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学術集会案内

第 16 回超音波骨折治療研究会

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Prevalence and distribution of intervertebral disc degeneration over the entire spine in a population-based cohort: the Wakayama Spine Study

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SUMMARY

Objectives: The purposes of this study were to investigate the prevalence and distribution of intervertebral disc degeneration (DD) over the entire spine using magnetic resonance imaging (MRI), and to examine the factors and symptoms potentially associated with DD.

Design: This study included 975 participants (324 men, mean age of 67.2 years; 651 women, mean age of 66.0 years) with an age range of 21–97 years in the Wakayama Spine Study. DD on MRI was classified into Pfirrmann's system (grades 4 and 5 indicating DD). We assessed the prevalence of DD at each level in the cervical, thoracic, and lumbar regions and the entire spine, and examined DD-associated factors and symptoms.

Results: The prevalence of DD over the entire spine was 71% in men and 77% in women aged <50 years, and >90% in both men and women aged >50 years. The prevalence of an intervertebral space with DD was highest at C5/6 (men: 51.5%, women: 46%), T6/7 (men: 32.4%, women: 37.7%), and L4/5 (men: 69.1%, women: 75.8%). Age and obesity were associated with the presence of DD in all regions. Low back pain was associated with the presence of DD in the lumbar region.

Conclusion: The current study established the baseline data of DD over the entire spine in a large population of elderly individuals. These data provide the foundation for elucidating the causes and mechanisms of DD.

Introduction

Intervertebral disc degeneration (DD) is thought to be the first step in degenerative spinal changes[1], and is typically followed by the gradual formation of osteophytes, disc narrowing, and spinal stenosis[2,3]. Furthermore, DD is considered to be one of the causes of several symptoms (neck pain or low back pain)[4–7]. Therefore, in terms of developing preventive strategies for spinal disorders, it will be important to obtain fundamental data on DD (prevalence, distribution, associated factors, etc.) in a population-based cohort.

We believe that the analysis of DD over the entire spine would provide more useful data than that of DD in the cervical, thoracic, or lumbar regions, separately. In particular, investigations on the extent of DD in these three regions using whole spine magnetic resonance imaging (MRI) could provide useful data concerning intra-individual factors in the development of DD. Several studies have examined degenerative changes in only cervical and lumbar discs because of the high susceptibility to DD in these regions[8–12]. As well, several previous studies have investigated the aging process of the intervertebral discs in the cervical and lumbar regions using MRI in population-based cohorts[13,14]. However, degenerative changes in the thoracic region and correspondingly over the entire spine are poorly understood, because DD in the thoracic region is considered to be an uncommon problem[15,16]. In particular, the stabilization of the thoracic region by the thoracic cage, which

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reduces the mechanical stress imposed on the intervertebral discs, is believed to reduce the incidence of degenerative diseases in this region[17].

Consistent with the above-mentioned previous studies, a population-based cohort analysis of DD in the different spinal regions using MRI could be used to examine the distribution of DD over the entire spine. However, to our knowledge, no previous studies have performed this type of investigation with a population-based cohort.

From the perspective of discogenic pain, the association between DD and symptoms remains controversial, although several reports have found that DD was a source of low back pain[4,5]. Moreover, reports on the association between the presence of DD in the cervical and thoracic regions and neck pain are rare[6,7]. Further, these studies were not performed with population-based cohorts and did not use whole spine MRI. Thus, no study has assessed neck pain and low back pain within individuals using whole spine MRI. To clarify the points described above, we established a population-based cohort study in which participants underwent whole spine MRI and were examined for symptoms associated with spinal disorders. This is our first report of DD over the entire spine based on a cross-sectional examination of a baseline population.

The aims of this study were to examine (1) the prevalence and distribution of DD over the entire spine using MRI in a population-based cohort, (2) the factors associated with DD (age, gender, and body mass index [BMI]) in the cervical, thoracic, and lumbar regions, and (3) the association between DD and symptoms (neck pain and low back pain).

Methods

Participants

The present study, entitled the Wakayama Spine Study, was performed with a sub-cohort of the second visit of the ROAD (Research on Osteoarthritis/osteoporosis Against Disability) study, which was initiated as a nationwide, prospective study of bone and joint diseases in population-based cohorts; the cohorts were established in three communities with different characteristics (i.e., urban, mountainous, and coastal regions) in Japan. A detailed profile of the ROAD study has already been described elsewhere[18,19]. Here, we briefly summarize the profile of the present study. The second visit of the ROAD study began in 2008 and was completed in 2010. All the participants in the baseline study were invited to participate in the second visit. In addition to the former participants, inhabitants aged 60 years and older in the urban area and those aged 40 years and younger in the mountainous and coastal areas who were willing to participate in the ROAD survey were also included in the second visit (both the mountainous and coastal areas were in Wakayama prefecture). Finally, 2674 individuals (900 men, 1774 women) participated in the second visit of the ROAD study, and comprised 1067 individuals (353 men, 714 women) in the urban area, 742 individuals (265 men, 477 women) in the mountainous area, and 865 individuals (282 men, 583 women) in the coastal area. Among these three communities in the ROAD study, the mountainous and coastal areas from which we invited all 1607 participants (547 men, 1060 women) to the Wakayama Spine Study are located in Wakayama prefecture. Of the 1607 participants, a total of 1011 individuals provided written informed consent and attended the Wakayama Spine Study with MRI examinations[20,21]. Among the 1011 participants, those who had MRI-sensitive implanted devices (e.g., pacemakers) and other disqualifiers were excluded. Consequently, 980 individuals underwent MRI of the whole spine. Furthermore, one participant who had undergone a previous cervical operation and four participants who had undergone a previous posterior lumbar fusion were excluded from the analysis. Finally, whole spine MRI results were available for 975 participants (324 men, 651 women) with an age range of 21–97 years (mean, 67.2 years for men and 66.0 years for women). Table I shows the demographic and baseline characteristics of the 975 participants in the present study.

For the purpose of analysis, the participants were divided into five age groups: (1) under 50 years, (2) 50–59 years, (3) 60–69 years, (4) 70–79 years, and (5) 80 years and over. The anthropometric measurements included height, weight, and BMI (weight [kg]/height^2 [m^2]). BMI was categorized according to the guidelines for Asians proposed by the World Health Organization and was thus defined as follows: underweight, less than 18.5; normal, 18.5–23; overweight, 23–27.5; and obesity, greater than 27.5[22]. Experienced orthopedists also asked all participants the following question regarding neck pain and low back pain: “Have you experienced neck pain on most days during the past month, in addition to now?” and “Have you experienced low back pain on most days during the past month, in addition to now?” Those who answered “yes” were defined as having neck pain or low back pain based on previous studies[23–26].

MRI

A mobile MRI unit (Excelart 1.5 T, Toshiba, Tokyo, Japan) was used in the present study, and whole spine MRI was performed for all participants on the same day as the examination. The participants were 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]: 4000 ms/echo, echo time [TE]: 120 ms, field of view [FOV]: 300 × 320 mm), and axial T2-weighted FSE (TR: 4000 ms/echo, TE: 120 ms, FOV: 180 × 180 mm).

Sagittal T2-weighted images were used to assess the intervertebral space from C2/3 to L5/S1. C2/3 to C7/T1, T1/2 to T12/L1, and L1/2 to L5/S1 were defined as the cervical region, thoracic region, and lumbar region, respectively. DD grading was performed by an

Table I
Characteristics of participants

	Overall	Men	Women
No. of participants	**975**	**324**	**651**
Age strata (years)			
<50	125	38	87
50–59	175	59	116
60–69	223	65	158
70–79	261	89	172
≧80	191	73	118
Demographic characteristics			
Age, years	66.4 ± 13.5	67.2 ± 13.9	66.0 ± 13.4
Height, cm	156.4 ± 9.4	164.6 ± 7.2	151.5 ± 7.2
Weight, kg	56.8 ± 11.5	64.5 ± 11.6	53.0 ± 9.4
BMI (kg/m^2)	23.3 ± 3.6	23.6 ± 3.4	23.1 ± 3.7
BMI (WHO-Asian category) (*N*)			
Underweight	61	16	45
Normal	425	124	300
Overweight	361	139	221
Obesity	128	44	84
Baseline characteristics			
Symptoms (%)			
Neck pain	24.9	19.4	27.7
Low back pain	43	36.7	42.1
Life style (%)			
Smoking	10.7	25.2	4.1
Alcohol consumption	31.4	56.8	18.8

BMI category for Asian was based on World Health Organization (WHO) guidelines defining underweight (<18.5), normal (18.5–23), overweight (23–27.5), and obese (>27.5). Values are the means ± standard deviation.

orthopedist (MT) who was blind to the background of the subjects. The degree of DD on MRI was classified into five grades based on Pfirrmann's classification system[27], with grades 4 and 5 indicating DD. As shown in Fig. 1, the signal intensity for grade 4 was intermediate to hypointense to the cerebrospinal fluid (dark gray), while the structure is inhomogeneous. Meanwhile, for grade 5, the signal intensity is hypointense to the cerebrospinal fluid (black), and the structure is likewise inhomogeneous. In addition, the disc space is collapsed. It has been reported that loss of signal intensity is significantly associated with the morphological level of the DD and is also associated with both the water and proteoglycan content in a disc[28]. Therefore, we used a grading based on signal intensity and disc height. For evaluating intraobserver variability, 100 randomly selected magnetic resonance images of the entire spine were rescored by the same observer (MT) more than 1 month after the first reading. Furthermore, to evaluate interobserver variability, 100 other magnetic resonance images were scored by two orthopedists (MT and RK) using the same classification. The intraobserver and interobserver variability for DD, as evaluated by kappa analysis, was 0.94 and 0.94, respectively.

"Prevalence of DD", which was defined as "the proportion of the number of participants who had DD at each intervertebral space or region or over the entire spine divided by the total number of participants", was used to describe the frequency of the presence of DD. In the analysis, to clarify the associated factors using multiple logistic regression analysis, we entered a variable of prevalence state (1, presence; 0, absence) of DD as a dependent variable.

Statistical analysis

Multiple logistic regression analysis was used to estimate the association between the presence of DD in each region (cervical, thoracic, and lumbar) as dependent variables and the age group, gender, and BMI category as nominal independent variables after adjustment for the age group, gender and BMI category, mutually.

Additionally, multiple logistic regression analysis was used to estimate the association between the presence of neck pain or low back pain and the presence of DD in each region after adjustment for age, gender, and BMI. Furthermore, in cases in which the presence of DD was significantly associated with a symptom, we examined as a sub-analysis the association between the presence of neck pain or low back pain and the number of DD (categorized into "0", "1 or 2", "3 or more" for ready assessment) in each region using multiple logistic regression analysis after adjustment for age, gender, and BMI. All statistical analyses were performed using JMP version 8 (SAS Institute Japan, Tokyo, Japan).

Results

As shown in Table II, the prevalence of DD in the cervical and thoracic regions and over the entire spine increased with the elevation of the age strata in both men and women. For both genders, the prevalence of DD in the lumbar region was also increased with the elevation of the age strata up to the 70-year-old age group but decreased in the 80-year-old age group. Table III

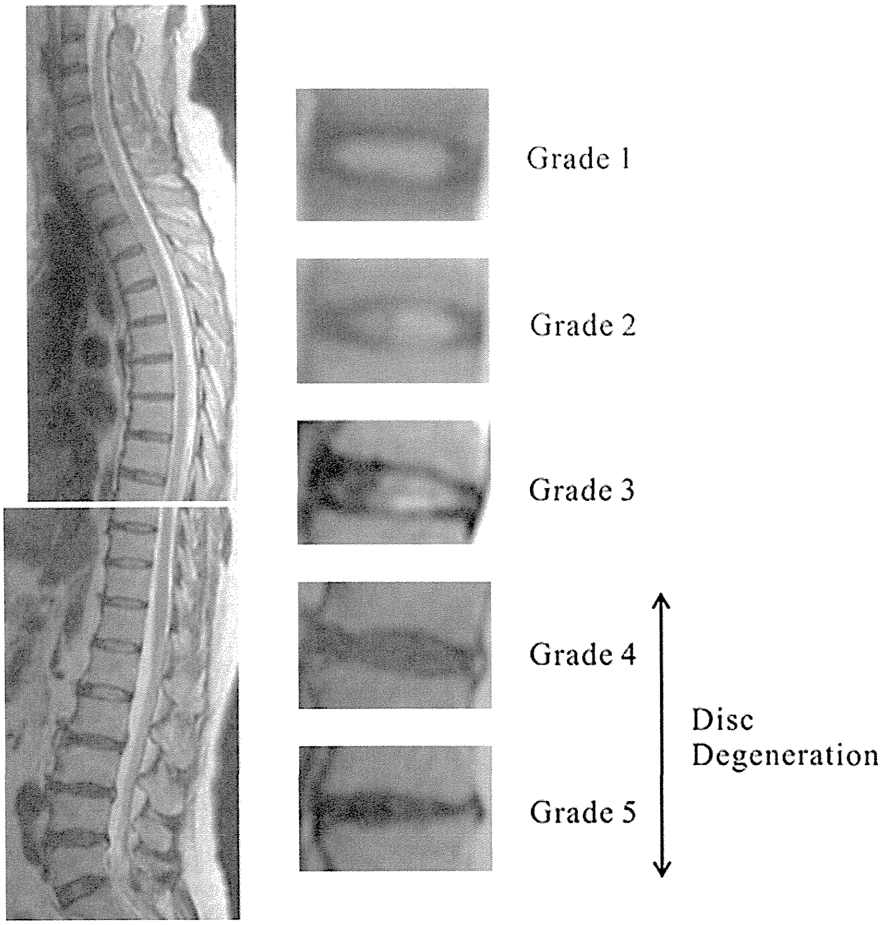

Fig. 1. Mid-sagittal view on T2-weighted images of the whole spine MRI with Pfirrmann classification. The grade is described according to Pfirrmann classification. Grades 4 and 5 were considered degenerated. The signal intensity for grade 4 was intermediate to hypointense to the cerebrospinal fluid (dark gray), while the structure is inhomogeneous. Meanwhile, for grade 5, the signal intensity is hypointense to the cerebrospinal fluid (black), and the structure is also inhomogeneous. Additionally, the disc space is collapsed.

shows the prevalence of intervertebral spaces with DD over the entire spine for the participants in this study. The three highest prevalence levels of DD in the intervertebral spaces in the cervical, thoracic, and lumbar regions were as follows. The prevalence at C5/6 was 51.5% (95% CI: 46.1–56.3) in men and 46% (95% CI: 42.2–49.9) in women, followed by the prevalence at C6/7 of 43.5% in men and 33.3% in women, and at C4/5 of 38.6% in men and 35.8% in women. The prevalence at T6/7 was 32.4% (95% CI: 27.5–37.6) in men and 37.7% (95% CI: 34.1–41.5) in women, followed by the prevalence at T7/8 of 31.8% in men and 36.2% in women, and at T5/6 of 28.4% in men and 35.9% in women. The prevalence at L4/5 was 69.1% (95% CI: 63.9–73.9) in men and 75.8% (95% CI: 72.3–78.9) in women, followed by that at L5/S1 of 66.7% in men and 70.9% in women, and at L3/4 of 59.3% in men and 61.9% in women.

An older age was significantly associated with the presence of DD in each region. Gender was not significantly associated with the presence of DD in each region, although men demonstrated a tendency for a greater number of DD than women in the cervical region. In addition, overweight status (BMI: 23–27.5) was a significantly associated factor in the cervical and thoracic regions, and obesity (BMI: >27.5) was a significantly associated factor in all regions compared with participants of a normal weight (BMI: 18.5–23) (Table IV).

The participants with DD in the cervical region did not significantly differ in terms of the presence of neck pain (OR 0.88, 95% CI: 0.63–1.22, $P = 0.53$). The presence of DD in the thoracic region was not significantly associated with neck pain (OR 0.84, 95% CI: 0.60–1.19, $P = 0.33$) and low back pain (OR 1.08, 95% CI: 0.80–1.47, $P = 0.60$). However, the presence of DD in the lumbar region was significantly associated with low back pain (OR 1.57, 95% CI: 1.02–2.49, $P < 0.05$). Moreover, in a sub-analysis, we investigated the association between low back pain and the number of DD in the lumbar region ("0", "1 or 2", "3 or more"). The presence of low back pain was significantly higher in participants with three or more DD (OR 1.75, 95% CI: 1.11–2.81, $P < 0.05$), but not in those with one or two DD (OR 1.34, 95% CI: 0.84–2.20, $P = 0.22$), as compared with participants without DD.

Discussion

This study is the first to report the prevalence and distribution of DD over the entire spine using whole spine MRI in a population-based cohort. The prevalence of DD over the entire spine and in each of the three spinal regions was higher in older participants. In addition, we noted that the presence of DD was significantly associated with low back pain in the lumbar region but not with neck pain in the cervical region.

Battié *et al.* reviewed the prevalence of DD in the lumbar region and noted that it ranged from 20% to 83%[29]. Consistent with the observations of this review, other reported prevalence levels of DD in the lumbar region have shown wide variation between samples and have often been quite high because the studies had certain drawbacks, including relatively small sample sizes[1,30], narrow age ranges[5,31], and asymptomatic subjects[32]. However, no previous study has assessed the prevalence of DD over the entire spine using whole spine MRI. We noted that the prevalence of DD over the entire spine exceeded 70% in participants less than 50 years of age and was greater than 90% in participants older than 50 years of age.

Table II
Prevalence of DD by age strata in men and women

	Entire spine		Cervical		Thoracic		Lumbar	
	Men	Women	Men	Women	Men	Women	Men	Women
Age strata (years)								
<50	71.0	77.0	26.3	27.9	15.7	11.4	55.2	71.2
50–59	91.5	93.1	47.4	49.1	49.1	35.3	86.4	91.3
60–69	98.4	95.5	66.1	54.4	61.5	63.2	96.9	94.3
70–79	95.8	99.4	80.9	72.0	73.0	79.6	96.6	96.5
≧80	93.2	97.4	86.3	85.5	79.4	88.9	82.1	84.5

Values are percentage.

Little epidemiological data are available concerning DD in the intervertebral space using MRI assessments in a population-based cohort. Matsumoto *et al.*[4] reported that the prevalence of DD in the cervical region was the highest at C5/6 (86% in men and 89% in women over the age of 60 years). In addition, Hanagai *et al.*[33] and Kanayama *et al.*[34] reported that the prevalence of DD in the lumbar region was the highest at L4/5 (67%; mean age 68.4 years) and L5/S1 (49.5%; mean age 39.7 years), respectively. In the present study, the prevalence of DD was the highest at C5/6 (51.5% in men and 46.0% in women) and L4/5 (69.1% in men and 75.8% in women). The prevalence of cervical DD in the previous study by Matsumoto *et al.*[4] was higher than that in the present study. However, the subjects were recruited from volunteers in the hospital rather than a population; thus, the capacity for strict comparisons are limited. Furthermore, few studies have reported age-related DD in the thoracic region. Matsumoto *et al.* reported that the highest prevalence of DD occurred at T7/8 (30.9%; mean age 48.0 y) followed by T6/7 in the thoracic region; however, all 94 participants in this report were asymptomatic[35]. In the present study, we confirmed a high prevalence of DD at T6/7 in the thoracic region. This finding is supported by results from thoracic MRI investigations demonstrating a high prevalence of DD in asymptomatic individuals.

The distribution of prevalence of DD was similar to the alignment of the spine in the sagittal plane, such as cervical lordosis (C3–C7), thoracic kyphosis (T1–T12), and lumbar lordosis (L1–L5)[36]. The high prevalence of DD in the lumbar region can potentially be explained by mechanical stress. Our results support the hypothesis that compressive stress affected DD, since compressive stresses are the highest in the mid-thoracic region of the entire spine[37]. Mechanical stress on the thoracic intervertebral disc is reduced due to stabilization by the thoracic cage, and therefore, the thoracic intervertebral disc may be affected by the detrimental effect of compressive stress caused by posture on the sagittal balance of the spine[38]. This study also provides the first mapping of intervertebral spaces with DD over the entire spine by MRI analysis, which adds to our knowledge of the distribution of prevalence of DD in the cervical, thoracic, and lumbar regions, which has been reported only fragmentarily in previous reports.

Our current results confirmed that age was a significant factor associated with the presence of DD in all three regions. Previous studies reported that the association of DD to factors such as height, weight, and gender was uncertain; however, age, obesity, smoking, and occupation have been suggested to be DD-associated factors[39–42]. The previous studies focused almost entirely on the lumbar region, and the identification of associated factors may be challenging for this region because it is affected to a greater extent by various factors, including mechanical stress. Moreover, it remains unknown what other factors (beyond age) are associated with DD in the cervical and thoracic regions[6,13]. In the present study, overweight and obesity significantly influenced DD in the cervical and thoracic regions (cervical; OR: overweight 1.38 [95% CI 1.00–1.90], obesity 1.60 [95% CI 1.04–2.51], thoracic; OR: overweight 1.64 [95% CI 1.17–2.29], obesity 3.12 [95% CI 1.91–5.19]), and obesity also significantly influenced DD in the lumbar region (OR: 2.56 [95% CI 1.20–6.14]). In a previous study, Samartzis *et al.* reported that DD in the lumbar region was significantly associated with overweight and obesity[39]. However, DD in the cervical and thoracic region did not demonstrate a significant association with BMI, as reported by Okada *et al.*[6] and Matsumoto *et al.*[35]. Of note, the previous studies were

Table III
Prevalence of intervertebral spaces with DD over the entire spine by age strata in men and women

Age strata (years)	C2/3	C3/4	C4/5	C5/6	C6/7	C7/T1	T1/2	T2/3	T3/4	T4/5	T5/6	T6/7	T7/8	T8/9	T9/10	T10/11	T11/12	T12/L1	L1/2	L2/3	L3/4	L4/5	L5/S1
Men																							
Total	28.3	30.2	38.6	51.5	43.5	26.8	20.3	23.4	22.2	24.0	28.4	32.4	31.8	28.7	31.4	25.0	24.0	17.5	30.0	51.5	59.3	69.1	66.7
<50	10.5	10.5	13.1	15.7	13.1	5.2	5.2	7.8	7.8	5.2	10.5	7.8	5.2	2.6	2.6	2.6	0.0	0.0	2.6	10.5	7.8	34.2	47.3
50–59	6.7	11.8	15.2	37.2	27.1	10.1	8.4	6.7	11.8	11.8	16.9	23.7	27.1	16.9	20.3	16.9	13.5	5.1	15.2	35.5	61.0	74.5	50.8
60–69	35.3	36.9	49.2	50.7	40.0	21.0	20.0	24.6	23.0	27.6	27.6	35.3	32.3	36.9	41.5	23.0	24.6	18.4	40.0	60.0	69.0	76.9	75.3
70–79	35.9	35.9	49.4	64.0	51.6	34.8	24.7	26.9	25.8	30.3	33.7	38.2	41.5	35.9	40.4	37.0	31.4	26.9	39.3	69.6	73.0	79.7	79.7
≧80	39.7	42.4	47.9	67.1	65.7	46.5	32.8	39.7	32.8	32.8	41.0	42.4	36.9	35.6	35.6	30.1	35.6	24.6	39.7	56.1	58.9	63.0	65.7
Women																							
Total	21.9	24.8	35.8	46.0	33.3	13.6	15.2	23.1	29.8	31.7	35.9	37.7	36.2	34.2	32.7	28.7	23.8	20.0	31.7	49.7	61.9	75.8	70.9
<50	2.2	3.4	10.3	20.6	10.3	1.1	0.0	1.1	4.5	0.0	1.1	4.5	3.4	5.7	4.5	4.5	1.1	0.0	4.5	12.6	18.3	49.4	56.3
50–59	11.2	9.4	23.2	36.2	23.2	3.4	6.8	12.0	15.5	15.5	16.3	18.1	19.8	12.9	13.7	10.3	6.9	6.9	15.6	35.6	55.6	73.9	70.4
60–69	13.9	20.8	31.0	43.6	29.1	11.3	13.2	18.3	29.7	32.2	37.9	39.8	31.6	32.2	30.3	19.6	15.8	14.5	25.3	55.0	66.4	85.4	75.9
70–79	33.7	34.8	46.5	53.4	42.4	16.2	22.0	34.3	41.2	44.7	50.0	50.0	47.0	45.9	44.7	42.4	34.3	26.1	44.7	64.5	80.2	86.0	81.9
≧80	40.6	46.6	57.6	66.9	52.5	32.2	27.1	40.6	45.7	51.6	57.6	61.0	66.9	61.8	57.6	56.7	52.9	46.1	57.2	62.3	67.5	69.2	58.9

Values are percentage.

conducted with asymptomatic healthy subjects. Therefore, based on our findings, obesity appears to have some influence on the process of DD over the entire spine.

An association between DD in the lumbar region and low back pain was previously demonstrated in a twin study[43]. Moreover, Okada *et al.*[6] reported an association between neck pain and DD in the cervical region, whereas Arana *et al.*[7] found an association between neck pain and DD in the upper thoracic region. Of interest, no agreement has been reached regarding the most appropriate definition of neck pain and low back pain in population cohorts[7]. Nonetheless, we observed a significant association between the presence of DD in the lumbar region and low back pain.

The present study has several limitations. First, it was a cross-sectional study, and therefore, the transition to DD cannot be clarified. Second, the participants included in the present study may not represent the general population, since they were recruited from only two local areas. To confirm whether the participants of the Wakayama Spine Study are representative of the Japanese population, we compared the anthropometric measurements and frequencies of smoking and alcohol consumption between the general Japanese population and the study participants. No significant differences in BMI were observed (men: 24.0 and 23.7, $P = 0.33$; women: 23.5 and 23.1, $P = 0.07$). Further, the proportion of current smokers and those who consumed alcohol (those who regularly smoked or consumed alcohol more than once per month) in men and the proportion of those who consumed alcohol in women were significantly higher in the general Japanese population than in the study population, whereas there was no significant difference in the proportion of current smokers in women (male smokers, 32.6% and 25.2%, $P = 0.015$; female smokers, 4.9% and 4.1%, $P = 0.50$; men who consumed alcohol, 73.9% and 56.8%, $P < 0.0001$; women who consumed alcohol, 28.1% and 18.8%, $P < 0.0001$). These results suggest the likelihood that in this study, participants had healthier lifestyles than those of the general Japanese population[44]. This "healthy" selection bias should be taken into consideration when generalizing the results obtained from the Wakayama Spine Study. Third, the Pfirrmann classification introduced a comprehensive MRI grading system based on the assessment of structure, the distinction of the nucleus and annulus fibrosis, the signal intensity[28], and the height of the intervertebral discs[27]. However, bony endplate alterations, osteophyte changes, spinal stenosis, and disc protrusion are not covered by the Pfirrmann classification. Therefore, it is necessary to perform investigations that include these morphological changes. Finally, the accurate measurement of obesity, such as abdominal obesity and/or body composition, might reveal that obesity has a stronger association with DD; however, the present study examined only BMI as a measurement of obesity. Thus, we plan to examine the girth of the abdomen and body composition using electrical impedance in the assessment of human body composition (the BIA method) in a future study.

In conclusion, this study is the first one to investigate the prevalence of DD over the entire spine in a large population of individuals to establish baseline data for a prospective longitudinal

Table IV
Multiple logistic regression of the association with presence of DD with age, BMI, and gender

	Cervical	Thoracic	Lumbar
	OR (95% CI)	OR (95% CI)	OR (95% CI)
Age group (years)			
<50	1	1	1
50–59 (vs <50)	2.45 (1.5–4.06)**	4.60 (2.53–8.76)***	4.47 (2.44–8.48)***
60–69 (vs <50)	3.62 (2.26–5.91)***	12.0 (6.77–22.7)***	9.95 (5.02–21.3)***
70–79 (vs <50)	7.87 (4.86–12.9)***	24.9 (13.8–47.6)***	15.0 (7.26–34.5)***
≧80 (vs <50)	16.9 (9.68–30.5)***	47.0 (24.5–95.6)***	2.94 (1.71–5.13)**
Men (vs women)	1.20 (0.89–1.64)	0.88 (0.64–1.21)	0.70 (0.45–1.09)
BMI (WHO-Asian category)			
Underweight (vs normal)	0.91 (0.49–1.70)	1.36 (0.71–2.67)	0.81 (0.38–1.84)
Normal	1	1	1
Overweight (vs normal)	1.38 (1.00–1.90)*	1.64 (1.17–2.29)*	1.14 (0.71–1.85)
Obesity (vs normal)	1.60 (1.04–2.51)*	3.12 (1.91–5.19)***	2.56 (1.20–6.14)*

BMI category for Asian was based on World Health Organization (WHO) guidelines defining underweight (<18.5), normal (18.5–23), overweight (23–27.5), and obese (>27.5). OR = odds ratio, CI = confidential interval.
$^{*}P < 0.05$, $^{**}P < 0.001$, $^{***}P < 0.0001$.

study. The prevalence of intervertebral spaces with DD was the highest at C5/6, T6/7, and L4/5 in the cervical, thoracic, and lumbar regions, respectively. DD in the cervical, thoracic, and lumbar regions was significantly associated with age and obesity. A significant positive association was observed between the presence of DD in the lumbar region and low back pain.

Author contributions

All authors worked collectively to develop the protocols and method described in this paper. MT, NY, SM, HO, YI, KN, NT, and TA were principal investigators responsible for the fieldwork in the Wakayama Spine study. MT and SM performed the statistical analysis. All authors contributed to the analysis and interpretation of results. MT wrote the report. All authors read and approved the final manuscript.

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The sponsors had no role in study design, data collection, data analysis, data interpretation, or in writing of the report.

Conflict of interest

The authors declare no conflicts of interest.

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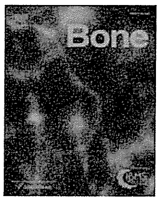

Original Full Length Article

Risk factors for falls in a longitudinal population-based cohort study of Japanese men and women: The ROAD Study

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ABSTRACT

The objective of this study was to clarify the associations of physical performance and bone and joint diseases with single and multiple falls in Japanese men and women using a population-based longitudinal cohort study known as Research on Osteoarthritis/osteoporosis Against Disability (ROAD). A total of 452 men and 896 women were analyzed in the present study (mean age, 63.9 years). A questionnaire was used to assess the number of falls during the 3-year follow-up. Grip strength, 6-m walking time, and chair stand time were measured at baseline. Knee osteoarthritis (OA) and lumbar spondylosis were defined as Kellgren Lawrence = 2, 3 or 4. Vertebral fracture (VFx) was assessed with the Japanese Society of Bone and Mineral Research criteria. Osteoporosis was defined by bone mineral density using dual energy X-ray absorptiometry based on World Health Organization criteria. Knee and lower back pain were estimated by an interview. During a 3-year follow-up, 79 (17.4%) men and 216 (24.1%) women reported at least one fall, and 54 (11.9%) men and 111 (12.4%) women reported multiple falls. Knee pain was a risk factor for multiple falls in women, but not in men. VFx tended to be associated with multiple falls in women, but not in men. A longer 6-m walking time was a risk factor for multiple falls in women, whereas a longer chair stand time was a risk factor for multiple falls in men. We found gender differences in risk factors for falls.

Introduction

Falls are one of the main causes of injury, disability, and death among the elderly [1,2]. In Japan, according to the 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, few population-based studies have been performed on the incidence of falls based on sex and age. Furthermore, 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, the association of bone and joint diseases, especially osteoarthritis (OA), with falls remains unclear.

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 [6,7]. The prevalence rates of radiographic knee OA and LS are 54.6% and 70.2%, respectively, in persons aged 40 years and older in Japan, which indicates that 25,300,000 and 37,900,000 persons aged 40 years and older are estimated to experience radiographic knee OA and LS, respectively [10]. 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 [11,12]. In previous studies, knee OA was assessed only by interview and not by radiography. The principal clinical symptom of knee OA is pain [13], but its correlation with the radiographic severity of knee OA is not as strong as expected [8]. In fact, in a study in Japan, approximately 20% of persons without knee OA had knee pain, and 30% of persons with severe knee OA had no knee pain [8]. 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 [8]. Our previous study showed that knee pain is significantly associated with falls in women [14], but that study used a cross-sectional design; thus, a causal relationship remains unclear. Regarding LS, to the best of our knowledge, no population-based studies have been performed

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regarding its association with falls except for our previous cross-sectional study [14], which showed that LS is not significantly associated with falls. In addition, among fractures due to osteoporosis (OP), vertebral fracture (VFx) is the most likely to lead to marked public health problems. VFx is reportedly associated with functional impairment [15], back pain, kyphosis [16,17], esophageal reflux [18], depressive mood [19], respiratory dysfunctions [20], and mortality [21]. However, whether VFx is an independent risk factor for the incidence of falls remains unclear.

Measuring walking speed is a simple way to assess health and function in older adults [22,23]. Walking speed has been found to be associated with falls in a few studies [4,24–26], although most studies were limited by a small sample size, a cross-sectional design [24,25], or evaluation of a single sex [4,26]. In addition, although walking abnormalities indicative by a slower walking speed are significantly associated with bone and joint diseases such as knee OA, LS, and their associated pain [14], no longitudinal studies have been performed to determine the associations of falls with bone and joint diseases and walking abnormalities at the same time. Furthermore, measuring the chair stand time is also reported to be a simple and established method to assess health and function in the elderly [27,28], but to the best of our knowledge, no longitudinal studies have been performed to determine the associations of falls with chair stand time.

Previous studies have shown that associations between individual risk factors and a single fall are few in number and weak compared to risk factors for multiple falls [12], indicating that single and multiple falls may have different backgrounds. Thus, to determine factors associated with falls, single and multiple falls should be analyzed separately.

The objective of this study was to clarify the associations of physical performance and bone and joint diseases with the incidence of single and multiple falls in Japanese men and women using a population-based longitudinal cohort study known as Research on Osteoarthritis/osteoporosis Against Disability (ROAD).

Methods

Participants

The ROAD study is a nationwide, prospective study designed to establish epidemiologic indices for evaluation of clinical evidence for the development of a disease-modifying treatment for bone and joint diseases (OP and OA are the representative bone and joint diseases, respectively). ROAD consists of population-based cohorts in three communities in Japan. A detailed profile of the ROAD study has been described elsewhere [8–10,29]; 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 participants (1,061 men and 1,979 women) ranging in age 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 list of the relevant region. Participants in the urban region were recruited from a randomly selected cohort from the Itabashi-ward residents' registration database [30]. 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.

Assessment of falls

Three years after the baseline data were obtained, we attempted to trace and review all 3,040 participants between 2008 and 2010; they were invited to attend a follow-up interview. All participants were interviewed with regard to falls by experienced interviewers and were asked the following questions: "Have you experienced falls during the 3-year follow-up, and if yes, how many falls did you experience"? At baseline, all participants were also interviewed regarding falls by experienced interviewers and were asked the following questions: "Have you experienced falls during the 12 months preceding baseline, and if yes, how many falls did you experience"? According to a previous study on falls [31], 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 participants were interviewed by experienced orthopedists regarding knee pain and lower back pain at baseline and were asked the following questions based on previous studies [8,9]: "Have you experienced knee pain on most days in the past month, in addition to now"? and "Have you experienced lower back pain on most days in the past month, in addition to now"? Those who answered "yes" were defined as having pain. Buttock pain and sciatica were not included as lower back pain in the present study.

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. VFx was assessed by lateral radiographs of the lumbar spine (L1-L5) in terms of a wedge, biconcave, or crush appearance according to the Japanese Society of Bone and Mineral Research criteria [32]. The films were marked up, and morphometric measurements of anterior, middle, and posterior heights on lateral radiography of the thoracic and lumbar spine were made. Wedge appearance was defined as a site at which the anterior height of the vertebra was $\leq$75% of the posterior height. Biconcave appearance occurred if the height of the central part of the vertebra was $\leq$80% of that of the anterior or posterior parts of the vertebra. Crush appearance occurred if the height of the anterior, central, and posterior parts of an axial vertebra were all reduced to $\leq$80% of the normal value (Supplementary Fig. 1). Knee and lumbar spine radiographs were also read without knowledge of the participant's clinical status by a single, experienced orthopedist (S.M.) using the Kellgren Lawrence (KL) radiographic atlas [33] to determine the severity of KL grading. Radiographs were scored as grade 0–4, with higher grades associated with more severe OA. We defined knee OA and LS as KL $\geq$2 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 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 intra- 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).

Bone mineral density (BMD) measurement

BMD was measured at the lumbar spine (L2–4) and the proximal femur using dual energy X-ray absorptiometry (DXA) (Hologic

Discovery; Hologic, Waltham, MA, USA) at baseline. For quality control, the same DXA equipment was used, and the same spine phantom was scanned daily to monitor the machine's performance in study populations at different regions. The BMD of the phantom was adjusted to 1.032 ± 0.016 g/cm^2 ($\pm 1.5\%$) during all examinations. In addition, the same physician (N.Y.) examined all participants to prevent observer variability. Coefficient of variance (CV) for L2–L4 in the phantom was 0.35%, and CVs for L2–L4, the proximal femur, Ward's triangle, and the trochanter examined in five volunteers were 0.61–0.90, 1.02–2.57, 1.97–5.45, and 1.77–4.17%, respectively [34].

OP was defined based on World Health Organization (WHO) criteria in which OP was diagnosed as T-scores of BMD ≤ 2.5 standard deviations (SDs) lower than peak bone mass [35]. Mean L2–4 BMD (SD) for young adult men and women measured using the Hologic QDR devices in Japan is reportedly 1.011 g/cm^2 (0.119 g/cm^2) [36]. Mean femoral neck BMD (SD) in Japan is reported to be 0.863 g/cm^2 (0.127 g/cm^2) for young men and 0.787 (0.109) for young women [36]. The present study therefore defined OP using these indices as lumbar spine BMD <0.714 g/cm^2 for both men and women, and as femoral neck BMD <0.546 g/cm^2 for men and <0.515 g/cm^2 for women.

Physical performance

At baseline, anthropometric measurements were taken, including height and weight, and body mass index (BMI) (weight [kg]/height^2 [m^2]) was estimated based on the measured height and weight. Grip strength was measured on bilateral sides using a TOEI LIGHT handgrip dynamometer (TOEI LIGHT CO., LTD, Saitama, Japan), 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. Participants 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. The average of two trials was recorded. These gait-speed trial measurements are considered highly reliable in community-dwelling elderly persons [37]. The time taken for five consecutive chair rises without the use of hands was also recorded. Hands were folded in front of the chest with feet flat on the floor, following the protocol described by Guralnik et al. [27] and used by other researchers [28]. Time was measured in seconds with a stopwatch and rounded to the nearest hundredth of a second. Timing began with the command "Go" and ended when the buttocks contacted the chair on the fifth landing. The reliability of this protocol is adequate [27].

Cognition assessment

At baseline, cognition was also evaluated for all participants using a Mini-Mental State Examination, and a cut-off score of <24 was used to select participants with cognitive impairment [38].

Statistical analyses

The differences in age and anthropometric measurements between the responders (those who completed the study) and non-responders (those lost to follow-up or who did not complete the study as described below) and between men and women were examined with a non-paired Student's *t*-test. Differences in physical performance measurements between the responders and non-responders and between men and women were examined with Wilcoxon signed-rank test. Differences in age and anthropometric measurements, among non-fallers, single fallers, and multiple fallers, were examined with one-way analysis of variance. Differences in physical performance measurements among non-fallers, single fallers, and multiple fallers were examined with the Kruskal–Wallis test. The prevalence of bone and joint diseases and cognitive impairment was compared between men and women and among non-fallers, single fallers, and multiple fallers with the chi square test. Multinomial logistic regression analysis after adjusting for age and BMI was used to determine the association of anthropometric measurements, physical performance, bone and joint diseases, and cognitive impairment with single and multiple falls compared with the absence of falls in men and women. Further, to determine an independent association of physical performance with single and multiple falls compared with the absence of falls, we used multinomial logistic regression analysis with age, BMI, 6-m walking time, and chair stand time as explanatory variables. To determine independent risk factors for single and multiple falls, we used multinomial logistic regression analysis with age, BMI, physical performance, bone and joint diseases, and cognitive impairment as explanatory variables. Data analyses were performed using SAS version 9.0 (SAS Institute Inc., Cary, NC, USA).

Results

Of the 1,690 participants in the mountainous and seaside cohorts at baseline in 2006 and 2007, 40 (2.4%) had died by the time of the review 3 years later, 97 (5.7%) did not participate in the follow-up study due to poor health, 16 (0.9%) had moved away, 51 (3.0%) declined the invitation to attend the follow-up study, and 47 (2.8%) did not participate in the follow-up study for other reasons. Among the 1,439 volunteers who did participate in the follow-up study, 68 (4.0%) provided incomplete fall questionnaires. In addition, six (0.4%) provided incomplete pain questionnaires; these were excluded. We also excluded eight (0.5%) participants who had undergone total knee arthroplasty before baseline. An additional nine (1.9%) participants did not perform the 6-m walking time or chair stand time, leaving a total of 1,348 (79.8%) participants (452 men and 896 women) from whom radiographs at baseline and complete fall and pain histories were obtained. The mean followup time was 2.93 ± 0.12 years, ranging from 2.65 to 3.22 years. Table 1 shows characterisctics of responders and non-responders. The responders were significantly younger than the non-responders (63.9 and 70.7 years, respectively). Physical performance measurements were better in responders than non-responders. Prevalence of knee OA, LS and knee pain was lower in responders (47.0, 61.6 and 9.7%,

Table 1
Baseline characteristics of responders and non-responders.

	Overall	Responders	Non-responders
Number of participants	1,690	1,348	342
Female (%)	64.7	66.5	57.9^{***}
Age (years)	65.2 ± 12.0	63.9 ± 11.8	$70.7 \pm 11.4^{*}$
Height (cm)	155.2 ± 9.3	155.6 ± 9.0	$153.6 \pm 10.1^{*}$
Weight (kg)	55.6 ± 10.8	56.1 ± 10.7	$53.7 \pm 10.8^{*}$
BMI (kg/m^2)	23.0 ± 3.4	23.1 ± 3.4	22.7 ± 3.4
Grip strength (kg) (median [IQR])	26.0 [21.0–33.0]	26.0 [21.0–34.0]	24.0 [18.0–30.0]**
6-m walking time (s) (median [IQR])	5.0 [4.0–7.0]	5.0 [4.0–6.0]	7.0 [5.0–9.0]**
Chair stand time (s) (median [IQR])	9.0 [7.0–12.0]	9.0 [7.0–11.0]	12.0 [8.25–15.0]**
Cognitive impairment (%)	4.5	2.8	11.4^{***}
Radiographic knee OA (%)	50.4	47.0	63.8^{***}
Radiographic LS (%)	63.2	61.6	69.1^{***}
Radiographic VFx	10.1	9.7	12.0
Knee pain (%)	24.3	22.2	32.6^{***}
Lower back pain (%)	21.1	20.6	22.9
Previous falls (%)	17.3	16.3	21.0^{***}

Values are mean ± SD, except where indicated.
BMI: body mass index, OA: osteoarthritis, LS: lumbar spondylosis, VFx: vertebral fracture, IQR: interquartile range.
* $p<0.05$ vs. responders by non-paired Student's *t*-test.
** $p<0.05$ vs. men by Wilcoxon signed-rank test.
*** $p<0.05$ vs. men by chi square test.

Table 2
Baseline characteristics of participants.

	Men	Women
Number of participants	452	896
Age (years)	64.9 ± 11.7	63.3 ± 11.8*
Height (cm)	164.0 ± 7.0	151.3 ± 6.6*
Weight (kg)	63.3 ± 10.7	52.5 ± 8.7*
BMI (kg/m^2)	23.5 ± 3.2	22.9 ± 3.4*
Grip strength (kg) (median [IQR])	37.0 [32.0–42.5]	23.5 [20.0–23.5]**
6-m walking time (s) (median [IQR])	5.0 [4.0–6.0]	5.0 [4.0–6.0]
Chair stand time (s) (median [IQR])	8.5 [7.0–11.0]	9.0 [7.0–11.0]
Cognitive impairment (%)	3.6	2.4
Radiographic knee OA (%)	37.4	51.9***
Radiographic LS (%)	76.1	54.2
Radiographic VFx	8.9	10.1
Knee pain (%)	15.3	25.7***
Lower back pain (%)	18.8	21.5
Previous falls (%)	13.1	18.0***

Values are mean ± SD, except where indicated.
BMI: body mass index, OA: osteoarthritis, LS: lumbar spondylosis, VFx: vertebral fracture, IQR: interquartile range.
* $p<0.05$ vs. men by non-paired Student's *t*-test.
** $p<0.05$ vs. men by Wilcoxon signed-rank test.
*** $p<0.05$ vs. men by chi square test.

respectively) than non-responders (63.8, 69.1 and 12.0, respectively). Prevalence of previous falls was significantly lower in responders than non-responders (16.3 and 21.0%, respectively).

Table 2 shows the age, anthropometric measurements, physical performance, and prevalence of cognitive impairment, bone and joint diseases, and previous falls of participants at baseline in men and women. Regarding physical performance, grip strength and chair stand time were significantly better in men (37.0 kg and 8.5 s, respectively) than in women (23.5 kg and 9.0 s, respectively), but the 6-m walking time was not (5.0 s and 5.0 s, respectively). The prevalence of radiographic knee OA and knee pain was significantly higher in women (51.9% and 25.7%, respectively) than in men (37.4% and 15.3%, respectively), whereas that of LS and lower back pain was not different between men and women. The prevalence of previous falls was significantly higher in women than in men (18.0% and 13.1%, respectively).

During the 3-year follow-up, 79 (17.4% [95% confidence interval [CI] 14.3–21.2]) men and 216 (24.1% [95% CI 21.4–27.0]) women reported at least one fall, and 54 (11.9% [95% CI 9.3–15.3]) men and 111 (12.4% [95% CI 10.4–14.7]) women reported multiple falls. The chi square test showed that the incidence of falls was significantly different between men and women ($p=0.0011$). The incidence of single and multiple falls was significantly higher in the mountainous regions (11.5% and 17.4%, respectively) than coastal regions (8.1% and 7.8%, respectively). With increasing age, the incidence of falls increased in women, but the incidence of falls was similar in men in their 60s and 70s (Fig. 1).

Table 3 shows the age, anthropometric measurements, physical performance, and BMD at baseline between non-fallers, single fallers, and multiple fallers. Age and BMI were significantly higher in female fallers than non-fallers, but this was not the case in men. Grip strength was worse in female fallers than non-fallers, but this was not the case in men. The 6-m walking time and chair stand time were longer in both male and female fallers than in non-fallers. LS and neck BMD were significantly lower in female fallers than non-fallers, but this was not the case in men.

We next examined the incidence rate of falls during the 3-year follow-up according to previous falls at baseline in men and women (Supplementary Fig. 2). The incidence rates of multiple falls were 7.9%, 22.7%, and 48.7% in men and 8.8%, 20.4%, and 43.1% in women among non-fallers, single fallers, and multiple fallers, respectively. The incidence rates of single falls were 5.9%, 9.1%, and 0.0% in men and 12.5%, 7.8%, and 8.6% in women among non-fallers, single fallers, and multiple fallers, respectively. The chi square test showed that the incidence of falls during the 3-year follow-up was significantly associated with previous falls at baseline in men and women ($p<0.0001$).

Fig. 2 shows the incidence rate of falls during the 3-year follow-up according to the presence of bone and joint diseases and cognitive impairment. The incidence rates of multiple falls were 16.6% and 9.2% in men and 14.8% and 9.7% in women in those with and without knee OA, respectively. The incidence rates of a single fall were 8.3% and 3.9% in men and 14.2% and 9.1% in women in those with and without knee OA, respectively. The chi square test showed that knee OA at baseline was significantly associated with the incidence rate of falls during the 3-year follow-up in men and women ($p<0.0001$). Regarding knee pain, the incidence rates of multiple falls were 18.8% and 10.7% in men and 18.7% and 10.2% in women in those with and without knee pain, respectively. The incidence rates of a single fall were 8.7% and 5.0% in men and 10.4% and 10.4% in women in those with and without knee OA, respectively. The chi square test showed that knee pain at baseline was significantly associated with the incidence of falls during the 3-year follow-up in men and women ($p<0.0001$). LS and lower back pain were not significantly associated with the incidence of falls in men ($p=0.52$ and 0.77, respectively) or in women ($p=0.45$ and 0.58, respectively). VFx at baseline was significantly associated with the incidence of falls in women (multiple falls 22.2% and 11.3%, single falls 14.4% and 11.4%, in those with and without VFx, respectively, $p=0.005$), but not in men ($p=0.06$). OP defined by L2–4 and femoral neck BMD was not associated with the incidence of falls in men and women. Cognitive impairment

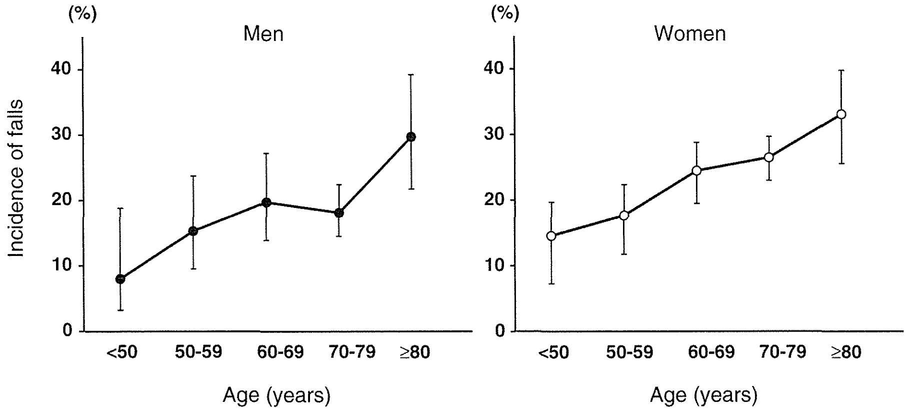

Fig. 1. Incidence rate of falls (error bars represent 95% confidence intervals) by gender and age strata.

Table 3
Comparison of characteristics among non-fallers, single fallers, and multiple fallers in men and women.

	Men				Women			
	Non-fallers	Single fallers	Multiple fallers	p value	Non-fallers	Single fallers	Multiple fallers	p value
Number of participants	373	25	54		680	105	111	
Age (years)	64.4 (11.7)	67.2 (13.2)	67.6 (10.1)	0.10	62.4 (11.6)	66.0 (12.6)	66.7 (11.4)	<0.001
BMI (kg/m^2)	23.4 (3.1)	24.6 (3.9)	23.7 (3.3)	0.16	22.8 (3.5)	22.7 (3.1)	23.8 (3.5)	0.01
Grip strength (kg) (median [IQR])	37.0 [32.0–43.0]	37.0 [30.0–41.5]	35.0 [28.8–40.0]	0.08	24.0 [20.0–27.0]	23.0 [19.5–27.0]	22.0 [18.0–26.0]	0.01
6-m walking time (s) (median [IQR])	4.5 [4.0–6.0]	5.5 [4.6–7.3]	6.2 [5.0–6.6]	<0.0001	5.0 [4.0–6.0]	5.0 [4.0–6.5]	5.5 [4.0–7.5]	<0.0001
Chair stand time (s) (median [IQR])	8.0 [7.0-10.0])	11.0 [9.0-12.0]	10.0 [8.0-13.0]	<0.0001	9.0 [7.0-11.0]	9.0 [8.0-12.0]	10.0 [8.0-12.25]	0.0001
LS BMD	1.05 (0.20)	1.05 (0.20)	1.05 (0.15)	0.99	0.89 (0.18)	0.85 (0.16)	0.86 (0.17)	0.04
Neck BMD	0.75 (0.13)	0.77 (0.12)	0.75 (0.10)	0.79	0.65 (0.13)	0.61 (0.11)	0.63 (0.11)	0.003

Values are the means (standard deviation), except where indicated.
One-way analysis of variance was used to determine the differences in age, height, weight and BMI among non-fallers, single fallers, and multiple fallers.
Kruskal–Wallis test was used to determine the differences in grip strength, 6-m walking time and chair stand time among non-fallers, single fallers, and multiple fallers.
The chi square test was used to determine the differences in the prevalence of cognitive impairment among non-fallers, single fallers, and multiple fallers.
BMI: body mass index, LS: lumbar spondylosis, BMD: bone mineral density.

was associated with the incidence of falls in men (multiple falls 31.3% and 10.9%, single falls 18.8% and 5.1%, in those with and without cognitive impairment, respectively, $p = 0.002$), but not in women ($p = 0.19$).

In men, multinomial logistic regression analysis after adjusting for age and BMI showed that a longer 6-m walking time, longer chair stand time, and previous falls were risk factors for falls, but grip strength, bone and joint diseases, and cognitive impairment were not

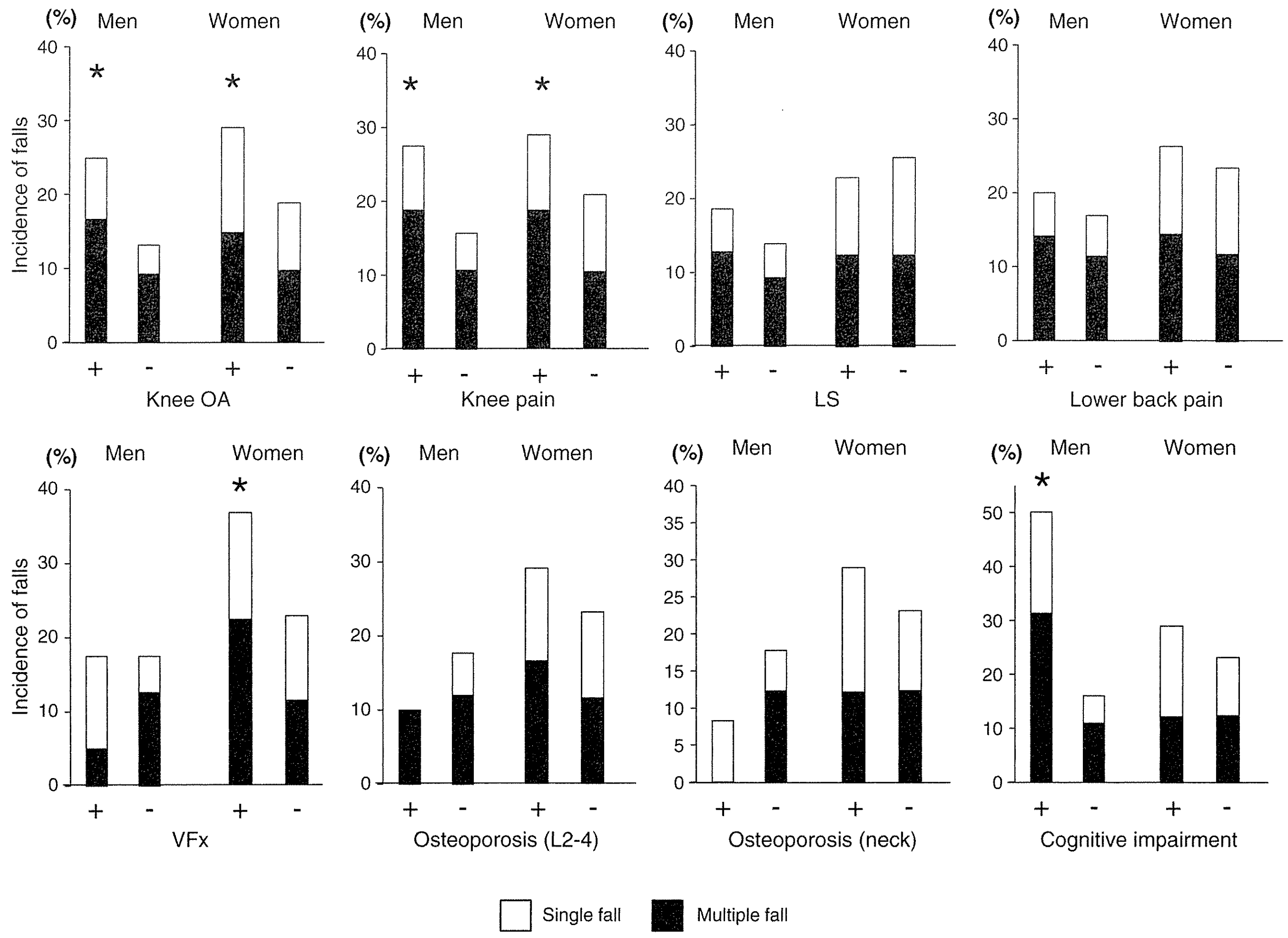

Fig. 2. Incidence of single and multiple falls by bone and joint diseases and cognitive impairment. *$p < 0.05$ vs. participants without each disease or pain, respectively, according to the chi square test. OA, osteoarthritis; LS, lumbar spondylosis; VFx, vertebral fracture.

Table 4
Risk factors for single and multiple falls in men.

	Crude OR (95% CI)		Adjusted OR (95% CI)	
	Single falls	Multiple falls	Single falls	Multiple falls
Grip strength (5 kg increase)	0.90 (0.71–1.14)	0.84 (0.71–0.99)	1.14 (1.01–1.29)	0.88 (0.72–1.08)
6-m walking time (1 s increase)	1.12 (0.98–1.27)	1.13 (1.03–1.26)	1.11 (0.95–1.25)	1.11 (1.01–1.23)
Chair stand time (1 s increase)	1.17 (1.03–1.32)	1.21 (1.11–1.33)	1.15 (1.00–1.32)	1.21 (1.09–1.33)
LS BMD (0.1 mg/cm^2 increase)	1.00 (0.80–1.22)	1.00 (0.86–1.16)	0.92 (0.73–1.15)	0.97 (0.83–1.13)
Neck BMD (0.1 mg/cm^2 increase)	1.10 (0.81–1.47)	0.98 (0.78–1.21)	1.07 (0.73–1.51)	1.01 (0.77–1.30)
Knee OA	2.44 (1.09–5.56)	2.08 (1.18–3.70)	2.07 (0.84–5.21)	1.77 (0.95–3.33)
Knee pain	2.04 (0.72–5.09)	2.05 (0.99–4.00)	1.65 (0.57–4.21)	1.78 (0.85–3.55)
VFx	2.58 (0.82–6.85)	0.40 (0.06–1.36)	2.48 (0.75–7.04)	0.32 (0.05–1.13)
Cognitive impairment	6.19 (1.29–23.1)	4.83 (1.41–15.1)	13.48 (0.98–178.64)	3.17 (0.44–21.99)
Previous falls				
Single fall	–	–	–	3.52 (1.07–9.97)
Multiple falls	1.18 (0.25–4.61)	9.54 (3.15–30.08)	–	12.6 (5.80–27.97)

Multinomial logistic regression analysis was used to calculate the crude odds ratio (OR) and 95% confidence interval (CI) compared with non-fallers.
Adjusted OR was calculated using multinomial logistic regression analysis after adjusting for age and body mass index (BMI).
OA: osteoarthritis, VFx: vertebral fracture, BMD: bone mineral density, LS: lumbar spondylosis.
Radiographic knee OA was defined as Kellgren Lawrence grade 3 or 4.

(Table 4). Previous falls were significantly associated with the incidence of multiple falls. In women, multinomial logistic regression analysis after adjusting for age and BMI showed that a longer 6-m walking time was a risk factor for multiple, but not single falls (Table 5). Chair stand time also tended to be associated with the incidence of single and multiple falls. Regarding bone and joint diseases, knee pain was a risk factor for single and multiple falls. VFx also tended to be associated with multiple falls, but radiographic knee OA was not associated with falls. Cognitive impairment was a risk factor for multiple falls, but not for single falls. A history of previous falls was a risk factor for multiple, but not single falls.

To determine the independent association of each physical performance parameter with the incidence of falls, multinomial logistic regression analysis was performed with age, BMI, 6-m walking time, and chair stand time as explanatory variables. We found that a longer chair stand time was an independent risk factor for multiple falls (OR 1.18, 95% CI 1.06–1.32), but a longer 6-m walking time was not (OR 1.05, 0.93–1.16). In women, a longer 6-m walking time tended to be associated with the incidence of multiple falls (OR 1.09, 95% CI 0.98–1.22), but a longer chair stand time was not (OR 1.01, 95% CI 0.94–1.07). After adjusting for previous falls, the independent association of a longer chair stand time with the incidence of falls remained in men (OR 1.15, 95% CI 1.02–1.30), and the independent association of a longer 6-m walking time with the incidence of falls remained in women (OR 1.12, 95% CI 1.00–1.25). In addition, knee pain and cognitive impairment in women were also significantly associated with falls, and VFx tended to be associated with falls with multinomial logistic regression analysis after adjusting for age and BMI. Thus, to determine the independent association of physical performance, bone and joint diseases, and cognitive impairment, multinomial logistic regression analysis was used with age, BMI, 6-m walking time, knee pain, VFx, and cognitive impairment as explanatory variables. We found that a longer 6-m walking time was an independent risk factor for multiple falls (OR 1.08, 95% CI 1.00–1.18), but the significant association of knee pain, VFx, and cognitive impairment with the incidence of falls disappeared (OR 1.47, 95% CI 0.91–2.35, OR 1.52, 95% CI 0.80–2.81, and OR 1.16, 95% CI 0.35–3.24, respectively).

Discussion

The present study is the first longitudinal population-based cohort study to examine whether physical performance, bone and joint diseases, and cognitive impairment are risk factors for single and multiple falls in men and women. We found gender differences in risk factors for

Table 5
Risk factors for single and multiple falls in women.

	Crude OR (95% CI)		Adjusted OR (95% CI)	
	Single falls	Multiple falls	Single falls	Multiple falls
Grip strength (5 kg increase)	0.84 (0.70–0.99)	0.81 (0.68–0.95)	0.94 (0.77–1.11)	0.91 (0.75–1.08)
6-m walking time (1 s increase)	1.10 (1.01–1.19)	1.16 (1.08–1.25)	1.04 (0.94–1.14)	1.11 (1.02–1.20)
Chair stand time (1 s increase)	1.07 (1.02–1.12)	1.07 (1.03–1.12)	1.04 (0.99–1.10)	1.04 (0.99–1.09)
LS BMD (0.1 mg/cm^2 increase)	0.88 (0.78–1.00)	0.90 (0.80–1.01)	0.96 (0.83–1.11)	0.92 (0.80–1.06)
Neck BMD (0.1 mg/cm^2 increase)	0.75 (0.63–0.90)	0.85 (0.72–1.01)	0.79 (0.62–1.01)	0.87 (0.69–1.10)
Knee OA	1.79 (1.18–2.78)	1.75 (1.16–2.63)	1.52 (0.94–2.50)	1.12 (0.79–1.82)
Knee pain	1.83 (1.17–2.83)	2.22 (1.44–3.37)	1.62 (1.00–2.60)	1.60 (1.00–2.54)
VFx	1.54 (0.78–2.85)	2.40 (1.35–4.12)	1.15 (0.57–2.20)	1.81 (0.98–3.24)
Cognitive impairment	0.42 (0.02–2.12)	2.12 (0.68–5.60)	0.73 (0.19–2.61)	4.95 (1.50–16.08)
Previous falls				
Single fall	0.55 (0.16–1.74)	1.51 (0.33–5.41)	0.70 (0.30–1.43)	2.48 (1.40–4.28)
Multiple falls	0.86 (0.39–1.81)	8.55 (3.80–19.20)	1.06 (0.35–2.62)	6.93 (3.76–12.72)

Multinomial logistic regression analysis was used to calculate the crude odds ratio (OR) and 95% confidence interval (CI) compared with non-fallers.
Adjusted OR was calculated using multinomial logistic regression analysis after adjusting for age and body mass index (BMI).
OA: osteoarthritis, VFx: vertebral fracture, BMD: bone mineral density, LS: lumbar spondylosis.
Radiographic knee OA was defined as Kellgren Lawrence grade 3 or 4.

falls. Regarding physical performance, a longer chair stand time was an independent risk factor for falls in men, whereas a longer 6-m walking time was an independent risk factor for falls in women. Knee pain, VFx, and cognitive impairment were associated with falls in women, but not in men.

The present study is a population-based longitudinal study to determine whether bone and joint diseases are risk factors for falls in Japanese men and women. After adjusting for age and BMI, knee pain was a risk factor for falls in women, but not in men. The sex differences regarding the association of knee pain with falls may be partly explained by the weaker quadriceps muscles in women, which is known to be an independent risk factor for falls [16]. Muscle strength is higher in men than in women in all decades [39], which may obscure the association of knee pain with falls. In addition, given the insignificant association of radiographic knee OA with falls, falls may occur due to symptoms such as pain rather than radiographic changes in the knee itself. Our study and other previous cross-sectional studies also suggested that knee pain is significantly associated with falls [11]. In other words, falls may be preventable when pain is relieved by medical care, even if patients have radiographic knee OA.

In the present study, LS and lower back pain were not associated with falls, whereas VFx was associated with falls. Lower BMD was not associated with falls in the present study, and thus, radiographic changes but not OP may be associated with falls. Studies of patients with VFx have reported increased kyphosis angles [16,17], which is an independent risk factor for injurious falls [40]. Previous studies [41,42] have demonstrated that people with kyphosis have greater balance abnormalities as assessed by computerized dynamic posturography. Specifically, they reported that women with OP-related kyphosis had greater mediolateral displacement and increased mediolateral velocity compared to controls [42]. In addition, lateral spontaneous sway amplitude has been reported to be the single best predictor of future risk of falls [43]. These observations may partly explain the association between VFx and falls.

In the present study, after adjusting for age and BMI, both a longer 6-m walking time and a longer chair stand time were associated with falls in men and women. A previous study also showed that slower walking speed is a risk factor for falls [44], although men and women were not separately analyzed in the study. To determine the independent association of the 6-m walking time and chair stand time, we further used multinomial logistic regression analysis with age, BMI, 6-m walking time, and chair stand time as explanatory factors, and found that in men, a longer chair stand time was an independent risk factor for multiple falls, but a longer 6-m walking time was not. In women, a longer 6-m walking time was associated with the incidence of multiple falls, whereas a longer chair stand time was not. This indicates that slower walking speed may more strongly affect the risk of falling in women than in men, whereas a longer chair stand time may more strongly affect the risk of falling in men than in women. The walking time and chair stand time can be easily and quickly measured in clinical and research settings without requiring monitoring devices or extensive training. The present study may indicate that walking time is a simple and quick option for measuring the risk of falling, particularly in women, and measuring the chair stand time is a simple and quick option for estimating the risk of falling, particularly in men.

The present study has several limitations. First, our participants lived in the community, and thus, our findings may not apply to elderly persons residing in institutions. Second, we did not include other anatomical locations of weight-bearing OA such as hip OA in the analysis, although this disorder also affects 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 lower than that of KL = 3 or 4 knee OA (12.2% and 21.0% in men and women, respectively) in the present study. Thus, it is possible that hip OA would not strongly affect the results of the present study. Third, non-responders were older, had lower physical performance and higher prevalence of knee pain, which were risk factors for falls. This means that the incidence of falls in the present study may have been underestimated. Fourth, the accuracy and reliability of recall of falls over the past 3 years was not assessed in the present study. Previous studies have shown that 13–32% of elderly subjects with confirmed falls did not recall falling over a 12-month period [47], even when excluding subjects with cognitive impairment. Therefore, the incidence of falls may be underestimated, particularly in older subjects and those with cognitive impairment. In addition, individuals are more likely to recall a fall that resulted in injury, which may have influenced the results of this study.

Conclusion

The present longitudinal analysis using a large-scale population from the ROAD study revealed gender differences in risk factors for falls. A longer walking time was a risk factor for falls in women, whereas a longer chair stand time was a risk factor for falls in men. Knee pain and VFx were risk factors for falls in women, but not in men. Further studies, along with continued longitudinal surveys in the ROAD study, will help elucidate the background of bone and joint diseases and their relationship with falls.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.bone.2012.10.020.

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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

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 ≥ 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