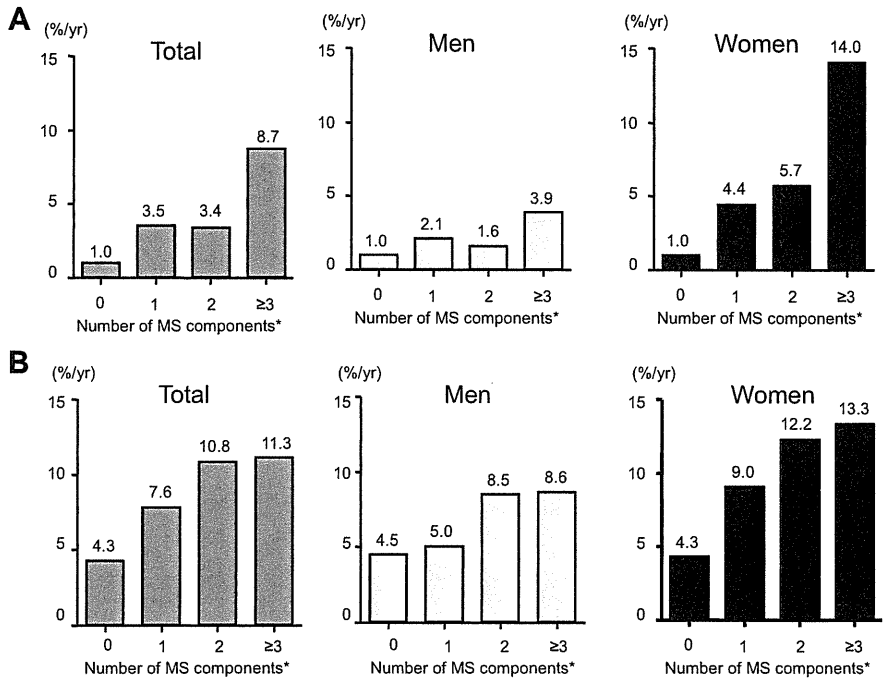
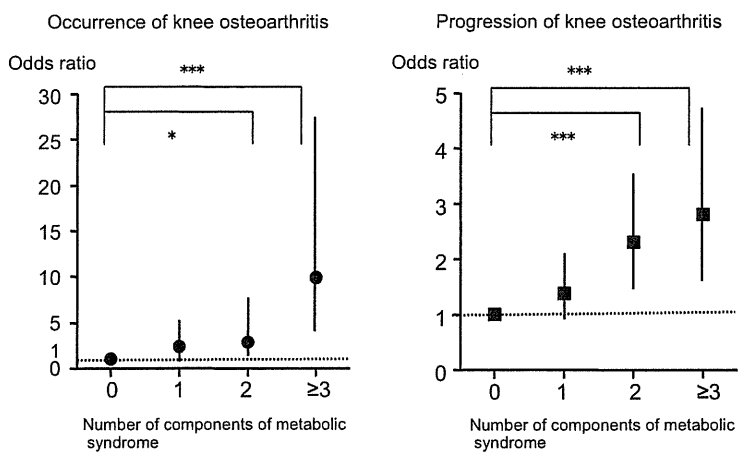


Fig. 2. Cumulative incidence (%/year) of KOA (A) and progression of the KL grade of either knee (%/year) (B) classified by the number of components of MS, including OW, HT, DL, and IGT.

for age and gender. The odds ratio (OR) and 95% CI for KOA occurrence were found to significantly increase with the number of MS components present (OR, 95% CI vs no component: one component, 2.16, 0.90–5.20, $P = 0.085$; two components, 2.49, 0.95–6.55, $P = 0.063$; ≥three components, 8.38, 3.12–22.5, $P < 0.001$). Similarly, KOA progression significantly increased with the number of MS components present (OR, 95% CI vs no component: one component, 1.41, 0.94–2.12, $P = 0.097$; two components, 2.25, 1.47–3.46, $P < 0.001$; ≥three components: 2.59, 1.57–4.27, $P < 0.001$).

Logistic regression model results obtained using KOA occurrence or progression as the objective variable and the number of MS components present as explanatory variables, after adjusting for age, gender, and the other potential risk factors listed in the Methods section, are shown in Fig. 3. The OR significantly increased with the number of MS components present after adjustment for



*:p < 0.05,***:p < 0.001

Multivariate logistic regression analysis using the occurrence or progression of KOA (over 3 years, 1: yes, 0: no) as the objective variable and the number of MS components as the explanatory variable, after adjusting for age, gender, region (0: coastal area, 1: mountainous area), smoking (0: ex- or non-smoker, 1: current smoker), alcohol consumption (0: ex- or non-drinker, 1: curre nt drinker), bicycling every day (0: no, 1: yes), regular exercise (0: no, 1: yes), and past history of knee injuries (0: no, 1: yes).

Fig. 3. ORs for occurrence and progression of KOA during the 3-year follow-up period vs the number of risk factors for MS.

other risk factors (OR, 95% CI vs no component: one component, 2.33, 0.96–5.65, $P = 0.065$; two components, 2.82, 1.05–7.54, $P = 0.039$; ≥three components, 9.83, 3.57–27.1, $P < 0.001$). Similarly, KOA progression significantly increased with the number of MS components present after adjustment for other risk factors (OR, 95% CI vs no component: one component, 1.38, 0.91–2.08, $P = 0.126$; two components, 2.29, 1.49–3.54, $P < 0.001$; ≥three components: 2.80, 1.68–4.68, $P < 0.001$). In both models, the OR for KOA occurrence significantly increased with the number of MS components present. Similar trends were observed for KOA progression with both models.

Discussion

In this study, we determined the cumulative incidence and progression rate of KOA diagnosed using the KL scale. We demonstrated that KOA occurrence and progression are associated with higher systolic BP, lower serum HDL-cho levels, and higher serum HbA1c levels, as well as higher BMI. Incorporating mutual adjustment for each MS component indicated that only BMI was significantly associated with KOA occurrence and progression. Regarding the risk factors for MS and KOA, even after adjusting for potential risk factors, multivariate analysis determined that HT and IGT were significantly associated with KOA occurrence, and OW and HT were significantly associated with KOA progression. The presence of a greater number of MS components was associated with a higher rate of KOA occurrence and progression. This tendency was much more pronounced in occurrence of KOA than in progression.

Numerous reports have presented an association between being OW or obese and KOA[1,7–12]. Lohmander *et al.* reported that being OW was associated with higher KOA incidence, and among measures of excess weight, BMI was observed to have the strongest relative risk gradient[28]. In the present study, we confirmed that BMI was the only continuous value significantly associated with KOA occurrence and progression among the MS risk factors (e.g., BMI, systolic BP, and serum levels of HDL-cho and HbA1c), consistent with previous studies. In contrast, several reports have shown that HT is associated with KOA presence, independent of OW[20,29–31]. In the present study, we confirmed a significant association between HT and IGT and KOA occurrence, and between OW and HT and KOA progression. Although several studies have found that obesity or increased BMI were risk factors for KOA onset[32–35], this appears to be the first report of associations between MS risk factors other than OW and KOA occurrence and progression.

There were differences between the results for continuous variables such as BMI, BP, and serum HDL-cho and HbA1c levels and those for categorical clinical criteria such as OW, HT, DL, and IGT. In analysis involving continuous variables, BMI was the only predictor of future KOA occurrence or progression. In contrast, clinical criteria-based analysis clearly showed associations between metabolic risk factors other than OW and KOA. This discrepancy suggests that the clinical criterion for OW (BMI ≥ 25 kg/m^2) may be less sensitive than continuous BMI values in reflecting the association of excess weight with KOA. We then performed additional analyses using KOA occurrence or progression as the objective variable and categorical risk factors for MS, such as HT, DL, and IGT, as explanatory variables. We also added continuous values for BMI at baseline rather than OW, after adjusting for multiple risk factors as listed for Model 2. The resulting overall ORs for HT, DL, and IGT adjusted for BMI on KOA occurrence or progression became smaller than those adjusted for OW. However, the association between HT and KOA occurrence remained significant (OR, 2.43; 95% CI, 1.14–5.18; $P = 0.021$), while IGT was no longer significant (OR, 1.70; 95% CI, 0.91–3.19; $P = 0.096$). Similarly, the association between HT and KOA progression remained significant (OR, 1.41; 95% CI, 1.00–2.00; $P = 0.049$). These results indicate that, even if associations between KOA and categorical MS components other than BMI are weak, if adjustments are made for OW using clinical criteria, then HT and IGT may be risk factors for KOA occurrence and HT may be a risk factor for KOA progression.

Regarding ethnic differences in KOA, we previously reported that KOA prevalence and incidence in the original ROAD study of 3,040 baseline participants was higher than those of Caucasians[36,37]. In contrast, with regard to ethnic differences in MS, Hoang *et al.* reviewed epidemiological studies and reported that MS prevalence in East Asians was lower than that in Caucasians[38]. MS prevalence in Asia may be increasing rapidly, as Nestel *et al.* reported a substantial increase in a cohort from Beijing from 9% in 1992 to 21% in 2002[39]. These ethnic differences have been suggested as resulting from genetic factors that modulate the association between KOA and obesity[40,41].

Regarding associations between risk factors of MS and KOA, Hart *et al.* attributed the effect of excess endogenous oestrogens to aromatization of oestrone in fat tissue[20]. Sowers *et al.* suggested that leptin and adiponectin levels influenced OA development[29]. Another hypothesis suggests that in obese subjects, metabolic changes in the striated muscles induced by interactions between insulin resistance and systemic inflammation may lead to fatigue and muscle weakness, influencing the balance between damage and repair mechanisms and ultimately leading to OA[42,43]. Inflammatory factors are suggested to be associated with both obesity and KOA[44,45]. Findlay evaluated the concept that vascular pathology might play a role in the initiation and/or progression of OA[46] and proposed that peripheral reduced blood flow associated with HT caused subchondral ischaemia. This ischaemia may in turn compromise nutrient and gas exchange into the articular cartilage and contribute to apoptosis of regional osteocytes of the subchondral bone. Furthermore, chondrocytes of OA exposed to high glucose concentrations exhibit impaired glucose transporter-1 downregulation[47]. Thus, impaired glucose transporter-1 downregulation may constitute an important pathogenic mechanism by which conditions characterized by hyperglycaemia may promote degenerative changes in chondrocytes, facilitating OA progression. However, in the present study, after adjustment for BMI, the effect of IGT was weak. Further studies are required to confirm whether IGT is a risk factor for KOA occurrence. Furthermore, because the present study aimed to identify associations between metabolic risk factors and future KOA occurrence or progression, we did not evaluate the effects of genetic factors and other risk factors potentially influencing MS and KOA. However, additional risk factors for both conditions should be addressed in further analysis of the ROAD study.

No previous studies have been performed on metabolic risk factor clustering and KOA occurrence or progression, although some cross-sectional epidemiological studies have evaluated the association between metabolic risk factor clustering and KOA presence[29,31]. In the present study, we demonstrated that KOA occurrence and progression are influenced not only by individual MS components but also by their clustering. An increase in the number of MS components significantly increases the risk of both KOA occurrence and progression. This effect of clustering was stronger for KOA occurrence than for KOA progression. Combining the present results with those of our previous report using the same analytical methods and adjustment factors[21], the ORs for ≥three components vs no components were 9.95, 2.79, and 2.72 for KOA occurrence, progression, and presence, respectively. Thus, preventing MS would aid in reducing every stage of KOA, including onset, worsening, and presence.

This study has several limitations. First, although it includes a relatively large number of participants, these participants do not

represent the entire general population because they were recruited from only two areas. Regarding potential selection bias of the ROAD study, we previously reported that no significant differences were identified between our participants and the general Japanese population, except that male participants aged 70–74 years in the ROAD study were significantly smaller in terms of body structure than the overall Japanese population ($P < 0.05$)[23]. Although we could locate and include baseline participants after 3 years with a high participation rate, this selection bias at baseline should be considered when generalising the results. Second, the definitions used for MS components were not completely identical to international criteria such as the National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) III, World Health Organization (WHO), or The American Association of Clinical Endocrinologists (AACE)[48]. As there has been considerable debate regarding abdominal circumference ($\geq$85 cm in men, $\geq$90 cm in women) in the Japanese criteria[49], we decided to utilize BMI $\geq$ 25 kg/m^2 to indicate OW rather than abdominal circumference. Furthermore, because not all blood samples were obtained under fasting conditions, we did not use blood glucose and serum TG levels as indicators. Therefore, our results may underestimate the presence of MS components, especially DL and IGT. However, we used the alternative index for each condition, recommended by the National Health and Nutrition Survey for cases where collecting samples under fasting conditions is difficult[26], and thus our criteria likely reflect dysfunction in lipid and glucose metabolism. Finally, we used KL grade $\geq$ 2 for diagnosing KOA. However, the KL scale is a categorical index, and it is impossible to evaluate the minimum joint space and osteophytosis separately. To evaluate KOA severity using quantitative parameters, a KOA computer-assisted diagnostic system[50] measuring minimum joint space width and osteophytosis area is under development; this system will provide increased accuracy in determining the association between MS components and KOA development for early prevention of disability.

In conclusion, this study revealed that HT and IGT influence KOA occurrence and that OW and HT are associated with KOA progression. KOA occurred or worsened more frequently with increase in the number of MS components. Preventing MS may be useful in preventing both KOA occurrence and progression.

Author contributions

NY conceptualized the study, was primarily responsible for developing the protocol, and acts as the guarantor for this study. SM, HO, and TA conducted data collection and X-ray assessment. All authors reviewed the protocol and contributed to interpretation of the results. All authors were involved in drafting the article and approved the final version submitted for publication. All authors had full access to all of the data in the study and take responsibility for the integrity and accuracy of the data analyses.

Role of the funding source

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Conflict of interest

All authors declare that (1) no authors have received corporate support for the submitted work; (2) the authors have no relationships with companies that might have an interest in the submitted work in the previous 3 years; (3) the authors' spouses, partners, or children do not have financial relationships that may be relevant to the submitted work; and (4) the authors have no non-financial interests that may be relevant to the submitted work.

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Prevalence of symptomatic lumbar spinal stenosis and its association with physical performance in a population-based cohort in Japan: the Wakayama Spine Study

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SUMMARY

Objective: The purpose of this study was to investigate the prevalence of symptomatic lumbar spinal stenosis (LSS) and to clarify the association between symptomatic LSS and physical performance using magnetic resonance imaging (MRI) in a population-based cohort.
Design: This cross-sectional study was performed as a part of the Research on Osteoarthritis/osteoporosis Against Disability (ROAD) in Japan and 1,009 subjects (335 men, 674 women, mean age 66.3 years, age range 21–97 years) were analyzed. An experienced orthopedic surgeon obtained the medical history and performed the physical testing for all participants. Symptomatic LSS diagnostic criteria required the presence of both symptoms and radiographic LSS findings. A 6-m walking time, chair standing time, and one-leg standing time were obtained from all participants.
Results: The prevalence of symptomatic LSS was 9.3% (95% confidence interval [CI]: 7.7–11.3) overall, 10.1% (CI: 7.4–13.8) in men and 8.9% (CI: 7.0–11.3) in women. There was a difference in the prevalence with increasing age by gender. The LSS prevalence showed little difference with age greater than 70 years for men, but the LSS prevalence for women was higher with increasing age. Among physical performance measures, 6-m walking time at a maximal pace was significantly associated with symptomatic LSS ($P = 0.03$).
Conclusion: The prevalence of symptomatic LSS was approximately 10% in a cohort resembling the general Japanese population. A 6-m walking time at a maximal pace was a more sensitive index than walking at a usual pace in assessing decreased physical performance associated with symptomatic LSS.

Introduction

Symptomatic lumbar spinal stenosis (LSS) is usually associated with impaired walking and other disabilities in the elderly. Symptomatic LSS has been shown to be the most frequent indication for spinal surgery in patients more than 65 years old[1,2]. However, little is known about the prevalence of symptomatic LSS in the general population. This is because the subjects in previous symptomatic LSS studies were limited to patients who visited the hospital[3,4]. Hence, people with minor symptomatic LSS who did not visit the hospital were not included in those studies. Furthermore, an examination that can capture minute changes of the intervertebral discs and ligaments using a tool like magnetic resonance imaging (MRI) is essential for the diagnosis of symptomatic LSS. This is because the definition of stenosis includes a morphological element. Many previous studies have reported the utility of MRI[5,6], but, to our knowledge, there have been no population-based cohort studies of symptomatic LSS using MRI.

It is well-known that the principal symptoms for LSS are sciatica and intermittent claudication (IC)[1,2]. Although most patients with MRI evidence of radiographic LSS are asymptomatic[7,8], when symptoms are present, severe symptoms are probably associated with poor physical performance. There have been few reports concerning physical performance of patients with symptomatic LSS[9,10]. According to a previous report concerning walking ability of

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subjects with three different degenerative musculoskeletal disorders (knee osteoarthritis, hip osteoarthritis, and symptomatic LSS) who were scheduled for either joint replacement or spinal decompression surgery, walking ability was limited in all three groups compared to healthy controls[9]. However, patients with symptomatic LSS showed the greatest restrictions in walking ability. In another report regarding subjects with symptomatic LSS in an orthopedic clinical practice, subjects in the healthy group showed greater functional mobility than those in the symptomatic LSS group[10]. The subjects included in the previous studies had enough symptoms to have visited the hospital, however, the association of physical performance measures with symptomatic LSS in subjects with minor symptoms who do not visit the hospital has not been well characterized. Although there may be a latent diminished physical functioning in symptomatic LSS with even minor radiographic changes and symptoms, there have been no population-based studies on symptomatic LSS that have included people with minor signs and symptoms of LSS.

Symptomatic LSS in this study was diagnosed by the presence of both clinical symptoms and radiographic LSS findings consistent with the clinical presentation. The aim of the present study was to clarify the prevalence of symptomatic LSS by gender and age strata using a population-based cohort. In addition, the association of symptomatic LSS with physical performance measures (walking speed, chair standing time, and one-leg standing time) was evaluated.

Methods

Participants

The present study, entitled "the Wakayama Spine Study: population-based cohort", was a population-based study for degenerative spinal disease and performed in a subcohort of the large-scale population-based cohort study called Research on Osteoarthritis/osteoporosis Against Disability (ROAD). ROAD is a nationwide, prospective study of bone and joint diseases consisting of population-based cohorts established in several communities in Japan. As a detailed profile of the ROAD study has already been described elsewhere, only a brief summary is provided here[11–14]. To date, creation of a baseline database including clinical and genetic information for 3,040 inhabitants (1,061 men, 1,979 women) in the age range of 23–95 years (mean, 70.6 years) has been completed. Participants were recruited from listings of resident registrations in three communities: an urban region in Itabashi, Tokyo; a mountainous region in Hidakagawa, Wakayama; and a coastal region in Taiji, Wakayama. All participants provided written informed consent, and the study was conducted with the approval of ethical committees of the University of Tokyo and the Tokyo Metropolitan Institute of Gerontology. Participants completed an interviewer-administered questionnaire of 400 items that included lifestyle information, underwent anthropometric measurements, and physical performance measures were recorded. A second visit of the ROAD study to the mountainous region of Hidakagawa and the seacoast region of Taiji was performed between 2008 and 2010. From inhabitants participating in the second visit of the ROAD study, 1,063 volunteers were recruited to undergo MRI examinations. Fifty-two of the 1,063 volunteers declined the MRI examination, therefore, 1,011 were registered in the present study. All participants provided another written informed consent for the MRI examination. Among those 1,011 participants, two participants with LSS symptoms for whom MRI was contraindicated (due to presence of a pacemaker) were excluded, because a final diagnosis of symptomatic LSS could not be made (Fig. 1). Thus, 1,009 participants (335 men and 674 women, mean age 66.3 years, age range of 21–97 years) were analyzed in the present study. Similar to the baseline study, participants in the second visit of the ROAD study completed an interviewer-administered questionnaire of 400 items that included lifestyle information such as smoking habits, alcohol consumption, family history, past history, physical activity, reproductive variables, and health-related quality of life (QOL). Anthropometric measurements included height, weight, bilateral grip strength, and body mass index (BMI) (weight [kg]/height^2 [m^2]). The ankle-brachial index (ABI) was measured using PWV/ABI (OMRON Co., Kyoto, Japan) for all participants. A timed 6-m walk at the participant's usual pace in a hallway was recorded to measure physical performance. Similarly, 6-m walking time at a maximal pace was measured[15–18]. The time taken for five consecutive chair rises without the use of hands was also recorded[18–20]. One-leg standing time with each leg was measured using a stopwatch (upper limit, 60 s) and the time adopted was the mean value of both legs[21,22].

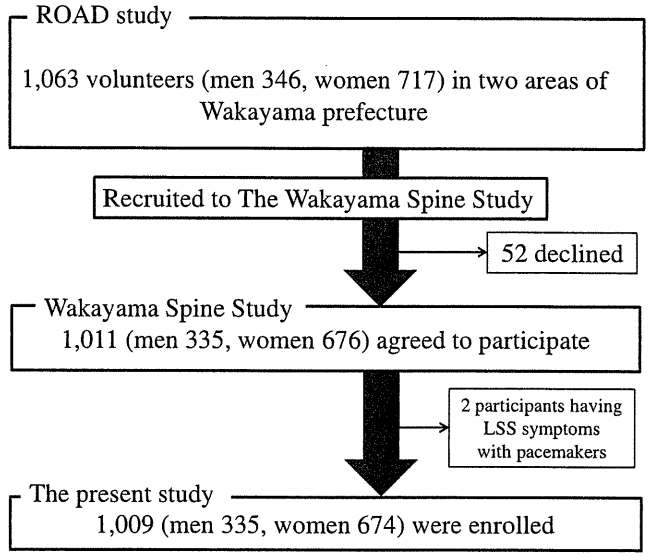

Fig. 1. Flow diagram depicting participants recruited to the Wakayama Spine Study from the ROAD study.

MRI

A mobile MRI (Excelart 1.5 T, Toshiba, Tokyo, Japan) unit was used in the present study, and total spinal MRI was performed for all participants on the same day as the examination. MRI exclusion criteria included presence of a cardiac pacemaker, claustrophobia, or other contraindications. The participants were positioned in supine during the MRI, and those with rounded backs used triangular pillows under their head and knees. The imaging protocol included sagittal T2-weighted fast spin echo (FSE) (repetition time (TR): 4,000 ms/echo, echo time (TE): 120 ms, field of view (FOV): 300 × 320 mm), and axial T2-weighted FSE (TR: 4,000 ms/echo, TE: 120 ms, FOV: 180 × 180 mm). Sagittal images were taken for the entire spine, but axial images were done at each lumbar intervertebral level (L1/2–L5/S1) parallel to the vertebral endplates.

Symptomatic LSS diagnosis

An experienced orthopedic surgeon (YI) consistently took the medical history and performed the physical testing for all the participants in this study. The history included information on the

presence of low back, buttock and leg pain, the area of pain or other discomfort, the presence of IC and its distance, and a modified Zurich Claudication Questionnaire[23] (excepting six items about satisfaction and a history of lumbar surgery for symptomatic LSS). Physical examinations included symptoms induced by lumbar extension, symptoms improved or induced with lumbar flexion, floor finger distance (cm), peripheral circulation (good or poor), a straight leg raising test, manual muscle testing of both upper and lower extremities, tendon reflex testing for both upper and lower extremities, and Babinski reflex testing. In addition, the MRI study of the entire spine was performed on all participants on the same day as the physical examination.

The diagnostic criteria for symptomatic LSS used in the present study were based on the LSS definition from the North American Spine Society (NASS) guideline, which requires presentation of both LSS symptoms and radiographic signs of LSS[24]. The orthopedic surgeon (YI) made the diagnosis of symptomatic LSS using this definition. The diagnosis for LSS symptoms required one or more of the following symptoms: pain, numbness and neurological deficits in the lower extremities and buttocks, and bladder/bowel dysfunction. The symptom characteristics should be induced or exacerbated with walking or prolonged standing and relieved with lumbar flexion, sitting and recumbency. The severity of radiographic LSS was assessed by qualitative measurements, which were performed by a well-experienced orthopedic surgeon (YI) and images were provided on films. The features assessed for LSS included severity of central, lateral recess, and foraminal stenosis, rated as four grades: none, mild, moderate and severe. The lateral recess was defined, as per Fardon and Millette[25], as extending from the medial edge of the facet to the edge of the neural foramen. We applied the general guideline classification of a[26] mild stenosis as narrowing of the normal area by one-third or less, moderate stenosis as narrowing between one-third and two-thirds, and severe stenosis as narrowing of more than two-thirds. Central and lateral recess stenosis was rated on the axial images and foraminal stenosis on the sagittal images. We used the most severe side for the rating of lateral and foraminal stenosis at each level. The same observer scored 50 randomly selected lumbar MRI films more than 1 month after the first reading to evaluate the intraobserver variability of the severity rating. Two experienced orthopedic surgeons also scored 50 different lumbar MRI films (YI & KN) for interobserver variability. The intraobserver variability was confirmed by a kappa analysis which dichotomized radiographic LSS severity as no/mild stenosis vs moderate/severe stenosis, and showed sufficient reliability for assessment of central, lateral and foraminal stenosis (0.77, 0.70 and 0.65, respectively). Interobserver variability was also sufficient for assessment using the kappa analysis (0.71, 0.65 and 0.65, respectively).

Radiographic LSS also required the severity to be more than moderate and the radiographic finding needs to be consistent with the symptoms as outlined above. An experienced orthopedic surgeon (YI) made the final diagnosis of symptomatic LSS using this definition, which requires presentation of both LSS symptoms and radiographic LSS findings. There were no participants with LSS symptoms due to tumor, inflammatory, or traumatic pathologies.

Statistical analysis

All statistical analyses were performed using JMP version 8 (SAS Institute Japan, Tokyo, Japan). Differences in age, height, weight, BMI, 6-m walking time at a usual pace, 6-m walking time at a maximal pace, chair standing time, and one-leg standing time between men and women were examined by the non-paired Student's *t*-test. The non-paired Student's *t*-test was also used to compare age between participants with and without symptomatic LSS. The prevalence of symptomatic LSS was also compared between men and women by the chi-square test. Differences in physical performance measures (6-m walking time at a usual pace, 6-m walking time at a maximal pace, chair standing time, and one-leg standing time) between participants with and without symptomatic LSS were examined by the non-paired Student's *t*-test. Furthermore, logistic regression analysis was used to estimate the odds ratios (ORs) of physical performance measures (6-m walking time at a usual pace, 6-m walking time at a maximal pace, chair standing time, and one-leg standing time) for symptomatic LSS after adjustment for age, gender and BMI.

Results

Table I shows the characteristics of 1,009 participants (335 men and 674 women, mean age 66.3 years, age range of 21–97 years) including age, anthropometric measurements, and physical performance in the present study. Two-thirds of the 1,009 participants were women. Mean age was not significantly different between men and women. BMI was significantly lower in women than in men ($P = 0.005$). Physical performance measures of the 6-m walking time at a usual pace and at a maximal pace were significantly shorter in men than in women ($P < 0.05$ for both), while chair standing time and one-leg standing time were not significantly different between men and women.

The prevalence of radiographic LSS findings was much greater than the prevalence of symptomatic LSS for the participants in this study. The percentage of participants with moderate or severe radiographic central stenosis was 76.5% (95% confidence interval [CI]: 73.7–79.0) in total, while the prevalence of symptomatic LSS was 9.3% (95% CI: 7.7–11.3) in total, 10.1% (CI: 7.4–13.8) in men, and 8.9% (CI: 7.0–11.3) in women. There was no significant difference between men and women ($P = 0.52$). The prevalence in men less than 39 years, 40–49, 50–59, 60–69, 70–79, and 80 years and older was 0%, 3.8% (CI: 0.7–18.9), 9.8% (CI: 4.6–19.8), 11.8% (CI: 6.1–21.5), 11.7% (CI: 6.7–19.8), and 10.7% (CI: 5.6–19.7), respectively, while that in women was 0%, 1.4% (CI: 0.2–7.3), 5.7% (CI: 2.8–11.3), 9.3% (5.7–14.8), 11.9% (CI: 7.9–17.5), and 13.3% (CI: 8.4–20.6), respectively (Fig. 2). The prevalence of both genders

Table I
Characteristics of participants

	Total	Men	Women	*P* value for gender
No. of participants	1009	335	674	
Age group (years)				
≦39	30	11	19	–
40–49	100	26	74	–
50–59	184	61	123	–
60–69	229	68	161	–
70–79	271	94	177	–
≧80	195	75	120	–
Demographic characteristics				
Age, years	66.3 ± 13.6	67.3 ± 13.8	65.9 ± 13.4	0.11
Height, cm	155.9 ± 9.4	164.5 ± 7.1	151.6 ± 7.2	<0.0001
Weight, kg	56.8 ± 11.5	64.4 ± 11.7	53.1 ± 9.4	<0.0001
BMI, kg/m^2	23.3 ± 3.6	23.7 ± 3.5	23.1 ± 3.6	0.005
Physical performance				
Six-meter walking time at a usual pace, s	5.7 ± 2.2	5.5 ± 1.5	5.8 ± 2.4	0.04
Six-meter walking time at a maximal pace, s	3.9 ± 1.4	3.6 ± 1.1	4.0 ± 1.6	<0.0001
Chair standing time, s	8.9 ± 4.0	8.8 ± 3.4	8.9 ± 4.2	0.61
One-leg standing time, s	36.0 ± 23.7	35.7 ± 24.0	36.1 ± 23.6	0.82

Non-paired *t*-test was used to determine differences in demographic characteristics and measurements of physical performance between men and women. Values are the means ± standard deviation.

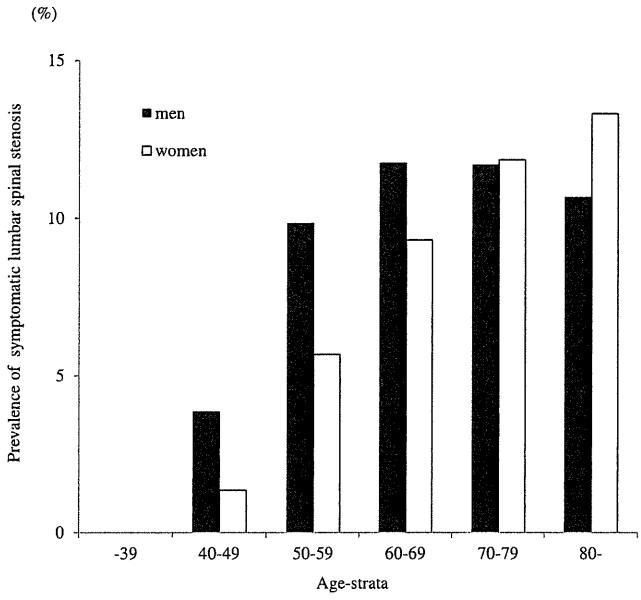

Fig. 2. Prevalence of symptomatic LSS classified by age and gender among 1,009 participants from a community cohort in Japan.

increased until reaching the 60–69 year old age group in which the prevalence in men was higher than that of women. However, the prevalence for women was higher than that of men after age 70. The prevalence of symptomatic LSS in men demonstrated little difference between age groups 60–69 years to over 80 years, but the prevalence for women became significantly higher with increasing aging ($P = 0.036$).

Fifty-five (58.5%) of 94 participants defined as having symptomatic LSS had IC. Five of these 55 participants presented with an ABI < 0.9. However, these five participants also had symptomatic LSS and their leg symptoms were positionally dependent. In this study, there were fifty neurogenic IC cases. There were five cases of unspecified IC, which was caused by both neurogenic and vascular claudication.

Table II shows the physical performance measures in participants with and without symptomatic LSS. In the overall population, 6-m walking time at a usual pace, 6-m walking time at a maximal pace, chair standing time, and one-leg standing time were significantly worse in participants with symptomatic LSS than those without symptomatic LSS ($P < 0.01$ for all). When analyzed in men and women separately, the results were similar to those overall, although the significant differences disappeared in some physical performance measures in men. The significant differences of 6-m walking time at a usual pace in both genders and one-leg standing time in men disappeared after a Bonferroni adjustment. Logistic regression analysis after adjustment for age, gender and BMI showed that 6-m walking time at a maximal pace was significantly associated with symptomatic LSS (OR: 1.17, 95% CI: 1.01–1.34). The physical performance measures of 6-m walking time at a usual pace, chair standing time, and one-leg standing time were not significantly associated with symptomatic LSS (OR: 1.04, 95% CI: 0.94–1.13, OR: 1.03, 95% CI: 0.97–1.09 and OR: 1.00, 95% CI: 0.98–1.01, respectively).

Discussion

The present study is the first to clarify the prevalence of symptomatic LSS by gender and age strata and the association of symptomatic LSS with physical performance measures using a population-based cohort. The prevalence of symptomatic LSS was found to be 9.3% in the general Japanese population, 10.1% in men, 8.9% in women, and there were no significant differences between genders. Interestingly, although the prevalence in women was higher with increasing age, the prevalence in men was the highest at 60–69 years, and little difference in prevalence was seen in men aged 60–69 years to 80 years or older. The prevalence of radiographic LSS was much greater than the prevalence of symptomatic LSS, with only a small proportion of participants with radiographic LSS actually showing symptoms suggestive of the clinical syndrome. The 6-m walking time at a maximal pace was significantly associated with symptomatic LSS, while the 6-m walking time at a usual pace was not.

We have identified no previous studies of symptomatic LSS prevalence. Johnsson[4] reported that the incidence of symptomatic LSS was 50/million person-years in southern Sweden in a study of patients who consulted the orthopedic department in two cities. However, as the author of that report described, the incidence of symptomatic LSS could be underestimated, because the studies did not include patients with minor symptoms who did not visit the hospital. This study is the first to clarify the prevalence of symptomatic LSS using a population-based cohort study.

Reported differences in prevalence of symptomatic LSS between men and women are mixed[27–29]. Verbiest reported a preponderance of symptomatic LSS in men as compared to women among his patients diagnosed by clinical symptoms and myelography[28]. However, Getty reported an equal gender distribution of symptomatic LSS prevalence in a series in which subjects were treated surgically for symptomatic LSS[29]. It is important to note that the subjects in those studies were patients who visited hospitals. In the present study, differences in the prevalence of symptomatic LSS between men and women in the general population were clarified. The prevalence of symptomatic LSS in men was slightly higher than in women, but there was no significant difference between genders. There was a difference in distribution of symptomatic LSS between men and women. The prevalence in women was higher with increasing age, but that in men was the highest at 60–69 years and

Table II
Measurements of each physical performance in participants with and without symptomatic LSS

	Total			Men			Women		
	LSS	Non-LSS	*P* value	LSS	Non-LSS	*P* value	LSS	Non-LSS	*P* value
Number of participants	94	915		34	301		60	614	
Physical performance									
Six-meter walking time at a usual pace, s	6.3 ± 2.7	5.6 ± 2.1	0.003	6.0 ± 1.6	5.4 ± 1.5	0.03	6.5 ± 3.1	5.7 ± 2.3	0.02
Six-meter walking time at a maximal pace, s	4.5 ± 2.1	3.8 ± 1.3	<0.0001	3.9 ± 1.1	3.6 ± 1.1	0.09	4.8 ± 2.4	3.9 ± 1.5	<0.0001
Chair standing time, s	10.1 ± 4.0	8.8 ± 3.9	0.002	9.7 ± 2.8	8.7 ± 3.4	0.10	10.3 ± 4.6	8.8 ± 4.1	0.008
One-leg standing time, s	27.9 ± 23.5	36.8 ± 23.6	0.0005	27.7 ± 25.4	36.7 ± 23.7	0.04	28.0 ± 22.6	36.9 ± 23.5	0.006

Values are the means ± standard deviation.
Non-paired *t*-test was used to determine differences in measurements of physical performance between LSS and non-LSS.

little different in men aged 60–69 years to 80 years and older. The prevalence of lumbar spondylosis (LS) diagnosed as Kellgren/Lawrence (KL) grade two or greater (defined as osteophyte formation with and without disc space narrowing) was found to be significantly higher in men than in women[30]. The prevalence of LS in women was found to be higher with increasing age, while that in men found little difference over 60 years[13]. Interestingly, these distribution patterns are similar to the prevalence of symptomatic LSS in the present study. Anatomical LSS arises from degenerative LS, and facet osteoarthritis and/or hypertrophy, which is associated with narrowing of the space available for the neural elements[1]. This may be one reason for the similarity between LS and symptomatic LSS prevalence.

The present study was the first to show that, among the general population, 6-m walking time at a maximal pace was significantly associated with symptomatic LSS, while 6-m walking time at a usual pace was not. This may mean that participants with symptomatic LSS appeared to have no disadvantage concerning activities of daily living compared to those without symptomatic LSS. However, when requiring greater functional reserve, such as 6-m walking time at a maximal pace, differences between participants with and without symptomatic LSS appeared. This is also the first study to indicate that tasks requiring greater functional reserve, such as walking at a maximal speed, could be a more sensitive index in assessment of decreased physical performance due to symptomatic LSS.

There are several limitations in the present study. First, although the present study included more than 1,000 participants, these participants may not represent the general population as they were recruited from only two areas. However, anthropometric measurements were compared between participants and the general Japanese population, and no significant differences were found in BMI (men: 23.71 (3.41) and 23.95 (2.64), $P = 0.33$, women: 23.06 (3.42) and 23.50 (3.69), $P = 0.07$)[31]. In addition, the proportion of current smokers and current drinkers (those who regularly smoked or drank more than one drink/month) in the general Japanese population was compared with that in the study population. Proportions of current smokers and drinkers in men and that of current drinkers in women were significantly higher in the general Japanese population than in the study population, but there were no significant differences in that of current smokers in women (smokers: men, 32.6% in the Japanese population, 25.2% in study participants, $P = 0.015$; women, 4.9% in the Japanese population, 4.1% in study participants, $P = 0.50$; drinkers: men, 73.9% in the Japanese population, 56.8% in study participants, $P < 0.0001$; women, 28.1% in the Japanese population, 18.8% in study participants, $P < 0.0001$), suggesting that it is likely that the participants (both men and women) had healthier lifestyles than the general Japanese population. Second, this is a cross-sectional study, so any causal relationship between symptomatic LSS and physical performance cannot be clarified. The Wakayama Spine Study is a longitudinal survey, so further progress will help to elucidate any causal relationships. Thirds, total walking distance/duration was not measured, and this metric for walking would likely have been of greater relevance to symptomatic LSS than speed of walking. In addition, this study only represents the Japanese population, hence, prevalence in other countries may be quite different.

In conclusion, the present study clarified that the prevalence of symptomatic LSS was about 10% in a cohort resembling the Japanese general population. There was a difference in the prevalence of symptomatic LSS distribution by age strata between men and women. The 6-m walking time at a maximal pace was a more sensitive index for assessing decreased physical performance due to LSS than the 6-m walking time at a usual pace. Further longitudinal surveys of the Wakayama Spine Study will help to further clarify the incidence and risk factors for symptomatic LSS.

Author contributions

All authors worked collectively to develop the protocols and methods described in this paper. YI, SM, KN, NO, HO, TA, and NY were principal investigators responsible for the fieldwork in the Wakayama Spine Study. YI and SM performed the statistical analysis. YI, HY, SM, KN, HH, HO, TA, MY, and NY contributed to the analysis and interpretation of results. YI wrote the report. All authors read and approved the final report.

Role of the funding source

The study sponsors played no role in the study design, the collection, analysis, and interpretation of data, writing of the report, or the decision to submit the paper for publication. The corresponding author had full access to all the data and had the final decision to submit for publication.

Conflict of interest

The authors declare that we have no conflicts of interest.

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Physical performance, bone and joint diseases, and incidence of falls in Japanese men and women: a longitudinal cohort study

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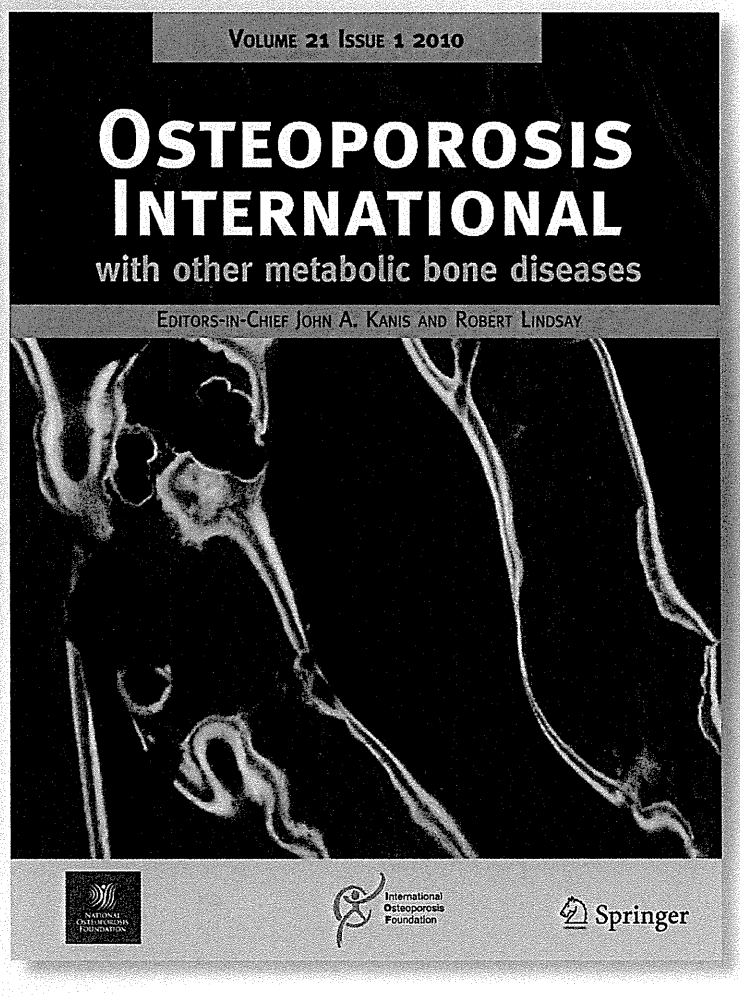

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ORIGINAL ARTICLE

Physical performance, bone and joint diseases, and incidence of falls in Japanese men and women: a longitudinal cohort study

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Abstract
Summary This study examined whether physical performance and bone and joint diseases were risk factors for falls in 745 men and 1,470 women from the Research on Osteoarthritis/osteoporosis Against Disability (ROAD) study (mean, 69.7 years). Slower walking speed was a risk factor for falls in men and women. Knee pain was a risk factor for falls in women.

Introduction The objective of the present study was to clarify the incidence of falls by sex and age and to determine whether physical performance and bone and joint diseases are risk factors for falls in men and women using a large-scale population-based cohort of the ROAD.
Methods A total of 745 men and 1,470 women were analyzed in the present study (mean age, 68.5 years). A questionnaire assessed the number of falls during 3 years of follow-up. Grip strength and walking speed were measured at baseline. Knee and lumbar spine radiographs were read by Kellgren–Lawrence (KL) grade; radiographic knee osteoarthritis and lumbar spondylosis were defined as KL=3 or 4. Knee and lower back pain were estimated by an interview.
Results During a mean follow-up of 3 years, 141 (18.9 %) men and 362 (24.6 %) women reported at least one fall. Slower walking speed was a risk factor for falls in men (0.1 m/s decrease; odds ratio [OR], 1.15; 95 % confidence interval [CI], 1.09–1.23) and women (0.1 m/s decrease; OR, 1.05; 95 % CI, 1.01–1.10). Knee pain was also a risk factor for falls (OR, 1.38; 95 % CI, 1.03–1.84) in women, but lower back pain was not.
Conclusion We examined the incidence and risk factors for falls in men and women. Slower walking speed was a risk factor for falls in men and women. Knee pain was a risk factor for falls in women.

Keywords Falls · Longitudinal study · Osteoarthritis · Pain · Walking speed

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Introduction

Falls are one of the main causes of injury, disability, and death among the elderly [1, 2]. In Japan, according to the

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recent National Livelihood Survey of the Ministry of Health, Labour and Welfare, falls and fractures are ranked fifth among diseases that cause disabilities and subsequently require support with activities of daily living [3]. However, there have been few population-based studies on the incidence of falls based on sex and age. Further, in terms of factors associated with falls, muscle strength, balance, vision, functional capacities, and cognitive impairment are traits that diminish with aging, and these factors have been suggested as predictive risk factors for falls and fractures [4, 5]. However, there have been few studies regarding the association of bone and joint diseases, especially osteoarthritis (OA), with falls [6–10].

The representative sites of OA are the knee and lumbar spine. Knee OA and lumbar spondylosis (LS) are major public health issues because they cause chronic pain and disability [11–16]. The prevalence of radiographic knee OA and LS is high in Japan [17, 18], with 25,300,000 and 37,900,000 subjects aged 40 years and older estimated to experience radiographic knee OA and LS, respectively [19]. The National Livelihood Survey ranked OA fourth among diseases that cause disabilities and subsequently require support with activities of daily living [3], but there have been few studies of the association between falls and OA [6–10]. In previous studies, knee OA was assessed only by interview and not by radiography [6, 7]. The principal clinical symptom of knee OA is pain [20], but its correlation with the radiographic severity of knee OA is not as strong as expected [17, 21–23]. Thus, knee OA diagnosed by interview could be limited by variable accuracy. In addition, men and women were not examined separately in these previous studies, although sex differences have been found in the prevalence of knee OA [17]. Further, prevalence of OA has been shown to be different between races [17]; thus, the association of OA with falls may be different among races. To the best of our knowledge, there are no population-based studies of Japanese men and women to determine the association of OA with falls in a longitudinal model. Our previous study showed that knee pain was significantly associated with falls in Japanese women [24], but that study used a cross-sectional design; thus, a causal relationship remains unclear. With regard to LS, to the best of our knowledge, there have been no population-based studies regarding its association with falls except for our previous cross-sectional study [24], which showed that LS was not significantly associated with falls.

Measuring walking speed is a simple way to assess health and function in older adults [25–27]. Walking speed has been found to be associated with falls in a few studies [4, 28–32], although most studies were limited by small sample size or cross-sectional design [29, 30] or evaluation of a single sex [4, 32]. In addition, although walking abnormalities such as slower walking speed are significantly associated with bone and joint diseases such as knee OA, LS, and their pain [24], there have been no longitudinal studies to determine the associations of falls with bone and joint diseases and walking abnormalities at the same time. Thus, whether the association of slower walking speeds with falls is independent of bone and joint diseases remains unclear.

The objectives of this study were to clarify the incidence of falls by sex and age in Japan using a population-based longitudinal cohort study known as Research on Osteoarthritis/osteoporosis Against Disability (ROAD). Further, we examined the associations of physical performance and bone and joint diseases with the incidence of falls in Japanese men and women.

Methods

Subjects

The ROAD study is a nationwide, prospective study designed to establish epidemiologic indexes for the evaluation of clinical evidence for the development of a disease-modifying treatment for bone and joint diseases (OA and osteoporosis are the representative bone and joint diseases, respectively). It consists of population-based cohorts in three communities in Japan. A detailed profile of the ROAD study has been described elsewhere [17–19, 33]; a brief summary is provided here. To date, we have completed the creation of a baseline database that includes clinical and genetic information for 3,040 subjects (1,061 men and 1,979 women) of age ranging from 23 to 95 years (mean, 70.6 years), who were recruited from resident registration listings in three communities: an urban region in Itabashi, Tokyo; a mountainous region in Hidakagawa, Wakayama; and a coastal region in Taiji, Wakayama.

Residents of these regions were recruited from the resident registration lists of the relevant region. Participants in the urban region were recruited from a randomly selected cohort from the Itabashi Ward residents' registration database [34]. The participation rate was 75.6 %. Participants in mountainous and coastal regions were also recruited from the resident registration lists, and the participation rates in these two areas were 56.7 and 31.7 %, respectively. The inclusion criteria, apart from residence in the communities mentioned above, were the ability to (1) walk to the survey site, (2) report data, and (3) understand and sign an informed consent form. The baseline survey of the ROAD study was completed in 2006. 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.

Falls assessment

In 2008–2010, we attempted to trace and review all 3,040 subjects; they were invited to attend a follow-up interview. All subjects were interviewed with regard to falls by experienced interviewers and were asked the following questions: "Have you experienced falls during 3 years of follow-up, and if yes, how many falls did you experience?" According to a previous study on falls [35], a fall is defined as a sudden, unintentional change in position causing an individual to land at a lower level on an object, the floor, or the ground, other than as a consequence of a sudden onset of paralysis, epileptic seizure, or overwhelming external force.

Pain assessment

All subjects were interviewed by experienced orthopedists with regard to knee pain and lower back pain at baseline and were asked the following questions based on previous studies [17, 18]: "Have you experienced knee pain on most days in the past year, in addition to now?" and "Have you experienced lower back pain on most days in the past year, in addition to now?" Those who answered yes were defined as having pain.

Radiographic assessment

At baseline, all participants underwent radiographic examination of both knees using anteroposterior and lateral views with weight-bearing and foot map positioning; radiographic examination of the anteroposterior and lateral views of the lumbar spine, including intervertebral levels L1/2 to L5/S, was also performed. Knee and lumbar spine radiographs were read without the knowledge of participant clinical status by a single, experienced orthopedist (S.M.) using the Kellgren–Lawrence (KL) radiographic atlas [36] to determine the severity of KL grading. Radiographs were scored as grade 0 through 4, with higher grades being associated with more severe OA. We defined knee OA and LS as KL $\geq$3 in at least one knee and one intervertebral level, respectively. To evaluate the intraobserver variability of KL grading, 100 randomly selected radiographs of the knee and the lumbar spine were scored by the same observer more than 1 month after the first reading. One hundred other radiographs were also scored by two experienced orthopedic surgeons (S.M. and H.O.) using the same atlas for interobserver variability. The intraobserver and interobserver variabilities evaluated were confirmed by kappa analysis to be sufficient for assessment (0.86 and 0.80 for knee OA and 0.84 and 0.76 for LS, respectively).

Physical performance

Anthropometric measurements included height, weight, and body mass index (BMI) (weight [in kilograms]/height^2 [in square meters]) at baseline. Grip strength was also measured on bilateral sides using a TOEI LIGHT handgrip dynamometer (TOEI LIGHT CO., LTD., Saitama, Japan) at baseline, and the best measurement was used to characterize maximum muscle strength. To measure physical performance, the time taken to walk 6 m at normal walking speed in a hallway was recorded. Subjects were told to walk from a marked starting line to a 6-m mark as if they were walking down their hallway at home. Time was measured in seconds with a stopwatch and rounded to the nearest hundredth of a second. These walking speed trial measurements are considered highly reliable in community-dwelling elderly subjects [34, 37–39].

Statistical analyses

The differences in age, anthropometric measurements, and physical performance measurements between men and women and between nonfallers and fallers were examined by a nonpaired Student's *t* test. The incidence of falls was also compared between men and women, among subjects with no severe knee OA (KL=0, 1, or 2) and KL=3 or 4 knee OA, among subjects with no severe LS (KL=0, 1, or 2) and KL=3 or 4 LS, among subjects with and without knee pain, and among subjects with and without lower back pain using the chi-square test. Multiple logistic regression analysis after adjustment for age and BMI was used to determine the association of anthropometric measurements, physical performance, radiographic knee OA and LS defined as KL= 3 or 4, and knee and lower back pain and with falls compared with nonfalls in men and women. Further, to determine an independent association of physical performance, radiographic knee OA, and knee pain with falls compared with nonfalls, we used multiple logistic regression analysis with age, BMI, walking speed, radiographic knee OA, and knee pain as independent variables. Data analyses were performed using SAS version 9.0 (SAS Institute Inc., Cary, NC,USA).

Results

Of the 3,040 subjects in the baseline study in 2005–2007, 125 (4.1 %) had died by the time of the review 3 years later, 123 (4.0 %) did not participate in the follow-up study due to bad health, 69 (2.3 %) had moved away, 83 (2.7 %) declined the invitation to attend the follow-up study, and 155 (5.1 %) did not participate in the follow-up study for other reasons. Among the 2,485 subjects who did participate in the follow-up study, 182 (6.0 %) provided incomplete fall questionnaires. In addition, 15 (0.5 %) provided incomplete pain questionnaires; these were excluded. We also excluded 14 (0.5 %) subjects who had undergone total knee arthroplasty at baseline. Further, 59 (1.9 %) subjects did not measure

walking speed, leaving a total of 2,215 (72.9 %) subjects (745 men and 1,470 women) from whom radiographs at baseline and complete fall and pain histories were obtained. The mean ± SD duration of follow-up between initial and second surveys was 3.3±0.6 years.

Table 1 shows the age, anthropometric measurements, physical performance, and prevalence of radiographic knee OA and LS as well as knee and lower back pain of participants at baseline. Regarding physical performance, grip strength and walking speed were significantly better in men than in women. The prevalence of radiographic knee OA and knee pain was significantly higher in women than in men, whereas that of LS and lower back pain was not different between men and women.

During the approximately 3-year follow-up, 141 (18.9 % [95 % confidence interval [CI], 16.3–21.9]) men and 362 (24.6 % [95 % CI, 22.5–26.9]) women reported at least one fall. Chi-square test showed that the incidence of falls were significantly different between men and women (p= 0.0025). With increasing age, the incidence of falls tended to increase in men and women (Fig. 1).

Table 2 shows the age, anthropometric measurements, and physical performance at baseline between nonfallers and fallers. Age was significantly higher in fallers than nonfallers in men and women. Height was higher in fallers than in nonfallers in women, whereas weight and BMI was not significantly different between nonfallers and fallers in men and women. Grip strength and walking speed were worse in fallers than nonfallers in men and women.

Figure 2 shows the incidence rate of falls according to knee OA, knee pain, LS, and lower back pain. The incidence rate of falls was higher in subjects with knee OA than those without knee OA in men (27.9 and 18.0 %, p<0.05, respectively) and women (33.1 and 22.6 %, p<0.05, respectively). The incidence rate of falls was also higher in subjects with knee pain than those without knee pain in men (30.4 and 17.1 %, p<0.05, respectively) and women (32.6 and 22.1 %, p<0.05, respectively). There were no significant differences in incidence rate of falls between subjects with and without LS in men (20.5 and 17.8 %, p=0.35, respectively) and women (25.5 and 23.5 %, p=0.39, respectively). Men with lower back pain had significantly higher incidence rate of falls than men without lower back pain (25.6 and 17.6 %, p<0.05, respectively), whereas women with lower back pain did not (23.8 and 24.8 %, p=0.76, respectively).

In men, multiple logistic regression analysis after adjustment for age and BMI showed that slower walking speed (p< 0.001) and knee pain (p=0.0046) were risk factors for falls, but grip strength (p=0.4903), radiographic knee OA (p= 0.1569), LS (p=0.8312), and lower back pain (p=0.0553) were not (Table 3). In women, multiple logistic regression analysis after adjustment for age and BMI showed that walking speed (p=0.013), knee OA (p=0.0218), and knee pain (p=0.0021) were risk factors for falls, whereas grip strength (p=0.1209) and lower back pain (p=0.5293) were not. LS was not significantly associated with falls in the crude model (p=0.3890). To determine independent associations of walking speed, radiographic knee OA, and knee pain, we used multiple logistic regression analysis with age, BMI, walking speed, radiographic knee OA, and knee pain as independent variables and found that slower walking speed was an independent risk factor for falls in men and women (p< 0.0001 and p=0.0104, respectively). Knee pain was an independent risk factor for falls in women (p=0.0305), but not in men (p=0.0632).

Table 1 Characteristics of participants

	Overall	Men	Women
Number of subjects	2,215	745	1,470
Age (years)	68.5±11.3	69.4±11.1	68.1±11.4*
Height (cm)	154.7±8.8	163.2±6.6	150.4±6.3*
Weight (kg)	55.5±10.2	62.2±9.9	52.0±8.5*
BMI (kg/m^2)	23.1±3.3	23.3±3.0	23.0±3.4*
Grip strength (kg)	26.3±9.3	34.5±8.8	22.1±6.2*
Walking speed (m/s)	1.24±0.34	1.26±0.35	1.23±0.33*
Radiographic knee OA (%)	15.8	9.1	19.1**
Radiographic LS (%)	43.7	42.6	44.2
Knee pain (%)	20.8	13.7	24.4**
Lower back pain (%)	18.7	16.8	19.7

Values are presented as the mean ± SD, except where indicated

BMI body mass index, *OA* osteoarthritis

*p<0.05 vs. men by nonpaired Student's t test; **p<0.05 vs. men by chi-square test

Discussion

The present study is a large-scale, population-based cohort study regarding the incidence of falls and their association with physical performance and radiographic knee OA and LS as well as pain in Japanese men and women. We found that slower walking speed was a risk factor for falls in men and women and knee pain was a risk factor for falls in women only.

The present population-based longitudinal study determined whether radiographic knee OA is a risk factor for falls in Japanese men and women. Jones et al. showed that individuals with self-reported arthritis had an increased tendency to fall [8]. In the present study, after adjustment for age and BMI, radiographic knee OA was a risk factor for falls in women, but not in men. The sex differences identified in the association between radiographic knee OA and falls may be partly explained by the weaker quadriceps

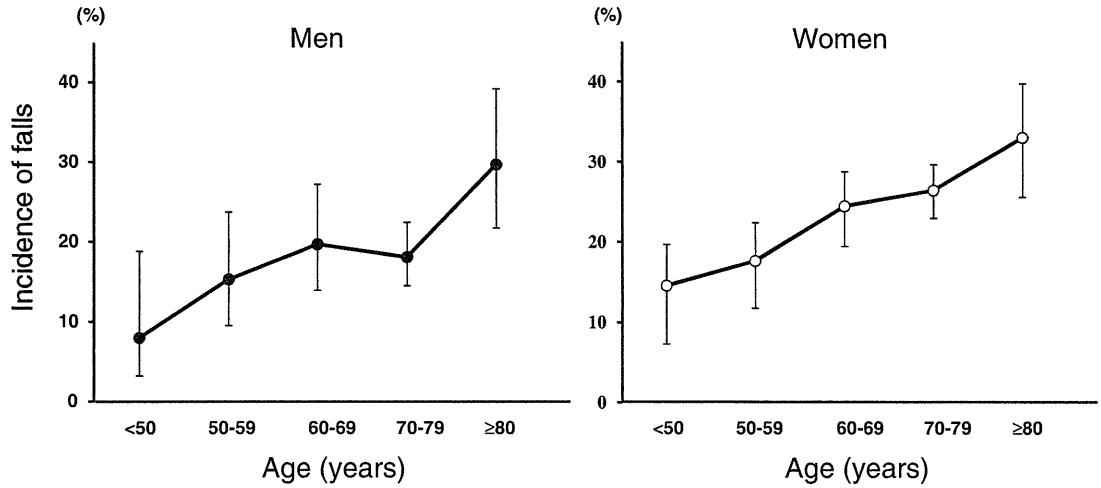

Fig. 1 Incidence rate of falls (95 % CI) by gender and age

muscles and increased postural sway associated with knee OA [8, 40], both of which are known to be independent risk factors for falls [7, 41]. In men, muscle strength is higher than that in women in all decades [42], which may obscure the association between radiographic knee OA and falls. LS was not a risk factor for falls in this study. Thus, falls may be more strongly associated with problems of the lower limbs rather than the trunk.

After adjustment for age, BMI, walking speed, and radiographic knee OA, knee pain was independently associated with the incidence of falls in women. Given that the significant association of radiographic knee OA with falls disappeared after adjustment, falls may occur due to symptoms such as pain caused by radiographic knee OA rather than radiographic changes in the knee itself. Our study and other previous cross-sectional studies also suggested that knee pain was significantly associated with falls [6, 24]. In addition, a prospective study also showed that knee pain increases in falls risk in Tasmanian men and women [10]. Jones et al. showed that, for the hand, the presence of pain is what weakens grip strength [43]. In a similar way, knee pain may weaken leg strength, leading to falls. In other words, falls may be preventable when pain is relieved by medical care, even if subjects have radiographic knee OA.

In the present study, after adjustment for knee OA and knee pain, slower walking speed was an independent risk factor for falls in men and women. Verghese et al. also showed that risk for falls increased to approximately 7 % as walking speed decreased per 0.1 m/s [44], although bone and joint diseases were not included and men and women were not separately analyzed in the study. In the present study, multiple logistic regression analysis after adjustment for knee OA and knee pain showed that, as walking speed decreased per 0.1 m/s, the risk for falls were 15 and 5 % higher in men and women, respectively, indicating that slower walking speed may more strongly affect the risk of falls in men than women. Although dependent on the availability of equipment, quantitative gait measures can be easily and quickly collected in clinical and research settings without requiring attachment of monitoring devices or extensive training. The present study may indicate that walking speed is a simple and quick option for measuring fall risk, particularly in men.

The present study has several limitations. First, our subjects lived in the community, and thus, our findings may not

Table 2 Comparison of characteristics among nonfallers and fallers in men and women

	Men			Women		
	Nonfallers	Fallers	*p* value	Nonfallers	Fallers	*p* value
Number of subjects	604	141		1,108	362	
Age (years)	68.9±11.2	71.8±10.2	0.003	67.3±11.4	70.3±10.8	<0.001
Height (cm)	163.3±6.9	162.6±5.4	0.18	150.8±6.2	149.0±6.5	<0.001
Weight (kg)	62.2±10.0	62.1±9.8	0.92	52.1±8.6	51.7±8.2	0.34
BMI (kg/m^2)	23.3±3.0	23.5±3.3	0.51	22.9±3.4	23.3±3.4	0.06
Grip strength (kg)	34.8±8.9	33.0±8.2	0.02	22.4±6.2	21.1±6.1	<0.001
Walking speed (m/s)	1.30±0.36	1.11±0.28	<0.001	1.25±0.33	1.15±0.33	<0.001

Values are presented as the mean ± SD, except where indicated. Nonpaired Student's *t* test was used to determine the differences in age, height, weight, BMI, grip strength, and walking speed between nonfallers and fallers

BMI body mass index

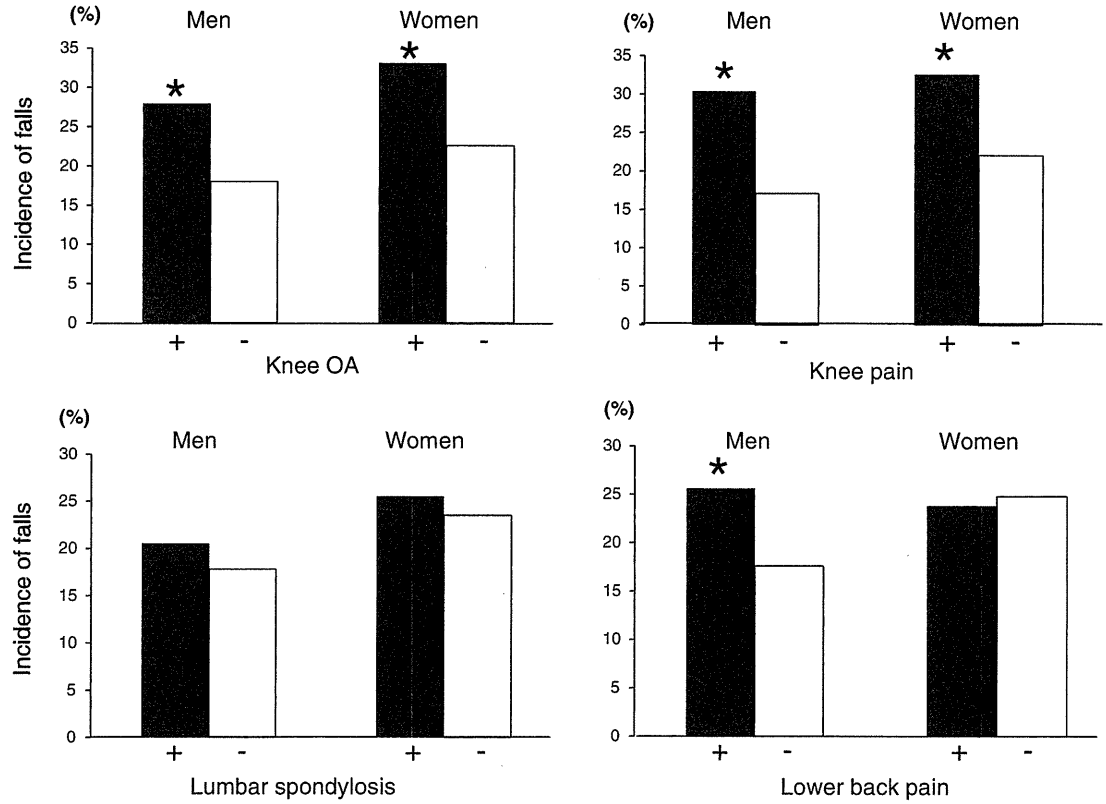

Fig. 2 Incidence of falls by knee OA, knee pain, LS, and lower back pain. *$p<0.05$ vs. subjects without knee OA, LS, knee pain, and lower back pain, respectively, by chi-square test

apply to elderly persons residing in institutions. Second, we did not include other weight-bearing OAs such as hip OA in the analysis, although this disorder also affect falls [45]. However, the prevalence of KL=3 or 4 hip OA is 1.4 and 3.5 % in Japanese men and women [46], respectively, which is smaller than that of KL=3 or 4 knee OA in the present study. Thus, it is possible that hip OA would not strongly affect the results of the present study.

In conclusion, the present longitudinal analysis using a large-scale population from the ROAD study revealed the incidence and risk factors for falls in men and women. Slower walking speed was a risk factor for falls in men

Table 3 Association of physical performance and bone and joint diseases with the incidence of falls in men and women

	Men			Women		
	Crude OR (95 % CI)	Adjusted OR_1 (95 % CI)	Adjusted OR_2 (95 % CI)	Crude OR (95 % CI)	Adjusted OR_1 (95 % CI)	Adjusted OR_2 (95 % CI)
Grip strength (5-kg decrease)	1.14 (1.02–1.27)	1.05 (0.92–1.20)	–	1.20 (1.09–1.33)	1.10 (0.98–1.25)	–
Walking speed (0.1-m/s decrease)	1.19 (1.11–1.25)	1.16 (1.10–1.25)	1.15 (1.09–1.23)	1.10 (1.05–1.14)	1.06 (1.02–1.11)	1.05 (1.01–1.10)
Radiographic knee OA	1.76 (0.98–3.06)	1.52 (0.83–2.67)	1.12 (0.59–2.08)	1.69 (1.27–2.24)	1.43 (1.05–1.93)	1.21 (0.87–1.66)
Knee pain	2.12 (1.31–3.36)	1.99 (1.22–3.18)	1.63 (0.96–2.70)	1.71 (1.31–2.22)	1.54 (1.17–2.02)	1.38 (1.03–1.84)
LS	1.19 (0.83–1.73)	1.04 (0.71–1.52)	–	0.90 (0.71–1.14)	0.74 (0.57–0.94)	–
Low back pain	1.61 (1.02–2.51)	1.59 (0.99–2.49)	–	0.95 (0.79–1.27)	0.91 (0.67–1.23)	–

Multiple logistic regression analysis was used to calculate the odds ratio (OR) and 95 % confidence interval (CI) compared with nonfallers. Adjusted OR_1 was calculated using multiple logistic regression analysis after adjustment for age and BMI. Adjusted OR_2 was calculated using multiple logistic regression analysis with age, BMI, walking speed, radiographic knee OA, and knee pain as independent variables. Radiographic knee OA and LS were defined as KL grade 3 or 4

OA osteoarthritis

and women. Knee pain was a risk factor for falls in women. Further studies, along with continued longitudinal surveys in the ROAD study, will help elucidate the background of knee OA and LS and their relationship with falls.

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Conflicts of interest None.

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