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ORIGINAL ARTICLE

Exercise habits during middle age are associated with lower prevalence of sarcopenia: the ROAD study

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Abstract
Summary The present cross-sectional study investigated the prevalence of sarcopenia and clarified its associated factors in 1,000 elderly participants of Japanese population-based cohorts. Exercise habit in middle age was associated with low prevalence of sarcopenia in older age, suggesting that it is a protective factor against sarcopenia in older age.
Introduction The present study investigated the prevalence of sarcopenia using the European Working Group on Sarcopenia in Older People (EWGSOP) definition, and clarified the association of sarcopenia with physical performance in the elderly participants of Japanese population-based cohorts of the Research on Osteoarthritis/osteoporosis Against Disability (ROAD) study.
Methods We enrolled 1,000 participants (aged ≥65 years) from the second visit of the ROAD study who had completed assessment of handgrip strength, gait speed, and skeletal muscle mass measured by bioimpedance analysis. Presence of sarcopenia was determined according to the EWGSOP algorithm. Information collected included exercise habits in middle age.
Results Prevalence of sarcopenia was 13.8 % in men and 12.4 % in women, and tended to be significantly higher according to increasing age in both sexes. Factors associated with sarcopenia, as determined by logistic regression analysis, were chair stand time (odds ratio [OR], 1.09; 95 % confidence interval [CI], 1.04–1.14), one-leg standing time (OR, 0.97; 95 % CI, 0.96–0.99), and exercise habit in middle age (OR, 0.53; 95 % CI, 0.31–0.90). Exercise habit in middle age was associated with low prevalence of sarcopenia in older age. Furthermore, linear regression analysis revealed that exercise habits in middle age were significantly associated with grip strength ($P<.001$), gait speed ($P<.001$), and one-leg standing time ($P=.005$) in older age.
Conclusions This cross-sectional study suggests that exercise habit in middle age is a protective factor against sarcopenia in older age and effective in maintaining muscle strength and physical performance in older age.

Keywords Elderly · Epidemiology · Exercise · Physical performance · Sarcopenia

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Introduction

Sarcopenia is characterized by generalized loss of skeletal muscle mass and muscle strength and/or function in the elderly, causing multiple adverse health outcomes, including physical disability, poor quality of life, and death [1–6]. Although cross-sectional studies have investigated prevalence of sarcopenia [7–13], epidemiologic evidence using population-based samples is insufficient despite the urgent need for strategies to prevent and treat this condition.

Japan is a super-aged society, and the proportion of the aged population is increasing. The percentage of individuals

aged ≥65 years was 23 % in 2010 and is expected to reach 30.1 % in 2024 and 39 % in 2051 [14]. The government of Japan reported that musculoskeletal disorders were present in 22.9 % of the entire population of those who were certified as requiring assistance or long-term care elderly in 2010 and were ranked first among its causes, together with joint diseases, falls, fractures, and spinal cord disorders [15]. For preventing and treating musculoskeletal disorders, there is an urgent need to develop and establish a prevention strategy and treatment programs that are effective in reducing the risk of disability among the elderly, which leads to requirement of assistance or long-term care. Although sarcopenia is a common musculoskeletal disease in the elderly, it is not clearly categorized [15]. There appears to be insufficient recognition of sarcopenia in daily clinical practice and society, leading to the disease being undiagnosed and untreated. One of the reasons may be the lack of a broadly accepted definition of sarcopenia until the European Working Group on Sarcopenia in Older People (EWGSOP) developed a practical clinical definition and consensus diagnostic criteria for this disease in 2010 [4]. There is a growing consensus that sarcopenia should not be defined merely on the basis of muscle mass but also with regard to muscle strength and function [4]. However, few epidemiologic studies have been based on the EWGSOP definition of sarcopenia using population-based samples, and no epidemiologic study has investigated the relationship between exercise habits in middle age and sarcopenia in older age.

The Research on Osteoarthritis/osteoporosis Against Disability (ROAD) study is a prospective cohort study aimed at elucidating the environmental and genetic background of musculoskeletal diseases [16, 17]. The present study investigated the prevalence of sarcopenia using the EWGSOP definition, and clarified the association of sarcopenia with exercise habits in middle age and physical performance in the elderly participants of Japanese population-based cohorts of the ROAD study.

Methods

Participants

From 2005–2007, we began a large-scale population-based cohort study entitled Research on Osteoarthritis/osteoporosis Against Disability consisting of 3,040 participants in three regions (baseline study) [16, 17]. The ROAD study is a prospective cohort study with the aim of elucidating the environmental and genetic backgrounds of musculoskeletal diseases. It is designed to examine the extent to which risk factors for these diseases are related to clinical features of the diseases, laboratory and radiographic findings, bone mass, bone geometry, lifestyle, nutritional factors, anthropometric and neuromuscular measures, and fall propensity. It also aims to determine how these diseases affect activities of daily living and quality of life of Japanese men and women. The subjects were residents of any one of three communities: an urban region in Itabashi, Tokyo; a mountainous region in Hidakagawa, Wakayama; and a coastal region in Taiji, Wakayama. The inclusion criteria were as follows: ability to (1) walk to the clinic where the survey was performed, (2) provide self-reported data, and (3) understand and sign an informed consent form. Participants from the urban region were aged ≥60 years and were recruited from those enrolled in a randomly selected cohort study from the previously established Itabashi Ward residential registration database [18]. Invitation letters were distributed only to inhabitants whose names were listed on this database. Participants from Hidakagawa and Taiji were aged ≥40 years and were recruited from residential registration listings. Residents aged <60 years from Itabashi and <40 years from Hidakagawa and Taiji who were interested in participating in the study were also invited. A total of 99.8, 84.3, and 54.7 % of the participants were aged ≥60 years in Itabashi, Hidakagawa, and Taiji, respectively. The response rates in the groups aged ≥60 years were 75.6 % in Itabashi, 68.4 % in Hidakagawa, and 29.3 % in Taiji. Two-thirds of the 3,040 participants in the baseline survey were women, and their mean age was 1 year less than that of the male participants. No significant difference was observed in body mass index (BMI) between the sexes.

After the baseline study, a second survey was performed in the same communities from 2008 to 2010, in which 2,674 inhabitants (892 men, 1,782 women) aged 21–97 years participated (second visit) [19]. Invitation letters were distributed to the inhabitants whose names were listed on the baseline database of the ROAD study. In addition to the former participants, inhabitants aged ≥60 years from Itabashi and those aged ≥40 years from Hidakagawa and Taiji who were willing to participate in the ROAD survey performed in 2008–2010 were also included in the second visit. In addition, residents aged <60 years from Itabashi and <40 years from Hidakagawa and Taiji who were interested in participating in the study were invited to be examined as well at the baseline. The inclusion criteria were as follows: ability to (1) walk to the clinic where the survey was performed, (2) provide self-reported data, and (3) understand and sign an informed consent form. No other exclusion criteria were used. Thus, 2,674 residents (892 men and 1,782 women) aged 21–97 years participated in the second visit. Of the 2,674 participants, 1,846 individuals aged ≥65 years visited the clinic and underwent an examination at the survey site located in Hidakagawa (504 individuals), Taiji (391 individuals), the University of Tokyo Hospital (132 individuals), or Tokyo Metropolitan Geriatric Hospital (819 individuals). For participants from Itabashi, the survey site was randomly assigned to either the University of Tokyo Hospital or Tokyo

Metropolitan Geriatric Hospital. Since gait speed was not measured at Tokyo Metropolitan Geriatric Hospital, 819 individuals who visited this hospital were removed from the present study. Of 1,846 participants, the remaining 1,019 individuals aged ≥65 years who visited the survey site located in Hidakagawa, Taiji, or at the University of Tokyo Hospital and underwent an examination including gait speed assessment were recruited for the present study. Of the 1,019 individuals, 19 were removed because 1 did not undergo handgrip strength measurement and 18 did not undergo skeletal muscle mass measurement. For the present study, we enrolled 1,000 participants (349 men and 651 women aged ≥65 years) from the second visit who completed assessment of handgrip strength, gait speed, and skeletal muscle mass. The mean age of the participants was 75.7 (SD, 5.9) years in men and 74.4 (SD, 6.1) years in women. All participants provided written informed consent, and the study was conducted with approval from the Ethics Committee of the University of Tokyo.

Participants completed an interviewer-administered questionnaire comprising 400 items regarding lifestyle information such as smoking habits, alcohol consumption, and physical activity. An interviewer asked the following question regarding past physical activity: "During the time you were aged 25–50 years, did you ever practice sports or physical exercise sufficient to produce sweating or shortness of breath?" Possible responses were as follows: never, occasionally, <2 hours per week, and ≥2 hours per week. Those who answered "occasionally, <2 hours per week, or ≥2 hours per week" were defined as having exercise habits in middle age. The following question was asked regarding current physical activity: "Do you practice walking more than 30 minutes every day?" Those who answered "yes" were defined as having a current walking habit.

Anthropometric and physical performance measurements

Anthropometric measurements, including height and weight, were obtained, and body mass index (weight [kg]/height [m^2]) was estimated based on the measured height and weight. Grip strength was measured on the right and left sides using a TOEI LIGHT handgrip dynamometer (TOEI LIGHT CO. LTD, Saitama, Japan), and the highest measurement was used to characterize maximum muscle strength. Subjects were defined as having low grip strength if grip strength was <30 kg in men and <20 kg in women, as reported by Lauretani and colleagues [20].

Skeletal muscle mass was measured by bioimpedance analysis [21–25] using the Body Composition Analyzer MC-190 (Tanita Corp., Tokyo, Japan). The protocol was described by Tanimoto and colleagues [10, 12], and the method has been validated [26]. Appendicular skeletal muscle mass (ASM) was derived as the sum of the muscle mass of the arms and the legs. Absolute ASM was converted to an appendicular muscle mass index (SMI) by dividing by height in meters squared (kg/m^2). Subjects were defined as having low skeletal muscle mass if the SMI was <2 SDs of the young adult mean. We used an SMI of <7.0 kg/m^2 in men and <5.8 kg/m^2 in women as cut-off points for low skeletal muscle mass based on the reference data of SMI measured by the MC-190 in 1,719 healthy young Japanese volunteers aged 18–39 years [10].

To measure physical performance, the time taken to walk 6 m at normal walking speed in a hallway was recorded, and usual gait speed was calculated. Subjects were defined as having low gait speed if usual gait speed was ≤0.8 m/s. The time taken for five consecutive chair rises without the use of hands was also recorded. Timing began with the command "Go" and ended when the buttocks contacted the chair on the fifth landing. One-leg standing time with eyes open was measured on both sides, and the best measurement was used. Participants were asked to stand on one leg while continuing to elevate their contralateral limb. Timing commenced when the participant assumed the correct posture and ended when any body part touched a supporting surface.

Statistical analysis

All statistical analyses were performed using STATA statistical software (STATA, College Station, TX). Differences in the values of the parameters between two groups were tested for significance using the nonpaired Student's *t* test and chi-square test. Trends in values were tested using the Jonckheere-Terpstra trend test. Factors associated with sarcopenia were determined using multivariate logistic regression analysis with sarcopenia as the dependent variable; the odds ratio (OR) and 95 % confidence interval were determined after adjusting for age, sex, and BMI. Factors associated with exercise habits in middle age were determined using multivariate linear regression analysis with exercise habits in middle age as the independent variable; the regression coefficient and 95 % CI were determined after adjusting for age, sex, and BMI.

Results

Table 1 shows the characteristics of the participants according to EWGSOP sarcopenia status. Age was significantly greater, while BMI, ASM, and SMI were significantly lesser in those with sarcopenia than in those without sarcopenia in both men and women. In physical performance, chair stand time was significantly greater and one-leg standing time was significantly lesser in those with sarcopenia than in those without sarcopenia in both men and women. The percentage of individuals with exercise habits in middle age was significantly lower in those with sarcopenia than in those without sarcopenia in both men and women.

Table 1 Characteristics of participants according to EWGSOP sarcopenia status

	Men		Women	
	No sarcopenia	Sarcopenia	No sarcopenia	Sarcopenia
No. of subjects	301	48	570	81
Age, years	75.1 (5.8)	79.9 (5.2)*	73.5 (5.6)	80.8 (5.8)*
Height, cm	161.9 (6.0)	158.5 (5.8)*	148.9 (6.4)	145.6 (6.6)*
Weight, kg	61.2 (9.5)	52.9 (6.5)*	52.4 (8.4)	42.6 (6.3)*
BMI, kg/m^2	23.3 (3.0)	21.0 (2.0)*	23.6 (3.3)	20.0 (2.3)*
ASM, kg	19.8 (3.0)	16.0 (1.7)*	13.8 (1.8)	11.4 (1.2)*
SMI, kg/m^2	7.54 (0.90)	6.36 (0.47)*	6.22 (0.66)	5.35 (0.30)*
Grip strength, kg	36.9 (6.8)	28.0 (4.0)*	23.9 (4.6)	16.8 (3.4)*
Usual gait speed, m/s	1.11 (0.25)	0.85 (0.27)*	1.06 (0.28)	0.82 (0.22)*
Chair stand time, s	9.6 (3.7)	11.9 (4.2)*	9.9 (4.2)	13.4 (5.9)*
One-leg standing time, median (IQR), s	31.0 (10.0–60.0)	8.0 (4.0–16.0)*	26.0 (8.0–60.0)	11.0 (5.0–23.0)*
Smoking, %	15.6	16.7	2.3	6.2
Alcohol consumption, %	58.8	45.8	14.7	18.8
Current walking habits, %	56.5	45.0	55.1	56.5
Exercise habits in middle age, %	69.9	46.2†	43.3	26.1†

Except where indicated otherwise, values are mean (SD)

ASM appendicular skeletal muscle mass, *BMI* body mass index, *EWGSOP* European Working Group on Sarcopenia in Older People, *IQR* interquartile range, *SMI* skeletal muscle mass index

*P<.001 vs. no sarcopenia in the same sex group by unpaired Student's t test; †P<.01 vs. no sarcopenia in the same sex group by chi-square test

Figure 1 shows sex- and age-wise distributions of prevalence of sarcopenia (Fig. 1a), low SMI (Fig. 1b), low grip strength (Fig. 1c), and low gait speed (Fig. 1d). The total prevalence of sarcopenia was 13.8 % in men and 12.4 % in women. Prevalence of sarcopenia (number of cases/subjects) in the age strata of 65–69, 70–74, 75–79, 80–84, and ≥85 years was 1.6 % (1/63), 5.7 % (5/88), 17.8 % (19/107), 23.2 % (16/69), and 31.8 % (7/22) in men and 0.6 % (1/163), 5.5 % (10/182), 13.8 % (22/160), 22.9 % (25/109), and 62.2 % (23/37) in women. Prevalence of sarcopenia tended to be significantly higher according to increasing age (P<.001 for trend) in both men and women. Prevalence of low grip strength and low gait speed also tended to be significantly higher according to increasing age (P<.001 for trend) in both men and women. However, the increasing tendency of prevalence of low SMI (P<.001 for trend) was milder compared with that of sarcopenia, low grip strength, and low gait speed.

Then, we determined the factors associated with sarcopenia by logistic regression analysis; the upper part of Table 2 shows the results using sarcopenia as the dependent variable. In the overall population, age (OR, 1.20; 95 % CI, 1.15–1.24) and BMI (OR, 0.68; 95 % CI, 0.63–0.75) were significantly associated with sarcopenia, whereas sex was not. In physical performance, chair stand time (OR, 1.09; 95 % CI, 1.04–1.14) and one-leg standing time (OR, 0.94; 95 % CI, 0.96–0.99) were significantly associated with sarcopenia in the overall population after adjusting for age, sex, and BMI. Current walking habit (OR, 0.69; 95 % CI, 0.42–1.12) was not significantly associated with sarcopenia. However, exercise habit in middle age (OR, 0.53; 95 % CI, 0.31–0.90) was associated with sarcopenia in the overall population after adjusting for age, sex, and BMI, indicating that exercise habit in middle age was significantly associated with low prevalence of sarcopenia in older age. The significance of the association did not change when current walking habit was added as an explanatory variable in this logistic regression model (OR, 0.53; 95 % CI, 0.32–0.90). In addition, we investigated the association of each category—occasionally, <2 h per week, and ≥2 h per week—with sarcopenia using "never" as a reference, in addition to the association of the presence of exercise habits in middle age with sarcopenia. The associated ORs for the three categories were comparable, but they did not reach significance level (occasionally: OR, 0.63; 95 % CI, 0.34–1.17; <2 h per week: OR, 0.30; 95 % CI, 0.09–1.01; ≥2 h per week: OR, 0.49; 95 % CI, 0.22–1.09).

The lower part of Table 2 shows the results of linear regression analysis using SMI, grip strength, gait speed, chair stand time, or one-leg standing time as the dependent variable and exercise habit in middle age as the independent variable. Exercise habit in middle age was significantly associated with grip strength in older age (P<.001), gait speed in older age (P<.001), and one-leg standing time in older age (P=.005) after adjusting for age, sex, and BMI in the overall population. We conducted the same analyses in men and women separately (Tables 3 and 4) and found results similar to those in the overall population. Some sex differences were observed in the present results. Exercise habit in middle age was significantly associated with grip strength and gait speed in older age in both men and women, whereas it was significantly associated with chair stand time and one-leg standing time only in men; however, the sample size of men was smaller than that of women. In the overall population, exercise habit in middle age was not associated with chair stand time.

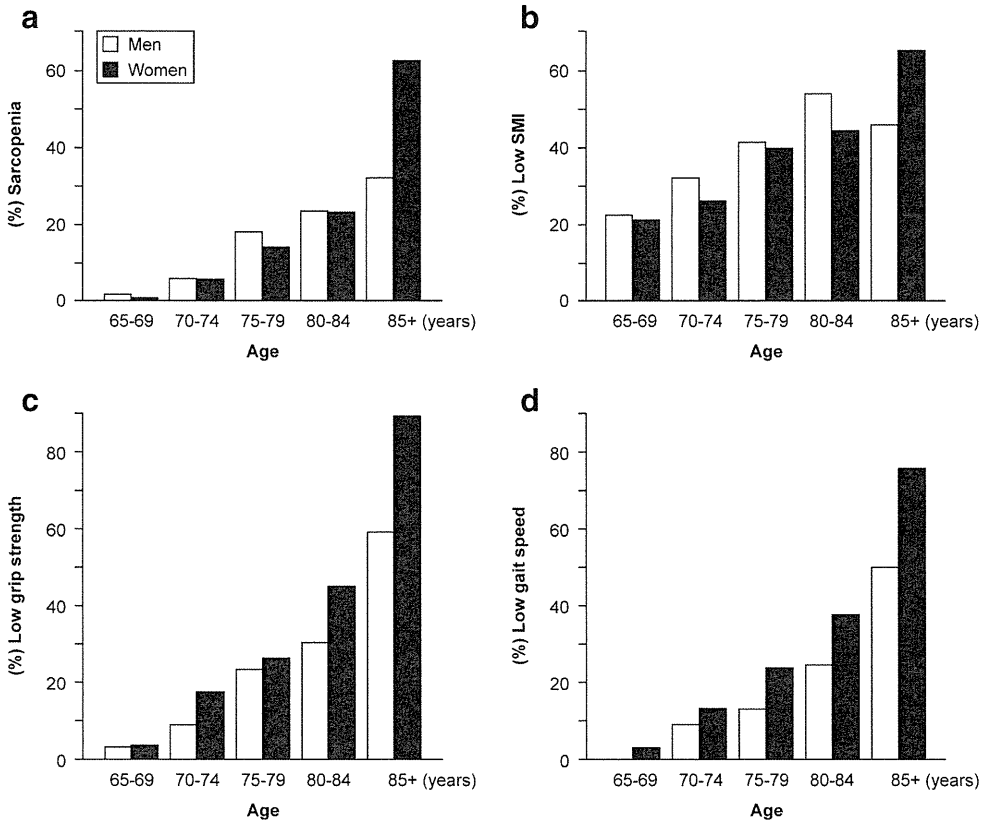

Fig. 1 Percentage of sarcopenia (**a**), low skeletal muscle mass index (*SMI*) (**b**), low grip strength (**c**), and low gait speed (**d**) in men and women in each age stratum (65–69, 70–74, 75–79, 80–85, and ≥85 years). Low SMI was defined as a value of <7.0 kg/m^2 in men and <5.8 kg/m^2 in women. Low grip strength was defined as a value of <30 kg in men and <20 kg in women. Low gait speed was defined as a value of ≤0.8 m/s

Discussion

The present study investigated the prevalence of sarcopenia using the EWGSOP definition in the elderly participants of Japanese population-based cohorts. We determined that age was positively associated with sarcopenia and that BMI was inversely associated, but sex was not. Exercise habit in middle age was associated with increased muscle strength and physical performance and low prevalence of sarcopenia in older age. To the best of our knowledge, this is the first study to show the relationship between exercise habits in middle age and sarcopenia in older age in the elderly participants of population-based cohorts.

Previous studies have reported the prevalence of sarcopenia and its associated factors. For example, Tanimoto and colleagues reported the prevalence of sarcopenia in

Table 2 Factors associated with sarcopenia and exercise habits in middle age in the overall population

Factors associated with sarcopenia	Odds ratio	95 % CI	*P* value
Age (+1 year)	1.20	1.15–1.24	<.001
Sex (women vs. men)	0.98	0.63–1.53	.9
BMI (+1 kg/m^2)	0.68	0.63–0.75	<.001
Chair stand time (+1 s)	1.09[a]	1.04–1.14	.001
One-leg standing time (+1 s)	0.97[a]	0.96–0.99	<.001
Smoking (yes vs. no)	1.86[a]	0.86–4.02	.1
Alcohol consumption (yes vs. no)	1.00[a]	0.60–1.67	.9
Current walking habits (yes vs. no)	0.69[a]	0.42–1.12	.1
Exercise habits in middle age (yes vs. no)	0.53[a]	0.31–0.90	.01
Factors associated with exercise habits in middle age	Regression coefficient	95 % CI	*P* value
SMI	0.09[b]	−0.02–0.19	.1
Grip strength	1.73[c]	1.02–2.44	<.001
Gait speed	0.07[c]	0.04–0.10	<.001
Chair stand time	−0.47[c]	−1.02–0.09	.09
One-leg standing time	4.14[c]	1.26–7.02	.005

BMI body mass index, *CI* confidence interval, *SMI* skeletal muscle mass index

[a] Odds ratio and 95 % CI were calculated by logistic regression analysis after adjusting for age, sex, and BMI

[b] Regression coefficient and 95 % CI were calculated by linear regression analysis after adjusting for age and sex

[c] Regression coefficient and 95 % CI were calculated by linear regression analysis after adjusting for age, sex, and BMI

Table 3 Factors associated with sarcopenia and exercise habits in middle age in men

Factors associated with sarcopenia	Odds ratio	95 % CI	*P* value
Chair stand time (+1 s)	1.09[a]	1.01–1.18	.03
One-leg standing time (+1 s)	0.97[a]	0.95–0.99	.001
Smoking (yes vs. no)	1.49[a]	0.59–3.75	.4
Alcohol consumption (yes vs. no)	0.78[a]	0.40–1.53	.4
Current walking habits (yes vs. no)	0.60[a]	0.28–1.27	.1
Exercise habits in middle age (yes vs. no)	0.48[a]	0.22–1.03	.06
Factors associated with exercise habits in middle age	Regression coefficient	95 % CI	*P* value
SMI	0.16[b]	−0.06 to 0.38	.1
Grip strength	3.17[c]	1.70 to 4.65	<.001
Gait speed	0.10[c]	0.04 to 0.15	.001
Chair stand time	−1.12[c]	−1.95 to −0.28	.009
One-leg standing time	7.81[c]	2.57 to 13.05	.004

CI confidence interval, *SMI* skeletal muscle mass index

[a] Odds ratio and 95 % CI were calculated by logistic regression analysis after adjusting for age and BMI

[b] Regression coefficient and 95 % CI were calculated by linear regression analysis after adjusting for age

[c] Regression coefficient and 95 % CI were calculated by linear regression analysis after adjusting for age and BMI

Japanese community-dwelling elderly individuals based on the EWGSOP definition using bioimpedance analysis (MC-190) [12]. They reported a prevalence of 11.3 % in men and 10.7 % in women [12], which is similar to our results. Although the cut-off value for low SMI was the same in these two studies, the cut-off value used for handgrip strength was different; we used cutoff values of <30 kg in men and <20 kg in women, in accordance with Lauretani and colleagues [20], while they used values of <30.3 kg in men and <19.3 kg in women, based on the lowest quartile of handgrip strength in their study population [12]. In the population of the present study, the lowest quartile of grip strength was 30.5 kg in men and 20.0 kg in women. Considering that these two studies showed similar results, cut-off values of 30 kg in men and 20 kg in women for handgrip strength [20] also may be appropriate for the practical case definition of the EWGSOP algorithm in the Japanese population.

Patel and colleagues reported the prevalence of sarcopenia in Caucasians using the EWGSOP definition, in which low muscle mass is defined as the lowest tertile of lean or fat-free

Table 4 Factors associated with sarcopenia and exercise habits in middle age in women

Factors associated with sarcopenia	Odds ratio	95 % CI	*P* value
Chair stand time (+1 s)	1.08[a]	1.02–1.15	.01
One-leg standing time (+1 s)	0.98[a]	0.96–1.00	.01
Smoking (yes vs. no)	2.44[a]	0.61–9.72	.2
Alcohol consumption (yes vs. no)	1.26[a]	0.58–2.71	.5
Current walking habits (yes vs. no)	0.75[a]	0.39–1.44	.3
Exercise habits in middle age (yes vs. no)	0.55[a]	0.27–1.13	.1
Factors associated with exercise habits in middle age	Regression coefficient	95 % CI	*P* value
SMI	0.06[b]	−0.05 to 0.17	.2
Grip strength	1.03[c]	0.29 to 1.78	.007
Gait speed	0.06[c]	0.01 to 0.10	.01
Chair stand time	−0.12[c]	−0.83 to 0.60	.7
One-leg standing time	2.19[c]	−1.24 to 5.62	.2

CI confidence interval, *SMI* skeletal muscle mass index

[a] Odds ratio and 95 % CI were calculated by logistic regression analysis after adjusting for age and BMI

[b] Regression coefficient and 95 % CI were calculated by linear regression analysis after adjusting for age

[c] Regression coefficient and 95 % CI were calculated by linear regression analysis after adjusting for age and BMI

mass [11]. They recommended use of the lowest tertile of muscle mass as a cut-off value if the reference value of muscle mass in a young healthy population is unavailable. In the population of the present study, the lowest tertile of SMI was 6.92 kg/m^2 in men and 5.80 kg/m^2 in women, which is similar to the cut-off value of <2 SDs of the young adult mean (7.0 kg/m^2 in men and 5.8 kg/m^2 in women) [10]. For evaluating low muscle mass, use of the lowest tertile may be an appropriate alternative method if the reference value of a young healthy population is unavailable.

The present study showed an association between sarcopenia and physical performance, including chair stand time and one-leg standing time, which is consistent with results of previous reports using the EWGSOP definition [11, 13]. However, these were comparisons between sarcopenia and current status of physical performance or exercise habit. Therefore, causal association was unclear whether sarcopenia was caused by decreased physical performance or activity or whether low physical performance or activity was due to sarcopenia. We also revealed that exercise habit in middle age was associated with increased muscle strength and physical performance and low prevalence of sarcopenia in older age. These results suggest that exercise habit in middle age is a protective factor against sarcopenia in older age and effective in maintaining muscle strength and physical performance in older age.

Some sex differences were observed in the present results. Exercise habit in middle age was significantly associated with grip strength and gait speed in older age in both men and women, whereas it was significantly associated with chair stand time and one-leg standing time only in men; however, the sample size of men was smaller than that of women. In the overall population, exercise habit in middle age was not associated with chair stand time; this finding may have been influenced by the fact that the sample size of women was almost twice that of men. The present results suggest that the impact of exercise habit in middle age on physical ability in older age is greater in men than in women.

Since exercise is a modifiable factor, it is a promising finding that exercise habit may be effective in preventing sarcopenia. In the present study, exercise habit was defined as physical activity in the period when the individual was aged 25–50 years, in which subjects practiced sports or physical exercise sufficient to produce sweating or shortness of breath, occasionally or more frequently. Although exercise habit was associated with low prevalence of sarcopenia at the age of ≥65 years, some details remain unclear, including exercise type, intensity, time, and other factors appropriate for prevention of sarcopenia. In addition to the association of the presence of exercise habit in middle age with sarcopenia, we further investigated the association of each category—occasionally, <2 h per week, and ≥2 h per week—with sarcopenia using "never" as a reference. Among the three categories, the analysis could not determine the best frequency and amount of exercise for protection from sarcopenia. The associated ORs for the three categories were comparable, and no dose–response tendency was seen in the relationship between frequency and amount of exercise and prevalence of sarcopenia; the associations also did not reach significance level. The present results suggest that abstaining from exercise during middle age is a risk factor for sarcopenia in older age. Furthermore, the presence of exercise habit in middle age might be much more important than the frequency and amount of exercise. Further studies are necessary to develop intervention programs and to test their effectiveness, along with accumulation of epidemiologic evidence including longitudinal studies.

The present study has several limitations. First, since this was a cross-sectional design, a causal relationship could not be determined. Second, information regarding exercise habits in middle age was obtained by self-report, and there is a possibility of recall bias. Third, the present study included participants who could walk to the survey site and could understand and sign an informed consent form. Since those who did not meet these inclusion criteria were not included in the analyses, the study participants do not truly represent the general population because of health bias. This should be considered when generalizing the results of the present study. Fourth, the results may have been affected by the characteristics of the population, including age and BMI. In the present study, age was positively associated with sarcopenia, whereas BMI was inversely associated with sarcopenia. Therefore, care should be taken when extrapolating the data to other populations with different characteristics, including age and BMI, which may confound the results.

In conclusion, the present study revealed prevalence of sarcopenia in the elderly participants of Japanese population-based cohorts. Exercise habit in middle age was associated with increased muscle strength and physical performance and low prevalence of sarcopenia in older age. These results suggest that exercise habit in middle age is a protective factor against sarcopenia in older age and is effective in maintaining muscle strength and physical performance in older age. Further long-term longitudinal epidemiological studies are necessary to develop effective intervention programs for the prevention and treatment of sarcopenia.

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Conflicts of interest None.

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ORIGINAL ARTICLE

Prevalence of sarcopenia in Japanese women with osteopenia and osteoporosis

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Abstract Sarcopenia and osteoporosis are both significant health burdens among postmenopausal women. This study examined associations between sarcopenia and osteopenia/osteoporosis in Japanese women and evaluated the prevalence of sarcopenia in women with osteopenia and osteoporosis. A total of 2400 Japanese women aged 40–88 years underwent dual-energy x-ray absorptiometry (DXA) scans of the whole body, lumbar spine, and total hip. Osteopenia and osteoporosis were defined according to World Health Organization criteria using bone mineral density (BMD) of the lumbar spine or hip. Sarcopenia was defined as a relative skeletal muscle index (RSMI) more than 2 standard deviations below the mean for a young adult reference population, calculated as the appendicular skeletal muscle mass (ASM) obtained from whole-body DXA divided by height in meters squared (RSMI = ASM/height^2). Significant and marginal/moderate positive correlations were observed between RSMI and lumbar spine/total hip BMDs ($r = 0.197$ and $r = 0.274$, respectively; $p < 0.0001$ each). The BMDs of the lumbar spine and total hip showed significant moderate negative correlations with age ($r = -0.270$ and $r = -0.375$, respectively; $p < 0.0001$ each), but RSMI showed no association with age in this population ($r = 0.056$). When osteopenia/osteoporosis was defined using lumbar spine BMD, prevalences of sarcopenia in subjects with normal BMD, osteopenia and osteoporosis were 10.4, 16.8, and 20.4 %, respectively. When osteopenia/osteoporosis was defined using total hip BMD, the prevalences of sarcopenia in these subjects were 9.0, 17.8, and 29.7 %, respectively. A Chi-square test for independence showed a significant association between sarcopenia and osteopenia/osteoporosis ($p < 0.0001$). These results indicate that sarcopenia is significantly associated with osteopenia and osteoporosis in Japanese women.

Keywords Sarcopenia · Osteopenia · Osteoporosis · Dual-energy X-ray absorptiometry · Muscle mass

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Introduction

Osteoporosis is a worldwide health problem that is age-related and three times more common in women than in men [1]. The loss of bone mass is a potent risk factor for fragility fractures, and osteoporosis-induced fractures represent a major burden on society [1]. Lifetime risk for hip, vertebral and forearm (wrist) fractures has been estimated as approximately 40 %, similar to that for coronary heart disease [1].

Sarcopenia is defined as the age-associated loss of skeletal muscle mass and function [2]. Sarcopenia is very common in older individuals, with a reported prevalence in 60- to 70-year-olds of 5–13 %, and a prevalence in >80-year-olds of 11–50 % [3]. Sarcopenia increases the risk of falls [4, 5], which enhance fragility fractures including osteoporotic hip fractures. The risk of falls appears more closely related to risk of limb fracture than bone mineral density (BMD) [6]. Concomitant sarcopenia and osteopenia/osteoporosis thus represents a greater risk than osteopenia/osteoporosis alone for limb fractures.

Several factors that play important roles in causing sarcopenia also contribute to bone loss, such as age-related

decreases in levels of sex steroid hormones [7, 8], impaired growth hormone and insulin-like growth factor-I signaling and activity with aging [9, 10], and changes in nutritional status, including vitamin D insufficiency [11]. Previous studies have shown a positive association between lean mass and BMD in postmenopausal women [12, 13]. Sarcopenia and osteoporosis may thus act together. The prevalence of sarcopenia has been reported as 10–52 % in the postmenopausal population, depending on the reference method used and the population examined [2]. However, the prevalence of sarcopenia in osteopenic and osteoporotic women has not been fully evaluated.

Given this background, the aims of this study were to examine associations between sarcopenia and osteopenia/osteoporosis in Japanese women ≥40 years old, and to evaluate the prevalence of sarcopenia among Japanese women with osteopenia and osteoporosis.

Materials and methods

Subjects

A total of 2400 consecutive women ≥40 years old (range, 40–88 years) who visited our orthopedic outpatient clinic and underwent whole-body and regional (lumbar spine and total hip) dual-energy X-ray absorptiometry (DXA) (QDR 4500A; Hologic, Waltham, MA, USA) were enrolled in this study. All subjects were orthopedic patients who had minor symptoms (i.e., sprain, contusion, transient joint pain, etc.) and requested examination for osteoporosis, or were examinees in a regional screening program for osteoporosis who were referred to our clinic for confirmation of whether osteoporosis was present. All subjects were informed about the objectives of DXA and consented. Subjects with a past history of medication using anti-osteoporosis drugs, malignancy, corticosteroid use, bone metabolic disorders other than osteoporosis (i.e., osteomalacia, hyperparathyroidism, etc.), paralysis or inability to walk for any reason (i.e., myelopathy, paraplegia, severe osteoarthritis, etc.) were excluded.

Definitions of osteopenia and osteoporosis

Osteopenia and osteoporosis were diagnosed using the criteria of the World Health Organization (WHO) [1]. Osteopenia was defined as a BMD more than 1.0 standard deviation (SD) below the young adult mean, but less than 2.5 SDs below this value (T-score < -1 and > -2.5), and osteoporosis was defined as a BMD 2.5 SDs or more below the young adult mean (T-score ≤ -2.5). The BMDs were measured from DXA of the lumbar spine (L2–L4) and total hip.

Sarcopenia definition

From the whole-body composition data obtained using DXA, appendicular skeletal muscle mass was calculated as the sum of skeletal muscle mass in the arms and legs, assuming that all non-fat and non-bone tissue is skeletal muscle [14, 15]. The DXA measurement methods and validation have been reported elsewhere [16, 17]. Relative skeletal mass index (RSMI) was derived from the appendicular skeletal muscle mass in kilograms divided by the square of the height in meters [14, 18]. Sarcopenia was considered present for an RSMI more than 2 SDs below the mean in young women [14]. In this study, the cut-off value for sarcopenia (<5.46 kg/m^2 for women) was referenced from normative data from the Japanese population using the same DXA device (QDR 4500A; Hologic) [19].

Prevalences of sarcopenia, osteopenia, and osteoporosis

The 2400 subjects were divided into five groups according to age decade: 40–49 ($n = 105$); 50–59 ($n = 459$); 60–69 ($n = 825$); 70–79 ($n = 874$); and 80–89 ($n = 137$) years. Prevalences of sarcopenia, osteopenia, and osteoporosis in each age group were then estimated. Prevalences of sarcopenia in subjects with osteopenia or osteoporosis in the total study population and in each age group were further calculated.

Statistical analyses

The correlation between estimated variables was analyzed using Pearson's correlation coefficient and simple regression analysis. Further analyses using multiple regression were conducted to evaluate the impact of RSMI on BMD. The association between sarcopenia and osteopenia/osteoporosis was investigated using the Chi-square test for independence. Values of $p < 0.05$ were considered statistically significant.

Results

Characteristics of the 2400 participants in this study are shown in Table 1. The correlations between variables are listed in Table 2. Significant and marginal/moderate positive correlations were observed among RSMI and lumbar spine/total hip BMDs. The RSMI showed a strong positive correlation with BMI. Age showed a significant, marginal positive correlation with BMI and a significant, marginal/moderate negative correlations with lumbar spine/total hip BMDs.

Multiple regression analysis on lumbar spine BMD using age, BMI, and RSMI as independent variables

Table 1 Characteristics of study subjects ($n = 2400$)

Variables	Mean	SD	Range
Age (years)	66.3	9.2	40–88
Height (cm)	151.7	6.4	127.0–172.0
Weight (kg)	53.0	8.5	25.0–110.0
Body mass index (kg/m^2)	23.1	3.4	13.6–41.9
Relative skeletal mass index (kg/m^2)	6.15	0.72	4.15–9.53
Lumbar spine-BMD (g/cm^2)	0.810	0.174	0.311–2.077
Total hip-BMD (g/cm^2)	0.719	0.127	0.320–1.230

BMD bone mineral density, *SD* standard deviation

Table 2 Correlations between estimated variables

	Age	BMI	RSMI	LS-BMD	Total hip-BMD
Age		0.124*	0.056	−0.270*	−0.375*
BMI			0.709*	0.237*	0.336*
RSMI				0.197*	0.274*
LS-BMD					0.636*
Total hip-BMD					

Data represent Pearson's correlation coefficient, *r*

BMI body mass index, *RSMI* relative skeletal mass index, *LS* lumbar spine, *BMD* bone mineral density

* $p < 0.0001$

Table 3 Multiple regression analysis on lumbar spine-BMD in study subjects

Variables	Coefficient (*r*)	Significance (*p*)
Intercept	0.842	<0.0001
Age	−0.006	<0.0001
BMI	0.013	<0.0001
RSMI	0.010	0.1281

BMI body mass index, *RSMI* relative skeletal mass index, *BMD* bone mineral density

identified age and BMI as significant contributors for lumbar spine BMD, but RSMI did not reach the level of statistical significance (Table 3). Multiple regression analysis for total hip BMD revealed that in addition to age and BMI, RSMI was also selected as a significant contributor to total hip BMD (Table 4).

A Chi-square test for independence showed a significant association between sarcopenia defined using RSMI and osteopenia/osteoporosis defined using both lumbar spine BMD and total hip BMD ($p < 0.0001$).

When osteopenia and osteoporosis were defined using lumbar spine BMD, the prevalence of osteopenia increased after the 50s and the prevalence of osteoporosis gradually increased with age (Fig. 1). When osteopenia and

Table 4 Multiple regression analysis on total hip-BMD in study subjects

Variables	Coefficient (*r*)	Significance (*p*)
Intercept	0.747	<0.0001
Age	−0.006	<0.0001
BMI	0.013	<0.0001
RSMI	0.009	0.0285

BMI body mass index, *RSMI* relative skeletal mass index, *BMD* bone mineral density

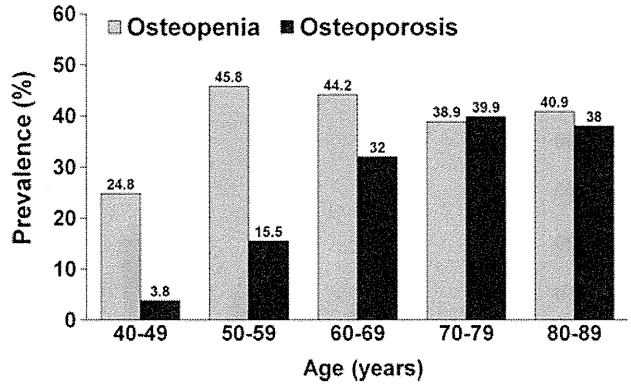

Fig. 1 Prevalences of osteopenia and osteoporosis with age, as evaluated by bone mineral density of the lumbar spine

osteoporosis were defined by total hip BMD, prevalence of osteopenia increased with age decade, but decreased slightly in the 80s , while the prevalence of osteoporosis increased exponentially with age group (Fig. 2). Prevalence of sarcopenia as defined using RSMI in this population was higher in the 40s compared to other age groups, and after the 50s , the prevalence appeared to almost plateau (Fig. 3).

In both definitions of osteopenia/osteoporosis by BMD measurement of the lumbar spine and total hip, the prevalence of sarcopenia defined with RSMI in subjects with osteopenia (16.8 or 17.8 %) was higher than the prevalence of sarcopenia in subjects with normal BMD (10.4 or 9.0 %), and the prevalence of sarcopenia in subjects with osteoporosis (20.4 or 29.7 %) was higher than the prevalence of sarcopenia in subjects with osteopenia. This relationship (lowest prevalence of sarcopenia in subjects with normal BMD and highest in osteoporotic subjects) was observed in all age groups (Figs. 4, 5).

Discussion

Sarcopenia and osteoporosis represent significant health burdens among postmenopausal women [5]. Associations with sarcopenia and osteopenia/osteoporosis in women have been reported in several studies. Gillette-Guyonnet

et al. [20] reported that among 129 healthy French women, appendicular skeletal muscle mass was significantly lower in osteoporotic women than in age- and sex-matched non-osteoporotic controls. Walsh et al. [18] investigated the prevalence of sarcopenia defined using RSMI in 213 healthy pre- and postmenopausal volunteers in the United States (97 % Caucasian) and reported that the prevalence of sarcopenia in that sample was 11.7 %, with prevalences of 12.5 % in premenopausal osteopenic women, 25 % in postmenopausal women with osteopenia, and 50 % in postmenopausal women with osteoporosis. Di Monaco et al. [4] recently assessed the prevalence of sarcopenia evaluated with RSMI and associations with osteoporosis in 313 hip-fracture women, and reported that 58 % of subjects were sarcopenic, whereas 74 % were osteoporotic. They concluded that the high prevalence of sarcopenia and its significant association with osteoporosis was present in a sample of hip-fracture women [4]. The present study with a larger number of Japanese women demonstrated significant associations of lumbar spine/total hip BMD and RSMI, and the prevalence of sarcopenia was highest in osteoporotic subjects, followed by osteopenic subjects, and lowest in normal BMD subjects in all age decade groups from the 40 s to 80 s.

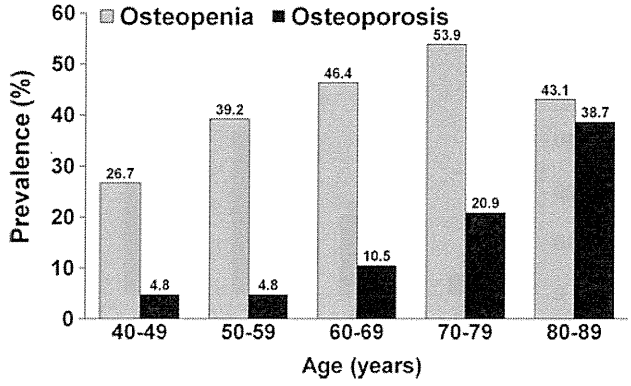

Fig. 2 Prevalences of osteopenia and osteoporosis with age, as evaluated by bone mineral density of the total hip

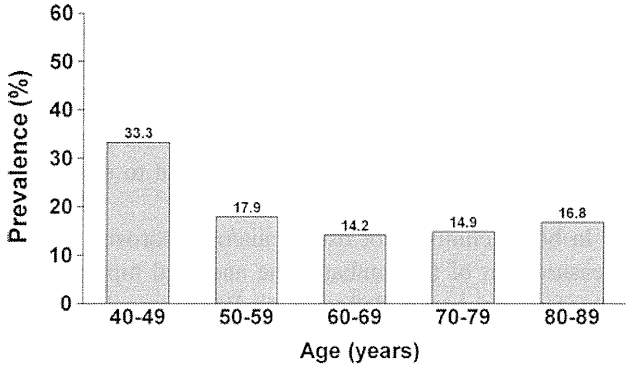

Fig. 3 Prevalence of sarcopenia with age

A study from the Third National Health and Nutrition Examination Survey (NHANES III) in the United States showed that prevalence of sarcopenia in women as estimated using bioelectrical impedance analysis (BIA) increased with age [21]. In the present study, osteopenia and osteoporosis were significantly associated with age, as with the wider literature including a report from the WHO [1]; however, RSMI and sarcopenia showed no significant association with age. Although the evaluation method in this study (RSMI) differed from that used in NHANES III (BIA), this discrepancy warrants closer attention. Study samples in the present study may have been biased compared to the normal population, because all participants in this study were subjects visiting an orthopedic clinic. Thus, the study participants might have had several underlying diseases/conditions modifying muscle mass and thus affecting the results. However, a cohort survey in Japan with a sample size of 2419 participants aged in their 40–80s showed that muscle strength (grip and knee extensor) decreased significantly with age in both men ($n = 1200$) and women ($n = 1219$), although age-related declines in the prevalence of sarcopenia as evaluated using RSMI were observed only in men, not in women [22]. Kirchengast et al. [23] also reported that significant age-related declines in lean body mass as evaluated with RSMI were observed only in men, not in women, among 282 healthy Austrian subjects aged 60–92 years. The reasons

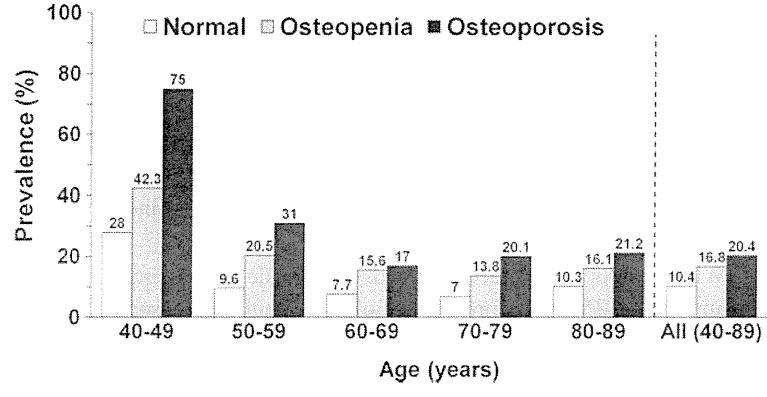

Fig. 4 Prevalences of sarcopenia in normal, osteopenic, and osteoporotic subjects with age, as evaluated by bone mineral density of the lumbar spine

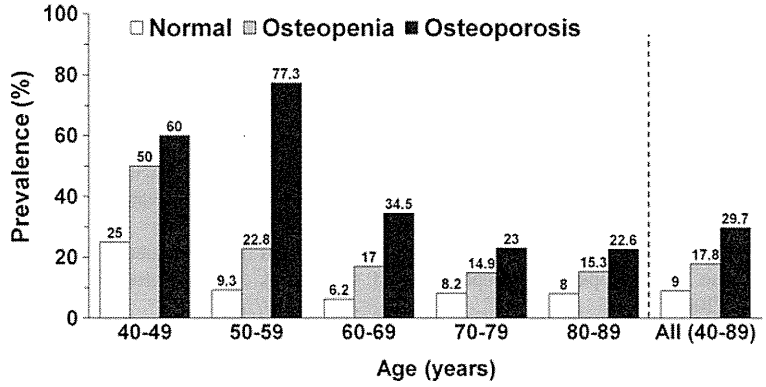

Fig. 5 Prevalences of sarcopenia in normal, osteopenic, and osteoporotic subjects with age, as evaluated by bone mineral density of the total hip

why these studies did not show age-related increases in sarcopenia among women remain unclear, but sex-specific differences may exist when sarcopenia is evaluated using RSMI.

In the present study, significant positive correlations between lumbar spine BMD and total hip BMD were observed, as previously reported [24]. However, multiple regression analysis showed that a significant impact of RSMI on BMD was only seen for total hip BMD, and not for lumbar spine BMD. We speculated that this discrepancy between total hip and lumbar spine BMDs might have been primarily attributable to the existence of spondylosis, which affects lumbar spine BMD. Although we could not evaluate the degree of spondylosis because spine X-rays were not available for many participants in this study population, previous studies have shown that lumbar osteophyte formation and intervertebral disc degeneration correlate positively with BMD [24]. In addition, from the perspective of muscle and bone interactions, RSMI of the arms and legs is considered to have a more significant relationship with BMD from an extremity (total hip BMD) rather than spine BMD.

The importance of BMD measurement for osteopenia/osteoporosis screening is widely accepted [1]. Screening for sarcopenia should also now be considered, because sarcopenia represents a major cause of disability and increased health costs, particularly among older individuals [2]. In this study, BMD and RSMI were simultaneously examined by DXA. As suggested by Walsh et al. [18], simultaneous screening for sarcopenia during BMD examinations by DXA may be of value in identifying osteopenic/osteoporotic women with sarcopenia, a group that may be most in need of exercise interventions to increase muscle and BMD.

Several limitations should be addressed. First, the definition of sarcopenia in this study only referred to RSMI, because the majority of diagnostic thresholds for sarcopenia have been developed based on this method [2, 5, 14, 18, 19, 25]. However, muscle mass does not correlate directly with muscle strength [5], and the European Working Group on Sarcopenia in Older People (EWGSOP) recommends the diagnosis of sarcopenia based on documentation of low muscle mass plus low muscle function (strength or performance) [25]. If we could have evaluated muscle function in addition to muscle mass in this study, age-related associations between sarcopenia and osteopenia/osteoporosis might have become more apparent. In future studies, for example, walking velocity should be included as a functional parameter in the definition of sarcopenia. Second, although the sample size was considered large, the present data cannot be generalized to the overall population, because the subject cohort may have suffered selection bias in that all subjects had visited orthopedic clinics. Further community-based studies with normal populations to evaluate both muscle mass and function are required to confirm the present findings.

In conclusion, this study examined associations between sarcopenia and osteopenia/osteoporosis in a total of 2400 Japanese women. The RSMI showed significant positive correlations with BMDs of the lumbar spine and total hip. Prevalence of sarcopenia defined with RSMI was highest in subjects with osteoporosis, followed by subjects with osteopenia, and lowest in subjects with normal BMD. These results suggest that sarcopenia is significantly associated with osteopenia and osteoporosis in Japanese women. However, the results should be interpreted with care, as the subject cohort may have suffered selection bias in that all subjects had visited orthopedic clinics.

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Conflict of interest None of the authors have any conflicts of interest to declare.

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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

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

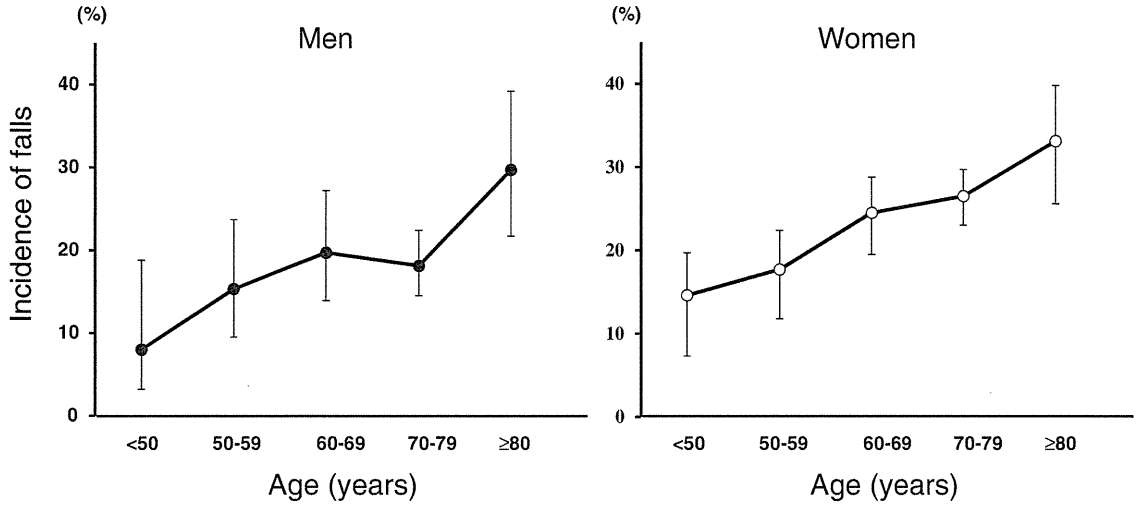

Fig. 1 Incidence rate of falls (95 % CI) by gender and age

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

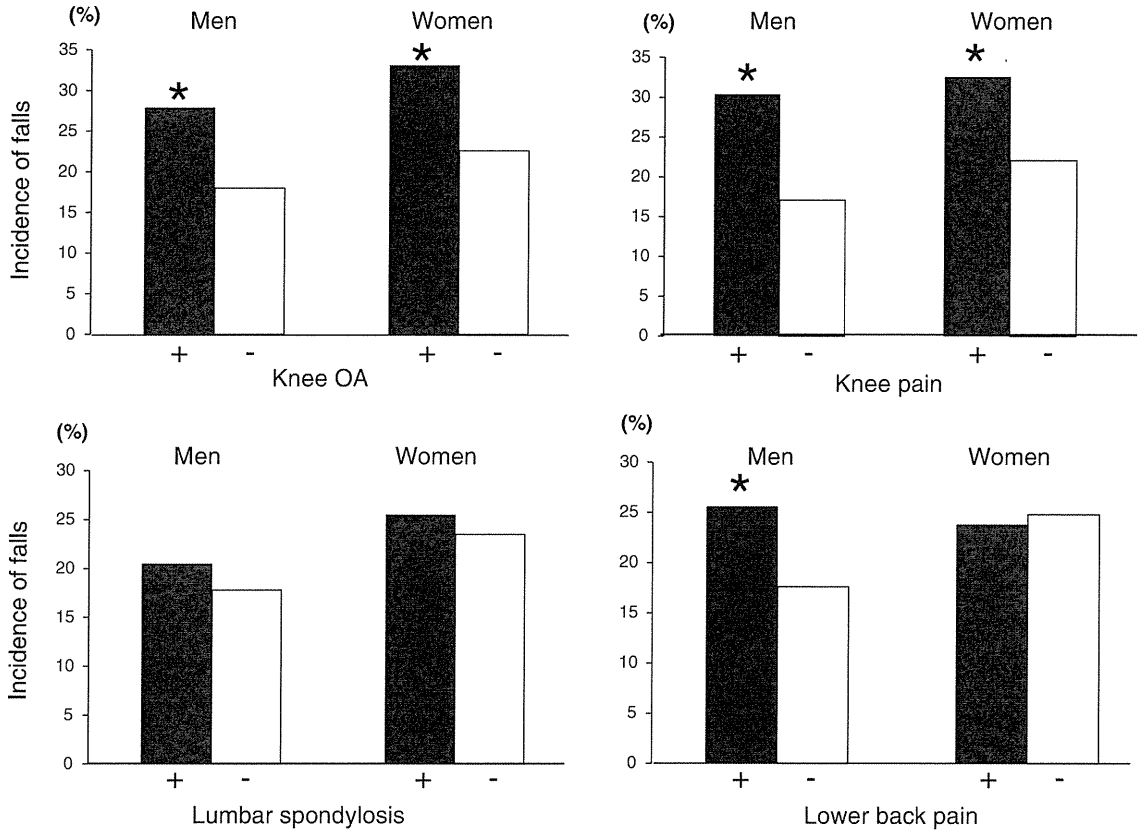

Fig. 2 Incidence of falls by knee OA, knee pain, LS, and lower back pain. *$p<0.05$ vs. subjects without knee OA, LS, knee pain, and lower back pain, respectively, by chi-square test

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