study are inferred to be among the top five leading conditions. Additional studies are necessary to identify those direct associations. Second, participants at baseline in the present study were those who could walk to the survey site and could understand and sign an informed consent form. Since those who could not were not included in the analyses, the study participants do not truly represent the general population due to health bias, which should be taken into consideration when generalizing the results of the present study.

In conclusion, the present study determined association of physical ADLs with the occurrence of certified need of care in the LTCI system in elderly participants of Japanese population-based cohorts. The severity of physical dysfunction is a predictor of the occurrence of certified need of care. Further studies are necessary to develop intervention programs that are safe and effective for elderly individuals who are at high risk of certified need of care.

Acknowledgments This study was supported by Grants-in-Aid for Scientific Research (S19109007, B20390182, B23390172, B23390356, and B23390357) from the Japanese Ministry of Education, Culture, Sports, Science and Technology; H17-Men-eki-009, H18-Choujyu-037, H20-Choujyu-009, H21-Chouju-Wakate-011, H22-Chouju-Wakate-007, H23-Chouju-002, and H25-Chouju-007 from the Ministry of Health, Labour and Welfare; and Research Aid from the Japanese Orthopaedic Association (JOA-Subsidized Science Project Research 2006-1 and 2010-2).

Conflict of interest There are no conflicts of interest.

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Osteoporos Int (2014) 25:1081–1088
DOI 10.1007/s00198-013-2550-z

ORIGINAL ARTICLE

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

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Received: 8 July 2013 / Accepted: 3 October 2013 / Published online: 22 October 2013

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.

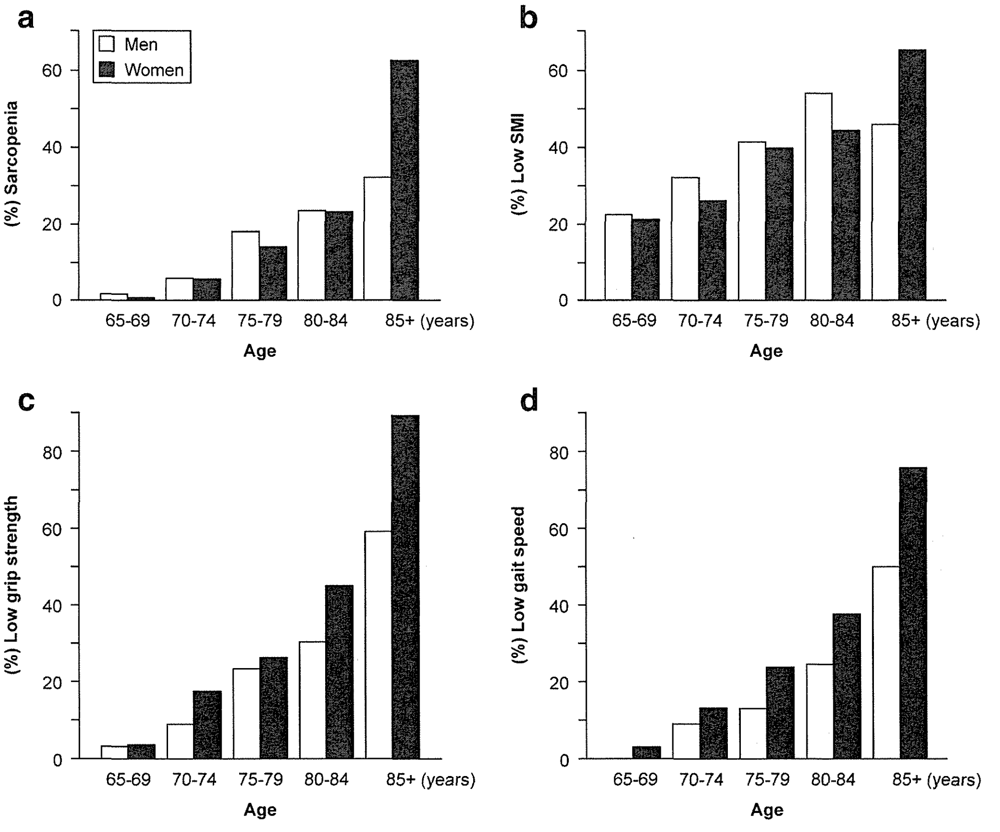

Fig. 1 Percentage of sarcopenia (**a**), low skeletal muscle mass index (*SMI*) (**b**), low grip strength (**c**), and low gait speed (**d**) in men and women in each age stratum (65–69, 70–74, 75–79, 80–85, and ≥85 years). Low SMI was defined as a value of <7.0 kg/m^2 in men and <5.8 kg/m^2 in women.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

Acknowledgments This study was supported by Grants-in-Aid for Scientific Research (S19109007, B20390182, B23390172, B23390356, and B23390357) from the Japanese Ministry of Education, Culture, Sports, Science and Technology; H17-Men-eki-009, H18-Choujyu-037, H20-Choujyu-009, H21-Chouju-Wakate-011, H22-Chouju-Wakate-007, and H23-Chouju-002 from the Ministry of Health, Labour and Welfare; and Research Aid from the Japanese Orthopaedic Association (JOA-Subsidized Science Project Research 2006–1 and 2010–2).

Conflicts of interest None.

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Osteoarthritis and Cartilage 22 (2014) 104–110

Osteoarthritis and Cartilage

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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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ARTICLE INFO

Article history:
Received 23 May 2013
Accepted 29 October 2013

Keywords:
Magnetic resonance imaging
Population-based cohort
Intervertebral disc degeneration
Entire spine
Prevalence
Distribution

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.

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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

1063-4584/$ – see front matter
http://dx.doi.org/10.1016/j.joca.2013.10.019

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

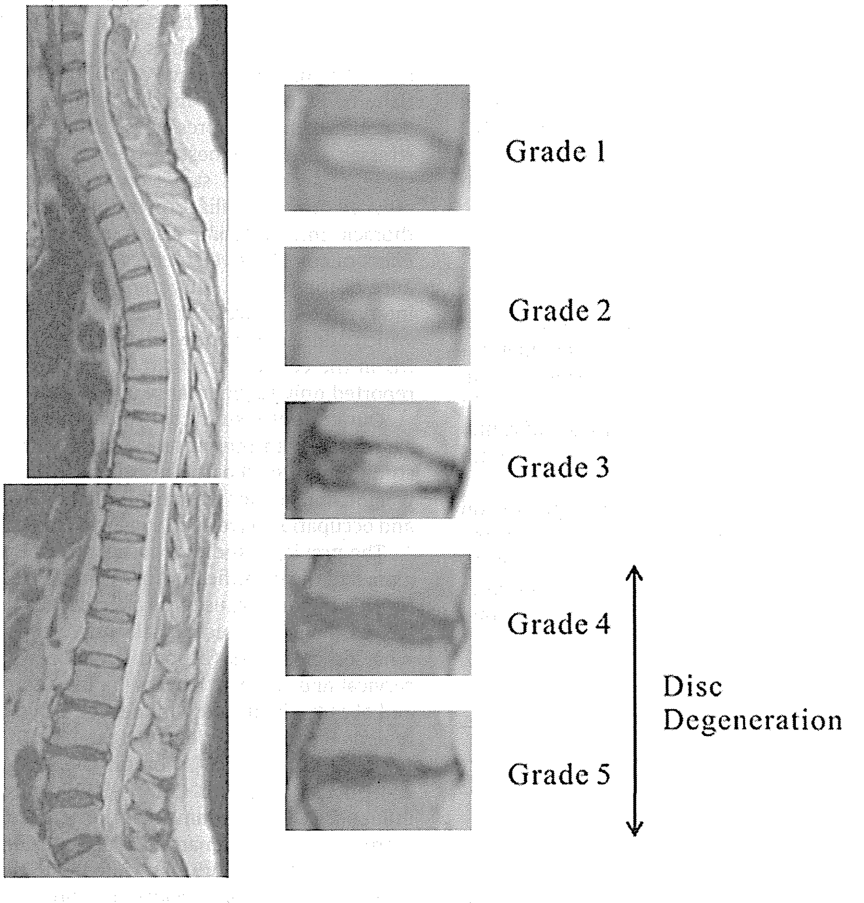

Fig. 1. Mid-sagittal view on T2-weighted images of the whole spine MRI with Pfirrmann classification. The grade is described according to Pfirrmann classification. Grades 4 and 5 were considered degenerated. The signal intensity for grade 4 was intermediate to hypointense to the cerebrospinal fluid (dark 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.

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 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.

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.

Role of the funding source

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.

Acknowledgments

This study was supported by a Grant-in-Aid for Scientific Research (B20390182, B23390357, C20591737, C20591774), and for Exploratory Research (19659305) from the Japanese Ministry of Education, Culture, Sports, Science and Technology, H17-Men-eki-009, H18-Choujyu-037, and H20-Choujyu-009 from the Ministry of Health, Labour and Welfare, Research Aid from the Japanese Orthopaedic Association, a Grant from the Japanese Orthopaedics and Traumatology Foundation, Inc. (No. 166), and a Grant-in-Aid for Scientific Research, Scientific Research (C22591639) from the Japanese Society for the Promotion of Science.

The authors wish to thank Mrs Tomoko Takijiri and other members of the Public Office in Hidakagawa Town, and Mrs Tamako Tsutsumi, Mrs Kanami Maeda, and other members of the Public Office in Taiji Town for their assistance in the location and scheduling of participants for examinations.

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The Spine Journal ■ (2015) ■

THE SPINE JOURNAL

Clinical Study

The association of combination of disc degeneration, end plate signal change, and Schmorl node with low back pain in a large population study: the Wakayama Spine Study

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Received 17 July 2014; revised 21 October 2014; accepted 20 November 2014

Abstract

BACKGROUND CONTEXT: Disc degeneration (DD) reportedly causes low back pain (LBP) and is often observed concomitantly with end plate signal change (ESC) and/or Schmorl node (SN) on magnetic resonance imaging.

PURPOSE: The purpose of this study was to examine the association between DD and LBP, considering ESC and/or SN presence, in a large population study.

STUDY DESIGN/SETTING: Cross-sectional population-based study in two regions of Japan.

PATIENT SAMPLE: Of 1,011 possible participants, data from 975 participants (324 men, 651 women; mean age, 66.4 years; range, 21–97 years) were included.

OUTCOME MEASURES: Prevalence of DD, ESC, and SN alone and in combination in the lumbar region and the association of these prevalence levels with LBP.

METHODS: Sagittal T2-weighted images were used to assess the intervertebral spaces between L1–L2 and L5–S1. Disc degeneration was classified using the Pfirrmann classification system (grades 4 and 5 indicated degeneration); ESC was defined as a diffuse high signal change along

FDA device/drug status: Not applicable.

Author disclosures: ***MT:*** Grant: Grant-in-Aid for Young Scientists, B26861206 (D, Paid directly to institution). ***NY:*** Grant: Grant-in-Aid for Scientific Research, B26293139 (F, Paid directly to institution) and Grant-in-Aid for Challenging Exploratory Research, 24659317 (D, Paid directly to institution). ***HH:*** Grant: Grant-in-Aid for Scientific Research, C26462249 (D, Paid directly to institution). ***SM:*** Grant: Grant-in-Aid for Scientific Research, B23390356 (F, Paid directly to institution). ***HY:*** Grant: Grant-in-Aid for Scientific Research, C25462305 (D, Paid directly to institution). ***HO:*** Grant: Grant-in-Aid for Challenging Exploratory Research, 24659666 (D, Paid directly to institution). ***AM:*** Nothing to disclose. ***HN:*** Nothing to disclose. ***YI:*** Grant: Grant-in-Aid for Young Scientists, B25860448 (D, Paid directly to institution). ***KNag:*** Nothing to disclose. ***RK:*** Grant: Grant-in-Aid for Young Scientists, B26860419 (D, Paid directly to institution). ***ST:*** Nothing to disclose. ***HK:*** Nothing to disclose. ***KNak:*** Nothing to disclose. ***TA:*** Grant: Grant-in-Aid for Challenging Exploratory Research, 25670293 (D, Paid directly to institution). ***MY:*** Grant: Health Labour Sciences Research Grant, H20-Choju-Ippan-009 (D, Paid directly to institution).

The disclosure key can be found on the Table of Contents and at www.TheSpineJournalOnline.com.

This study was funded by the Ministry of Education, Culture, Sports, Science and Technology, and the Ministry of Health, Labour and Welfare in Japan. The sponsors did not contribute to the study design, data collection, data analysis, data interpretation, or the writing of the manuscript.

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http://dx.doi.org/10.1016/j.spinee.2014.11.012
1529-9430/

either area of the end plate, and SN was defined as a small well-defined herniation pit with a surrounding wall of hypointense signal. Logistic regression analysis was used to determine the odds ratios (ORs) and confidence intervals (CIs) for LBP in the presence of radiographic changes in the lumbar region and at each lumbar intervertebral level, compared with patients without radiographic change, after adjusting for age, body mass index, and sex.

RESULTS: The prevalence of lumbar structural findings was as follows: DD alone, 30.4%; ESC alone, 0.8%; SN alone, 1.5%; DD and ESC, 26.6%; DD and SN, 12.3%; and DD, ESC, and SN, 19.1%. These lumbar structural findings were significantly associated with LBP in the lumbar region overall, as follows: DD, ESC, and SN, OR 2.17, 95% CI 1.2–3.9; L1–L2, OR 6.00, 95% CI 1.9–26.6; L4–L5, OR 2.56, 95% CI 1.4–4.9; and L5–S1, OR 2.81, 95% CI 1.1–2.3. The combination of DD and ESC was significantly associated with LBP as follows: L3–L4, OR 2.43, 95% CI 1.5–4.0; L4–L5, OR 1.82, 95% CI 1.2–2.8; and L5–S1, OR 1.60, 95% CI 1.1–2.3.

CONCLUSIONS: Our data suggest that DD alone is not associated with LBP. By contrast, the combination of DD and ESC was highly associated with LBP.

Keywords: Disc degeneration; End plate signal change; Schmorl node; Low back pain; Large population study; ROAD study

Introduction

Low back pain (LBP) causes functional impairment, diminished quality of life, loss of working ability, potential psychological distress, and increased health-care costs [1–3]. Magnetic resonance imaging (MRI) has become widely used in LBP diagnosis [4–15].

From the perspective of discogenic pain, the association between disc degeneration (DD) and symptoms remains controversial. Several reports have found that DD was a source of LBP [4–7], but others reported no association between DD and LBP [8,9]. This discrepancy is partly explained by the fact that DD often occurs concomitantly with various radiographic changes such as end plate signal change (ESC) and Schmorl node (SN). However, few studies have reported on the association of ESC and SN with LBP [10–14], and furthermore, to the best of our knowledge, no population-based study has examined the association of the combination of DD, ESC, and SN with LBP.

The purposes of this study were to examine the prevalence of combinations of DD, ESC, and SN in the lumbar region overall and to clarify the associations between LBP and combinations of DD, ESC, and SN in a large population.

Methods

Participants

The Wakayama Spine Study is a population-based study of degenerative spinal disease [15–17] performed in a subcohort of the large-scale population-based cohort study Research on Osteoarthritis/Osteoporosis against Disability (ROAD) [18,19]. Research on Osteoarthritis/Osteoporosis against Disability is a nationwide prospective study of bone and joint diseases consisting of population-based cohorts established in three communities in Japan. The participants were recruited from listings of resident registrations in three communities that have different characteristics: an urban region in Itabashi, Tokyo; a mountainous region in Hidakagawa, Wakayama; and a coastal region in Taiji, Wakayama. The inclusion criteria, apart from residence in the communities mentioned previously, were the ability to walk to the survey site, report data, and understand and sign an informed consent form. The age of the participants recruited from the urban region was 60 years or older and that of the participants from the other two regions was 40 years or older [18]. A second visit of the ROAD study to the mountainous region of Hidakagawa and the coastal region of Taiji was performed between 2008 and 2010. From the inhabitants participating in the second visit of the ROAD study, 1,063 volunteers were recruited to MRI examinations. Among these volunteers, 52 declined to attend the examination and 1,011 provided an additional written informed consent for the mobile MRI examination and were recruited for registration in the Wakayama Spine Study. Among the 1,011 participants, those who had an MRI-sensitive implanted device (e.g., pacemaker) or other disqualifier were excluded. Ultimately, 980 individuals underwent whole-spine MRI. One participant who had undergone a previous cervical operation and four participants who had undergone previous posterior lumbar fusion were excluded from the analysis. Thus, whole-spine MRI results were available for 975 participants (324 men and 651 women) with an age range of 21 to 97 years (mean, 67.2 years for men and 66.0 years for women). Experienced board-certified orthopedic surgeons also asked all participants the following question regarding LBP: "Have you experienced LBP on most days during the past month, in addition to now?" Those who answered "yes" were defined as having LBP based on the previous studies [20–24]. All study participants provided informed consent, and the study design was approved by the appropriate ethics review boards.

Magnetic resonance imaging

A mobile MRI unit (Excelart 1.5 T; Toshiba, Tokyo, Japan) was used, 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 (repetition time, 4,000 ms/echo; echo time, 120 ms; and field of view, 300×320 mm) and axial T2-weighted fast spin echo (repetition time, 4,000 ms/echo; echo time, 120 ms; and field of view, 180×180 mm). Sagittal T1-weighted images were omitted owing to cost and time limitations; only T2-weighted images were obtained.

Radiographic assessment

Sagittal T2-weighted images were used to assess DD, ESC, and SN at all intervertebral levels from C2–C3 to L5–S1. The present study assessed L1–L2 to L5–S1 in the lumbar region.

Disc degeneration

Disc degeneration grading was performed by a board-certified orthopedic surgeon who was blinded to the background of the participants. The degree of DD on MRI was classified into five grades based on the Pfirrmann classification system [25], with grades 4 and 5 indicating DD. To evaluate intraobserver variability, 100 randomly selected MR images of the entire spine were rescored by the same observer more than 1 month after the first reading. Furthermore, to evaluate interobserver variability, 100 other MR images were scored by 2 orthopedic surgeons using the same classification. The intraobserver and interobserver variabilities of DD, as evaluated by kappa analysis, were 0.94 and 0.94, respectively.

End plate signal change

End plate signal change was defined as diffuse areas of high signal change along the end plates, tending to be linear and always parallel to the vertebral end plates on sagittal T2-weighted images. However, discerning the type of Modic changes [26,27] was not possible because of cost and time limitations of this large-scale study. Because the T1 sequence was not obtained, we considered Modic Type I/II (T2 high signal intensity end plate change) to reflect the presence of ESC and T2 isosignal intensity and Modic Type III (T2 low signal intensity end plate change) to reflect the absence of ESC. To evaluate the intraobserver and interobserver variabilities, two orthopedic surgeons scored MR images in the same manner. The intraobserver and interobserver variabilities of ESC evaluated by kappa analysis were 0.86 and 0.82, respectively.

Schmorl node

Schmorl node was characterized by a localized defect at the rostral, caudal, or both end plates, with a well-defined herniation pit in the vertebral body with or without a surrounding sclerotic rim (low signal on T2-weighted image) [14,28]. Erosive defects in the end plate in degenerate segments were not considered as SN [14,28]. To evaluate intraobserver and interobserver variabilities, two orthopedic surgeons scored MR images in the same manner. The intraobserver and interobserver variabilities for SN evaluated by kappa analysis were 0.92 and 0.84, respectively.

Statistical analyses

Radiographic changes were compared between sexes using the chi-square test. Multivariate logistic regression analysis was used to estimate the radiographic changes of DD, ESC, and SN presence in the lumbar region as dependent variables, with LBP as the independent variable, after adjustment for age, body mass index (BMI), and sex. Multivariate logistic regression analysis was used to estimate the respective associations of eight combinations of radiographic changes (none; DD alone; SN alone; ESC alone; DD and SN; DD and ESC; SN and ESC; and DD, ESC, and SN) in the lumbar region as dependent variables, with LBP as the independent variable, after adjustment for age, BMI, and sex. Multivariate logistic regression analysis was also used to estimate the association of 8 combinations of radiographic changes at each intervertebral level (L1–L2 to L5–S1) in the lumbar region after adjustment for age, BMI, and sex. All statistical analyses were performed using JMP, version 8 (SAS Institute Japan, Tokyo, Japan).

Prevalence of DD, ESC, and/or SN, defined as the proportion of the number of participants who demonstrated the presence of DD, ESC, and/or SN in the lumbar region divided by the total number of participants, was used to describe the frequency of DD, ESC, and/or SN. In this analysis, to clarify the associated factors using multivariate logistic regression analysis, we entered a variable reflecting the observation of DD, ESC, and/or SN (1, presence; 0, absence) as a dependent variable.

Table 1
Characteristics of the 975 participants in the present study

	Overall	Men	Women
No. of participants	975	324	651
Demographic characteristics			
Age, y	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
Symptom			
LBP (%)	393 (40.3)	119 (36.7)	274 (42.1)

BMI, body mass index; LBP, low back pain.
Note: Values are the mean±standard deviation.

Table 2
Prevalence of combination of radiographic change in the lumbar region according to sex

	Overall (%)	Men (%)	Women (%)
Total	975	324	651
None	85 (8.7)	35 (10.8)	50 (7.7)
DD alone	296 (30.4)	104 (32.1)	192 (29.5)
ESC alone	8 (0.8)	3 (0.9)	5 (0.8)
SN alone	15 (1.5)	6 (1.9)	9 (1.4)
DD and ESC	259 (26.6)	85 (26.2)	174 (26.7)
DD and SN	120 (12.3)	37 (11.4)	83 (12.8)
SN and ESC	6 (0.6)	0 (0)	6 (0.9)
DD, ESC, and SN	186 (19.1)	54 (16.7)	132 (20.3)

DD, disc degeneration; ESC, end plate signal change; SN, Schmorl node.

Note: Chi-square test was used to determine differences in radiographic change between men and women.

Table 3
Association between LBP and radiographic changes in the lumbar region

	Proportion of participants with LBP (%)	OR (95% CI)
None	25/85 (29.4)	1
DD alone	112/296 (37.8)	1.35 (0.8–2.3)
ESC alone	0/8 (0)	—
SN alone	5/15 (33.3)	1.14 (0.3–3.6)
DD and ESC	107/259 (41.3)	1.51 (0.9–2.6)
DD and SN	45/120 (37.5)	1.26 (0.7–2.3)
SN and ESC	3/6 (50.0)	2.06 (0.4–11.9)
DD, ESC, and SN	96/186 (51.6)	2.17 (1.2–3.9)*

CI, confidence interval; DD, disc degeneration; ESC, end plate signal change; LBP, low back pain; OR, odds ratio; SN, Schmorl node.

Note: Proportion of participants with LBP means the number of participants with LBP/the number of participants with each radiographic change. ORs were calculated by multivariate logistic regression analysis after adjustment for age, body mass index, and sex.

* $p<.01$.

Results

Table 1 shows the characteristics of the 975 participants in the present study including age and demographic measurements. Two-thirds of the participants were women.

The prevalence of DD, ESC, and SN in the lumbar region overall, without considering other radiographic changes, was 86.7%, 44.1%, and 29.6% in men and 89.6%, 48.7%, and 35.2% in women, respectively. Table 2 shows the prevalence of combinations of radiographic changes according to sex. DD alone demonstrated the highest prevalence, followed by DD and ESC and DD, ESC, and SN in both sexes. The prevalence of SN alone, ESC alone, or the combination of SN and ESC was small. The prevalence of combinations of radiographic changes in the lumbar region did not significantly differ between men and women.

When we evaluated DD, ESC, and SN in the lumbar region overall without considering other radiographic change, DD presence and ESC presence in the lumbar region were each significantly associated with LBP (DD: odds ratio [OR] 1.58, 95% confidence interval [CI] 1.02–2.49; ESC: OR 1.36, 95% CI 1.04–1.76). On the other hand, SN presence in the lumbar region was not significantly associated with LBP (OR 1.27, 95% CI 0.96–1.68). Next, to determine the effect of the combination of DD, ESC, and SN on LBP, we classified participants into eight groups: none; DD alone; ESC alone; SN alone; DD and ESC; DD and SN; SN and ESC; and DD, ESC, and SN. As shown in Table 3, the combination of DD, ESC, and SN in the lumbar region was significantly associated with LBP. Disc degeneration alone was not an associated factor for LBP.

Furthermore, as shown in Table 4, the effect of combinations of radiographic change at each intervertebral level from L1–L2 to L5–S1 on LBP was evaluated: the combination of DD, ESC, and SN was significantly associated with LBP at L1–L2, L4–L5, and L5–S1. Furthermore, the combination of DD and ESC was significantly associated with LBP at L3–L4, L4–L5, and L5–S1.

Discussion

The prevalence of DD, ESC, or SN in the lumbar region has been examined in some previous studies [11–15,26–32], but, to the authors' knowledge, no population-based studies have assessed the prevalence of the combination of DD, ESC, and SN in a large population using MRI. First, we found that prevalence of combinations of DD, ESC, and SN in the lumbar region was approximately 20%. By contrast, the prevalence of ESC alone, SN alone, and combination of SN and ESC was quite small, which is partly explained by the fact that DD was reported to have a strong positive linear relationship with ESC and/or SN in the previous studies [14,28,33].

The association of DD with LBP remains controversial. An association between DD in the lumbar region and LBP was previously demonstrated in a twin study and other previous studies [15,30,31]. However, some reports have observed a high prevalence of DD among asymptomatic volunteers, with no association between DD and LBP [8,9]. These studies may have been limited in that they did not account for interactions between radiographic changes including DD, ESC, and SN. The present study found that the combination of DD, ESC, and SN was significantly associated with LBP, whereas DD alone was not.

The association of Modic changes, which are the gold standard to diagnose ESC, with clinical symptoms, has been controversial in the clinical studies based on patient series and a population-based cohort [10–12,29,32]. The present study found that the combination of DD and ESC at L3–L4, L4–L5, and L5–S1 was significantly associated with LBP. Degenerative change of end plates becomes a source of LBP and affects DD. Because the lumbar vertebral end plate contains immunoreactive nerves, as shown in the studies of sheep and humans [33,34], it has been reported that an increased number of tumor necrosis factor–immunoreactive spinal nerve cells and fibers are present in end plates