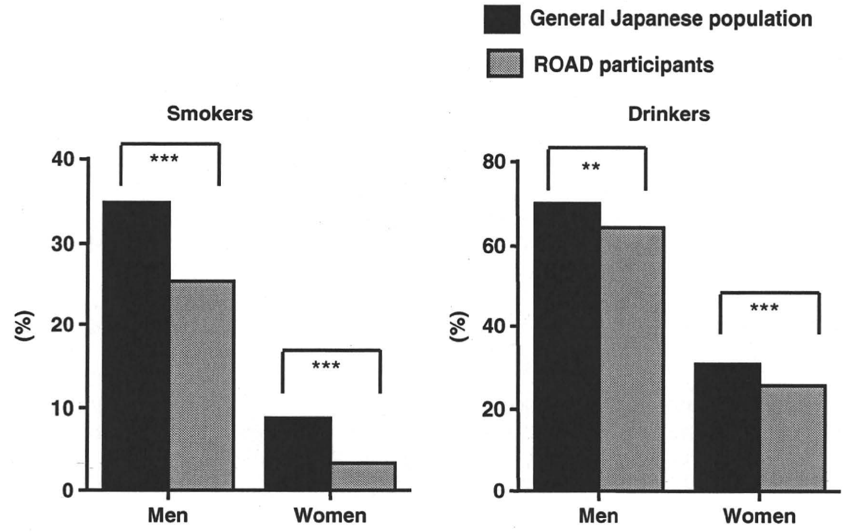

Figure 4 Comparison of the proportion of current smokers and drinkers between the participants of the ROAD study and the general Japanese population. $^{**}P < 0.01$, $^{***}P < 0.001$

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

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Conflict of interest: None declared.

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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

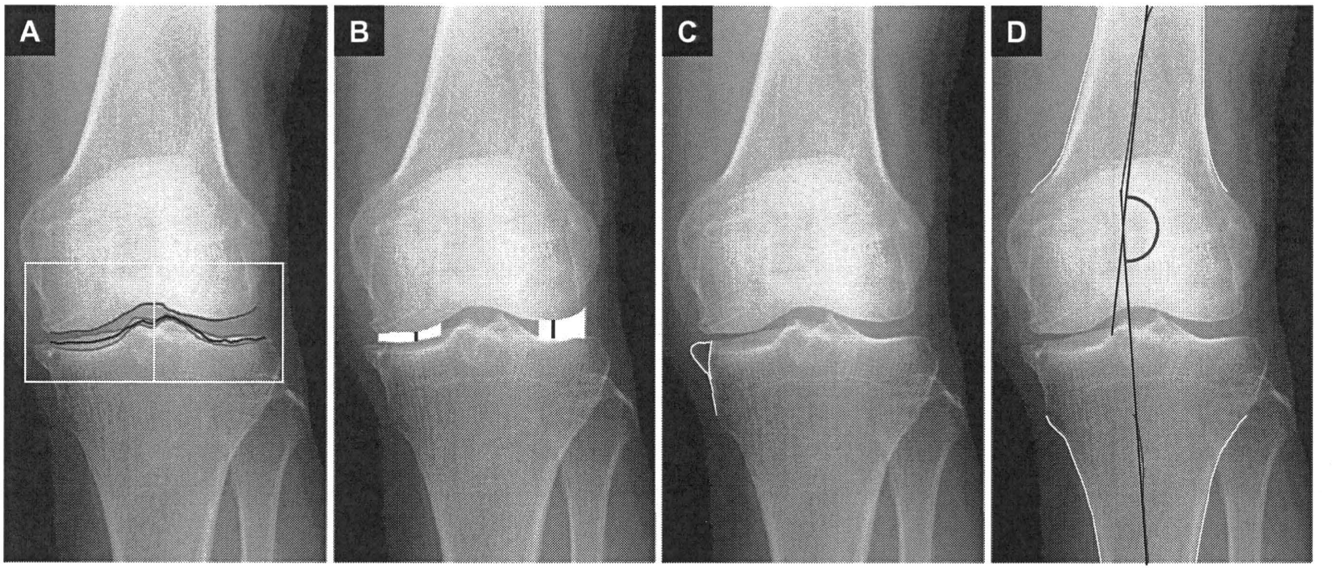

Fig. 1. Schema of image processing by the knee osteoarthritis computer-aided diagnosis (KOACAD) measuring system. **A** Outlines of anterior and posterior margins of the tibial plateau. The *middle line* between these two outlines represents the lower rim of the joint space. **B** Medial and lateral 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 (mm²)	Lateral JSA (mm²)	OPA (mm²)	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 failure, three moved to distant areas and three lost contact. Twelve other patients who showed symptoms in the lower extremities due to cerebral infarction, myelopathy or dementia during the postoperative follow-up period were excluded. Symptoms in the lower extremities of the remaining 89 patients (56 males and 33 females; mean ± SD, 66.3 ± 11.2 years) were surveyed 2 years after surgery. There was no complication in the surgical procedure except for slight dural tears in four patients, which were repaired without additional treatment. During the follow-up period, a superficial infection, a pseudomembranous enteritis, a disc herniation at the operated level and a compression vertebral fracture occurred, all of which were cured with conservative therapies. None of the patients underwent spinal re-operation because of progression of stenosis or instability.

The background data of the 89 patients are shown in Table 1. Comparison of preoperative and postoperative JOA scores on symptoms in the lower extremities of all the patients revealed that both leg pain/numbness (1.0–2.0) and gait disturbance (0.7–2.4) were significantly improved by surgery (Table 1). The stratified comparisons by gender, preoperative presence of the above findings and the number of decompressed levels showed that the JOA scores of both symptoms were significantly improved by the surgery in all subgroups. However, the subgroup with preoperative drop foot showed somewhat less improvement in both leg pain/numbness ($P = 0.009$) and gait disturbance ($P = 0.007$) than other subgroups ($P < 0.0001$).

Predictors of the residual symptoms in lower extremities

According to the definition of residual symptoms as above, 27 (30.3%) and 13 (14.6%) patients showed residual leg pain/numbness and gait disturbance, respectively (Table 2). To identify the predictors of residual symptoms in the lower extremities, we compared the number (percentage) of patients with and without residual symptoms in the stratified subgroup according to the variables. Among the variables, preoperative resting numbness was positively associated with both residual leg pain/numbness ($P = 0.03$) and residual gait disturbance ($P = 0.02$). Furthermore, preoperative drop foot was more strongly associated with residual gait disturbance ($P = 0.0002$), although not with residual leg pain/numbness. Age, gender, preoperative presence of cauda equina syndrome, degenerative spinal deformity, myelographic complete filling defect or the number of decompressed levels was not associated with either of the residual symptoms in the lower extremities.

To further identify the principal predictors, we further performed logistic regression analysis after adjustment for age and gender to estimate OR and 95% CI. We confirmed the significant association of resting numbness with residual leg pain/numbness and gait disturbance, as well as the significant association of drop foot with residual gait disturbance (Table 3).

Table 1 Comparison of preoperative and postoperative JOA scores on symptoms in lower extremities

		n	Leg pain/numbness				Gait disturbance			
			Preop. (SD)	Postop. (SD)	Change (SD)	*P* value	Preop. (SD)	Postop. (SD)	Change (SD)	*P* value
All		89	1.0 (0.5)	2.0 (0.8)	10 (0.8)	<0.0001	0.7 (0.8)	2.4 (0.8)	1.8 (1.0)	<0.0001
Gender	Male	56	1.0 (0.6)	2.1 (0.8)	1.1 (0.8)	<0.0001	0.7 (0.8)	2.4 (0.8)	1.7 (0.9)	<0.0001
	Female	33	0.9 (0.4)	1.8 (0.8)	0.9 (0.8)	<0.0001	0.6 (0.8)	2.4 (0.8)	1.8 (1.0)	<0.0001
Resting numbness	(+)	40	0.9 (0.5)	1.4 (0.7)	0.6 (0.7)	<0.0001	0.6 (0.7)	2.2 (0.9)	1.6 (1.0)	<0.0001
	(–)	49	1.1 (0.6)	2.5 (0.5)	1.4 (0.6)	<0.0001	0.8 (0.8)	2.7 (0.6)	1.9 (0.9)	<0.0001
Drop foot	(+)	9	0.9 (0.8)	1.9 (0.6)	1.0 (0.9)	0.009	0.6 (0.9)	1.9 (1.2)	1.3 (1.1)	0.007
	(–)	80	0.9 (0.5)	2.0 (0.8)	1.0 (0.8)	<0.0001	0.7 (0.8)	2.5 (0.7)	1.8 (0.9)	<0.0001
Cauda equina syndrome	(+)	66	0.9 (0.5)	1.9 (2.2)	1.0 (0.8)	<0.0001	0.6 (0.7)	2.4 (0.8)	1.8 (0.9)	<0.0001
	(–)	23	1.0 (0.7)	2.2 (0.9)	1.0 (0.8)	<0.0001	0.9 (0.9)	2.4 (0.7)	1.5 (1.0)	<0.0001
Degenerative spinal deformity	(+)	47	1.0 (0.6)	2.0 (0.8)	1.0 (0.8)	<0.0001	0.7 (0.8)	2.4 (0.7)	1.7 (0.9)	<0.0001
	(–)	42	0.9 (0.4)	2.0 (0.9)	1.1 (0.9)	<0.0001	0.6 (0.7)	2.5 (1.0)	1.9 (1.0)	<0.0001
Complete filling defect	(+)	56	0.9 (0.6)	1.9 (0.8)	1.0 (0.8)	<0.0001	0.7 (0.8)	2.4 (0.8)	1.7 (1.0)	<0.0001
	(–)	33	1.0 (0.5)	2.2 (0.9)	1.2 (0.7)	<0.0001	0.7 (0.8)	2.5 (0.8)	1.8 (0.9)	<0.0001
Number of decompressed levels	1	50	1.0 (0.5)	2.1 (0.7)	1.1 (0.7)	<0.0001	0.9 (0.8)	2.6 (0.6)	1.7 (0.8)	<0.0001
	≥2	39	0.9 (0.6)	1.9 (0.8)	0.9 (0.9)	<0.0001	0.4 (0.7)	2.2 (0.9)	1.8 (1.2)	<0.0001

P value was determined by the paired *t* test

Table 2 Number (percentage) of patients with and without residual symptoms in the lower extremities

		Leg pain/numbness			Gait disturbance		
		(+) $n = 27$	(–) $n = 62$	*P* value	(+) $n = 13$	(–) $n = 76$	*P* value
Mean age (years)		72.0	68.1	0.10	64.6	69.1	0.10
Gender	Male	17 (30.4)	39 (69.6)	0.26	10 (17.9)	46 (82.1)	0.26
	Female	10 (30.3)	23 (69.7)		3 (9.0)	30 (91.0)	
Resting numbness	(+)	26 (65.0)	14 (35.0)	0.03*	9 (22.5)	31 (77.5)	0.02*
	(–)	1 (2.0)	48 (98.0)		4 (8.2)	45 (91.8)	
Drop foot	(+)	4 (44.4)	5 (55.6)	0.33	5 (55.6)	4 (44.4)	0.0002*
	(–)	23 (28.8)	57 (61.2)		8 (10.0)	72 (90.0)	
Cauda equina syndrome	(+)	23 (34.8)	43 (65.2)	0.11	9 (13.6)	57 (86.4)	0.66
	(–)	4 (17.4)	19 (82.6)		4 (17.4)	19 (82.6)	
Degenerative spinal deformity	(+)	17 (36.2)	30 (63.8)	0.60	7 (14.9)	40 (55.1)	0.60
	(–)	10 (23.8)	32 (76.2)		6 (14.3)	36 (55.7)	
Complete filling defect	(+)	21 (37.5)	35 (62.5)	0.06	8 (14.3)	48 (85.7)	0.91
	(–)	6 (18.2)	27 (81.8)		5 (15.2)	28 (84.8)	
Number of decompressed levels	1	11 (22.0)	39 (78.0)	0.05	4 (8.0)	46 (92.0)	0.05
	≥2	16 (41.0)	23 (59.0)		9 (23.1)	30 (76.9)	

P value was determined by the chi-square test

Table 3 Logistic regression analyses for odds ratio (OR) and 95% confidence interval (CI) of the variables for residual symptoms in the lower extremities

	Leg pain/numbness		Gait disturbance	
	OR	(95% CI)	OR	(95% CI)
Resting numbness	85.6*	(15.9–1603.1)	4.5*	(1.2–23.2)
Drop foot	2.1	(0.5–9.0)	11.6*	(2.5–59.1)
Cauda equina syndrome	2.6	(0.09–4.1)	1.3	(0.006–2.5)
Degenerative spinal deformity	0.7	(0.1–4.9)	0.6	(0.1–2.2)
Complete filling defect	2.2	(0.9–2.4)	1.4	(0.004–2.3)
Number of decompressed levels	2.5	(1.0–2.7)	4.2	(0.06–9.8)

Data were calculated by logistic regression analysis after adjustment for age and gender, $*P < 0.01$

Discussion

This prospective observational study for the first time identified the specific predictors for the remaining major symptoms of LSS after decompression surgery: leg pain/numbness and gait disturbance. Preoperative resting numbness was found to be a predictor of both residual leg pain/numbness and gait disturbance, and preoperative drop foot was a predictor of residual gait disturbance. It would seem to be natural that preoperative resting numbness eventually leads to postoperative leg pain/numbness. In fact, 65.0% (26 of 40 patients) of patients with preoperative resting numbness still showed residual leg pain/numbness 2 years after the operation (Table 2). Numbness caused by LSS has been reported to be more difficult to alleviate by surgery than other neurological symptoms such as muscle weakness or pain [2, 6]. Also, it is not surprising that preoperative drop foot eventually leads to postoperative gait disturbance. More than half (55.6%; 5 of 9 patients) the patients with preoperative drop foot showed residual gait disturbance (Table 2). A previous study on the surgical outcome of LSS patients with drop foot revealed that especially those with a preoperative MMT score of 0 or 1 for ankle dorsiflexion exhibited poor alleviation of this disorder [1]. In the present study as well, there were three patients with an MMT score of 0 or 1, and all of them showed residual gait disturbance due to the unchanged drop foot (data not shown). Furthermore, comparison of preoperative and postoperative JOA scores revealed that the subgroup with preoperative drop foot showed less improvement of symptoms in the lower extremities than other subgroups (Table 1). Taken together, resting numbness and drop foot may be derived from less reversible neurological disorders, so that they are difficult to restore by decompression. The preoperative durations of these symptoms may influence the surgical outcomes, which we should examine as a next task. More interesting is that preoperative resting numbness, a sensory disorder, was identified as a predictor of residual gait disturbance, which is a motor disorder. Although the underlying mechanism remains unclear, we speculate a possible involvement of irreversible peripheral neural damage that is related to both resting numbness and gait disturbance.

In addition to resting numbness and drop foot, the number of decompressed levels also showed a trend toward positive association with residual leg pain/numbness and residual gait disturbance, although not statistically significant (Table 2, $P = 0.05$ in both symptoms; Table 3, OR = 2.5 and 4.2, respectively). Although the present comparison was performed between a single level of decompression and two or more levels of decompression, a comparison between one or two levels ($n = 80$) and three or more levels ($n = 9$) showed a significant association of the number of decompressed levels with residual leg pain/numbness ($P = 0.01$, OR = 7.5, 95% CI = 1.6–50.0), but not with residual gait disturbance ($P = 0.50$, OR = 1.3, 95% CI = 0.1–6.3) (data not shown in the tables). Indeed, there is greater possibility of multiple levels of decompression to cause surgical invasion, which may eventually result in the residual symptoms. Alternatively, independently of the surgery itself, residual symptoms may be derived from irreversible symptoms of the preoperative disorders, since the multi-level canal stenosis, which is an indication of multi-level decompression, may cause more damages to the nerve root, cauda equina and the blood circulation [13, 14, 18]. Hence, unlike preoperative symptoms such as resting numbness and drop foot, the number of decompressed levels may not be suitable for the predictor. In fact, previous reports on the relationship between the number of decompressed levels and the surgical outcome have been controversial, depending on the outcome measures including standardized instruments and self-reported satisfaction by patients [7, 9].

As the decompression surgery, the present study utilized our original technique called modified fenestration with restorative spinoplasty. Since this technique was developed to achieve good visibility of the spinal canal and safe decompression even in patients with narrow and steep facet joints, the ability to decompress the spinal canal and nerve roots is sufficient, similar to conventional laminectomy/foraminotomy techniques [11]. Hence, we believe that the present results obtained using this unique technique are applicable generally to typical decompression surgeries.

Although approximately 30 and 15% of patients were shown to have residual symptoms after the decompression surgery, respectively (Table 2), the present residual symptoms were defined according to our original criteria based on the JOA score and were not completely or directly linked with the dissatisfaction of the patients. Indeed, there are other factors such as back pain and psychological status to be considererd for the recommendation of the surgery. Furthermore, since the JOA scores of leg pain/numbness and gait disturbance were significantly improved after the surgery, regardless of the presence or absence of these predictors (Table 1), decompression surgery is definitely worth performing to decrease the severity of these symptoms. Hence, the present study suggests that it is desirable for this surgery to be performed before the onset of resting numbness or drop foot at least to prevent residual symptoms in the lower extremities. Even in the presence of these preoperative predictors, however, we encourage this surgery with sufficient informed consent, including the findings obtained from this study, to avoid misunderstanding or over-expectation of the patient with regard to the surgical outcome.

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