

Table 1 Comparison of baseline characteristics of subjects without and with mild cognitive impairment (MCI)

	Total (n=1676)			Men (n=591)			Women (n=1085)		
	Without MCI	With MCI	p Value	Without MCI	With MCI	p Value	Without MCI	With MCI	p Value
	(N=1601)	(N=75)	(Without vs with MCI)	(N=561)	(N=30)	(Without vs with MCI)	(N=1040)	(N=45)	(Without vs with MCI)
Number of subjects (prevalence, %) classified by age-strata									
<39 (year)	45	0 (0.0)		14	0 (0.0)		31	0 (0.0)	
40–49	148	1 (0.7)		43	1 (2.3)		105	0 (0.0)	
50–59	314	2 (0.6)	<0.001***	106	1 (0.9)	<0.001***	208	1 (0.5)	<0.001***
60–69	467	10 (2.1)		151	5 (3.2)		316	5 (1.6)	
70–79	496	35 (6.6)		202	14 (6.5)		294	21 (6.7)	
≥80	131	27 (17.1)		45	9 (16.7)		86	18 (17.3)	
Total	1601	75 (4.5)		561	30 (5.1)		1040	45 (4.2)	
Mean values (SDs) of MMSE summary score	28.5 (1.7)	21.2 (3.2)	<0.0001***	28.4 (1.8)	20.7 (4.4)	<0.0001***	28.6 (1.7)	21.5 (2.1)	<0.0001***
Mean values (SDs) of selected characteristics									
Age (year)	64.7 (11.9)	75.8 (8.1)	<0.0001***	65.8 (11.7)	74.0 (9.3)	0.0002***	64.1 (12.0)	77.0 (6.9)	<0.0001***
Height (cm)	155.5 (9.1)	148.7 (9.8)	<0.0001***	163.8 (7.1)	157.4 (5.8)	<0.0001***	151.1 (6.7)	142.9 (7.4)	<0.0001***
Weight (kg)	55.8 (10.7)	51.7 (11.7)	0.0011**	62.5 (10.8)	57.7 (12.1)	0.0181*	52.2 (8.8)	47.7 (9.6)	0.0007***
BMI (kg/m ²)	23.0 (3.4)	23.2 (3.7)	0.5845	23.2 (3.2)	23.2 (3.9)	0.9346	22.9 (3.5)	23.2	0.4877
Grip strength (better side) (kg)	27.8 (9.5)	20.8 (8.5)	<0.0001***	36.4 (8.8)	27.6 (8.2)	<0.0001***	23.3 (6.0)	16.5 (5.3)	<0.0001***
Grip strength (worse side) (kg)	24.6 (9.3)	16.8 (9.3)	<0.0001***	32.8 (9.1)	22.4 (10.6)	<0.0001***	20.1 (5.6)	13.1 (6.2)	<0.0001***
Percentage of selected characteristics (%)									
Residing in a coastal area	50.1	28.0	<0.001***	47.8	26.7	0.024*	51.4	28.9	0.003**
Current smoking habit (more than once a month)	13.3	10.0	0.428	30.4	21.4	0.312	3.9	2.4	0.624
Current alcohol consumption (more than once a month)	40.5	24.0	0.004**	67.6	46.7	0.018*	26.0	8.9	0.010*
Regular exercise after graduation from school	14.9	4.0	0.008**	34.4	6.7	0.002**	4.4	2.2	0.478
Prevalence of KOA at the baseline (%)	48.8	75.7	<0.001***	41.0	50.0	0.328	53.0	93.2	<0.001***

*p<0.05, **p<0.01, ***p<0.001

BMI, body mass index; KOA, knee osteoarthritis; MMSE, mini-mental state examination; n, number of subjects.

significantly higher than the percentage in the without-MCI group (48.8%, $p < 0.001$). This significant tendency was observed in women, while in men the association was not significant.

Occurrence of radiographic KOA in participants with and without MCI

The baseline prevalence of KOA in the 1384 individuals who attended follow-up was 46.8% (men 37.3%; women 51.6%). After the exclusion of participants with a baseline KL grade ≥ 2 at one or both knees, the cumulative incidence of OA during the 3-year follow-up period was estimated using an at-risk population of 728 individuals (290 men, 438 women) without OA in either knee at baseline. Among these, 71 participants (18 men, 53 women) were newly diagnosed with KOA, and the annual cumulative incidence was estimated as 3.3% (men 2.1%; women 4.0%). The incidence of KOA increased with age (table 2).

The MMSE score was significantly lower in participants with, compared to those without, incident radiographic KOA ($p < 0.0001$), and the prevalence of MCI at baseline was significantly higher ($p = 0.003$). Those with KOA tended to reside in a mountainous area, were significantly taller, had greater BMI and weaker grip strength in both hands and were less likely to smoke, drink alcohol or exercise regularly compared with those without OA. History of knee injury was more common among those without KOA (table 2).

On univariate regression analysis, a one-digit increase in the MMSE score was associated with a 24% decreased risk of incident radiographic KOA ($p < 0.001$; table 3). This trend remained after adjustment for age, gender, regional differences and BMI in model 1 (OR 0.85 for +1 MMSE score; $p = 0.015$) and after adjustment for age, gender, regional differences, BMI, grip strength (kg) on the worse side, smoking, alcohol consumption, regular exercise and history of knee injury in model 2 (OR 0.83; $p = 0.010$). The presence of MCI was associated with a fivefold increased risk of incident KOA ($p = 0.008$), with ORs of 4.59 ($p = 0.027$) in model 1 and 4.90 ($p = 0.027$) in model 2.

Progression of radiographic KOA with and without MCI

We excluded 88 participants (21 men, 67 women) with a baseline KL grade of 4 at one or both knees, before estimating the cumulative rate for the progression of KOA during a 3-year follow-up. We estimated the rate of progression rate in KL grades over the 3 years using the population at risk comprising 1296 individuals (445 men, 851 women). Among these, 311 individuals (86 men, 225 women) had a higher KL grade assigned to one or both knees at follow-up than at baseline. The annual rate of progression in KL grades for either knee over the 3-year period was 8.0% (men 6.4%, women 8.8%) in the overall population at risk, and the rate increased with age (table 4). The MMSE summary score was significantly lower ($p < 0.0001$) and the baseline

prevalence of MCI was significantly higher ($p = 0.008$) in participants with, than in those without, progression of radiographic KOA. Participants with progression of radiographic KOA tended to reside in a mountainous area, were significantly older and taller, had greater BMI and weaker grip strength in both hands and were less likely to smoke, drink alcohol or take regular exercise compared to those who did not have progression of KOA (table 4).

A one-digit increase in the MMSE was associated with a 16% increased risk of progression of radiographic KOA (OR 0.84; $p < 0.001$). This tendency was no longer significant after adjustment for age, gender, regional differences and BMI in model 1 (OR 0.95; $p = 0.131$), and for age, gender, regional differences, BMI, grip strength (worst side), smoking, alcohol consumption, regular exercise and history of knee injuries in model 2 (OR 0.96; $p = 0.232$; table 5). On univariate analysis, the presence of MCI was associated with a 2.5-fold increased risk of progression of KOA (OR 2.54; $p = 0.010$), but this was not significant after adjustment for confounding factors in model 1 (OR 1.56; $p = 0.242$) or model 2 (OR 1.38; $p = 0.416$).

Association of inflammation and metabolic risk factors with both KOA and MCI

In addition to the factors adjusted in model 2, we assessed the following two factors as potential confounders influencing both KOA and MCI: subclinical inflammation and metabolic risk factors.

As an index of inflammation, baseline serum C reactive protein (CRP) level was added as an explanatory factor in a logistic regression analysis similar to that performed in model 2. The adjusted ORs for the occurrence of OA in relation to the MMSE summary score (OR 0.83; 95% CI, 0.72 to 0.96 for +1 MMSE score; $p = 0.010$) or to the presence of MCI (OR 5.18; 95% CI, 1.24 to 21.6 for presence of MCI; $p = 0.024$) remained unchanged, and the serum CRP level was not significantly associated with occurrence (OR 0.47; 95% CI, 0.09 to 2.40 for +1 CRP level; $p = 0.365$) or progression of OA (OR 0.96; 95% CI, 0.67 to 1.37; $p = 0.818$).

Then, we performed logistic regression analysis, similar to that performed in model 2, by using the metabolic risk factors overweight (1: BMI ≥ 25 kg/m², 0: BMI < 25 kg/m²), hypertension (1: systolic blood pressure (BP) ≥ 130 mm Hg and/or diastolic BP ≥ 85 mm Hg, 0: systolic BP < 130 mm Hg and diastolic BP < 84 mm Hg), dyslipidaemia (1: serum high-density lipoprotein cholesterol (HDL-cho) level < 40 mg/dl, 0: HDL-cho level ≥ 40 mg/dl) and impaired glucose tolerance (1: serum haemoglobin A1c (HbA1c) level $\geq 5.5\%$, 0: HbA1c level $< 5.5\%$). Furthermore, subjects receiving medication for hypertension, dyslipidaemia or diabetes mellitus were regarded as having hypertension, dyslipidaemia or impaired glucose tolerance, respectively. The adjusted ORs for the occurrence of KOA in relation to the MMSE summary score (OR 0.84; 95% CI, 0.73 to

Table 2 Mean values (SDs) of anthropometric factors, mini-mental state examination (MMSE) and prevalence of mild cognitive impairment (MCI) and selected characteristics vs the occurrence of knee osteoarthritis

	Occurrence of KOA			Men			Women		
	KOA (-) (n=657)	Total KOA (+) (n=71)	p Value	KOA (-) (n=272)	KOA (+) (n=18)	p Value	KOA (-) (n=385)	KOA (+) (n=53)	p Value
Number of subjects classified by age-strata (cumulative incidence, %/year)									
<39 (year)	38	0 (0.0)		10	0 (0.0)		28	0 (0.0)	
40-49	118	1 (0.3)		36	0 (0.0)		82	1 (0.4)	
50-59	201	15 (2.3)	<0.001***	77	0 (0.0)	0.009**	124	(3.6)	<0.001***
60-69	177	27 (4.4)		76	11 (4.2)		101	(4.6)	
70-79	108	23 (5.9)		62	6 (2.9)		46	17 (9.0)	
≥80	15	5 (8.3)		11	1 (2.8)		4	4 (16.7)	
Mean values (SDs) for MMSE summary score and prevalence of MCI									
MMSE summary score	29.1 (1.6)	28.0 (2.3)	<0.0001***	28.8 (1.9)	27.3 (2.7)	0.0017**	29.3 (1.3)	28.2 (2.1)	<0.0001***
Prevalence of MCI (%)	7/654 (1.1)	4/71 (5.6)	0.003**	6/270 (2.2)	2/18 (11.1)	0.026*	1/384 (0.3)	2/53 (3.8)	0.004*
Mean values (SDs) for age, anthropometric factors and neuromuscular function									
Age (year)	58.2 (11.8)	67.3 (8.2)	<0.0001***	61.0 (11.8)	70.0 (6.1)	0.0021**	56.4 (11.4)	66.4 (8.7)	<0.0001***
Height (cm)	158.8 (8.6)	153.9 (7.6)	<0.0001***	165.6 (7.0)	162.0 (5.0)	0.0360*	154.0 (6.0)	151.2 (6.2)	0.0018**
Weight (kg)	56.8 (11.0)	56.0 (8.8)	0.5560	63.7 (11.0)	63.7 (9.2)	0.9859	51.9 (8.1)	53.4 (7.1)	0.2051
BMI (kg/m ²)	22.4 (3.2)	23.6 (2.9)	0.0035**	23.2 (3.2)	24.2 (3.1)	0.1709	21.9 (3.1)	23.4 (2.8)	0.0012**
Grip strength (better side) (kg)	31.3 (9.9)	26.7 (8.1)	0.0002***	39.4 (8.8)	35.9 (7.1)	0.0996	25.6 (6.0)	23.5 (5.6)	0.0171*
Grip strength (worse side) (kg)	28.0 (9.6)	23.0 (8.5)	<0.0001***	35.9 (9.0)	30.7 (11.0)	0.0188*	22.5 (5.1)	20.4 (5.5)	0.0065**
Percentage of selected characteristics, %									
Residing in a coastal area	70.8	56.3	0.012*	66.9	55.6	0.324	73.5	56.6	0.011*
Current smoking habit (more than once a month)	16.9	7.1	0.034*	34.2	27.8	0.577	4.7	0.0	0.110
Current alcohol consumption (more than once a month)	47.9	35.2	0.041*	70.0	61.1	0.428	32.5	26.4	0.375
Regular exercise after graduation from school	19.9	7.0	0.008**	37.5	27.8	0.408	7.5	0.0	0.039*
Past injury of either knee	1.8	5.6	0.038*	0.4	5.6	0.010*	2.9	5.7	0.277

*p<0.05, **p<0.01, ***p<0.001

BMI, body mass index; KOA, knee osteoarthritis; KOA(-), non-occurrence of KOA; KOA(+), occurrence of KOA; n, number of subjects.

Table 3 ORs for occurrence of knee osteoarthritis during the 3-year follow-up period versus mild cognitive impairment (MCI)

MMSE summary score		Univariate analysis			Logistic regression model 1			Logistic regression model 2		
Explanatory variables	Reference	OR	95% CI	p Value	OR	95% CI	p Value	OR	95% CI	p Value
MMSE summary score	+1 score	0.76	0.68 to 0.85	<0.001***	0.85	0.73 to 0.97	0.015*	0.83	0.72 to 0.96	0.010*
Other potential risk actors										
Age (year)	1 year				1.09	1.06 to 1.13	<0.001**	1.10	1.06 to 1.14	<0.001***
Gender	0: men, 1: women				4.36	2.33 to 8.16	<0.001**	4.02	1.50 to 10.74	0.006**
Region	0: mountainous area, 1: coastal area				0.78	0.45 to 1.35	0.380	0.76	0.43 to 1.35	0.354
BMI (kg/m ²)	+1 kg/m ²				1.23	1.12 to 1.34	<0.001**	1.22	1.11 to 1.34	<0.001***
Grip strength (worse side) (kg)	+1 kg							1.01	0.96 to 1.06	0.730
Smoking	0: exsmoker or never smoker, 1: current smoker							1.01	0.35 to 2.91	0.986
Alcohol consumption	0: exdrinker or never drinker, 1: current drinker							1.11	0.60 to 2.04	0.746
Regular exercise after graduation from school	0: no, 1: yes							0.57	0.20 to 1.65	0.302
History of knee injuries	0: no, 1: yes							4.76	1.26 to 17.97	0.021*
MCI										
Explanatory variables		Univariate analysis			Logistic regression model 1			Logistic regression model 2		
MCI	0: absence, 1: presence	5.52	1.57 to 19.34	0.008**	4.59	1.18 to 17.7	0.027*	4.90	1.20 to 20.05	0.027*
Other potential risk actors										
Age (year)	1 year				1.10	1.07 to 1.14	<0.001**	1.10	1.07 to 1.15	<0.001***
Gender	0: men, 1: women				4.36	2.32 to 8.17	<0.001**	3.80	1.42 to 10.19	0.008**
Region	0: mountainous area, 1: coastal area				0.75	0.44 to 1.30	0.310	0.73	0.41 to 1.29	0.280
BMI (kg/m ²)	+1 kg/m ²				1.23	1.13 to 1.35	<0.001**	1.23	1.12 to 1.34	<0.001***
Grip strength (worse side) (kg)	+1 kg							1.00	0.96 to 1.05	0.870
Smoking	0: exsmoker or never smoker, 1: current smoker							1.08	0.38 to 3.12	0.885
Alcohol consumption	0: exdrinker or never drinker, 1: current drinker							1.10	0.59 to 2.02	0.770
Regular exercise after graduation from school	0: no, 1: yes							0.57	0.20 to 1.65	0.304
Past history of knee injuries	0: no, 1: yes							4.28	1.13 to 16.19	0.032*

*p<0.05, **p<0.01, ***p<0.001.

BMI, body mass index; n, number of subjects; MMSE, mini-mental state examination.

Table 4 Mean values (SDs) of anthropometric factors, mini-mental state examination (MMSE) and prevalence of mild cognitive impairment (MCI) and selected characteristics versus progression of knee osteoarthritis

	Progression of KOA Women			Men			Women		
	Progression		p Value	Progression		p Value	Progression		p Value
	(-) (n=985)	(+) (n=311)		(-) (n=359)	(+) (n=86)		(-) (n=626)	(+) (n=225)	
Number of subjects classified by age-strata (Proportion of progression, %/year)									
≤39 (year)	37	2 (1.7)		9	1 (3.3)		28	1 (1.1)	
40–49	128	7 (1.7)		38	2 (1.7)		90	5 (1.8)	
50–59	248	44 (5.0)	<0.001***	89	8 (2.8)	<0.001***	159	36 (6.2)	<0.001***
60–69	292	105 (8.2)		101			191	79 (9.8)	
70–79	241	115 (10.8)		105	38 (8.9)		136	77 (12.1)	
≥80	39	38 (16.5)		17	11 (13.1)		22	27 (18.4)	
Mean values (SDs) for MMSE summary score and prevalence of MCI									
MMSE summary score	28.7 (1.8)	28.0 (2.2)	<0.0001***	28.5 (1.9)	27.9 (2.3)	0.0056**	28.8 (1.8)	28.1 (2.1)	<0.0001***
Prevalence of MCI (%)	18/980 (1.8)	14/295 (4.5)	0.008**	9/357 (2.5)	5/85 (5.9)	0.112	9/623 (1.4)	9/224 (4.0)	0.022*
Mean values (SDs) for age, anthropometric factors and neuromuscular function									
Age (year)	61.6 (11.9)	68.7 (9.3)	<0.0001***	63.3 (11.8)	70.0 (9.4)	<0.0001***	60.7 (11.9)	68.2 (9.3)	<0.0001***
Height (cm)	156.7 (8.9)	153.1 (8.6)	<0.0001***	164.6 (7.1)	161.8 (6.2)	0.0010**	152.2 (6.4)	149.7 (6.9)	<0.0001***
Weight (kg)	56.0 (10.9)	55.6 (9.9)	0.5496	63.1 (10.9)	62.8 (10.2)	0.8520	52.0 (8.6)	52.9 (8.4)	0.1883
BMI (kg/m ²)	22.7 (3.3)	23.6 (3.1)	<0.0001***	23.2 (3.2)	23.9 (3.1)	0.0643	22.4 (3.3)	23.5 (3.1)	<0.0001***
Grip strength (better side) (kg)	29.3 (9.7)	25.7 (8.0)	<0.0001***	38.1 (8.7)	34.4 (7.2)	0.0003***	24.3 (6.0)	22.4 (5.3)	<0.0001***
Grip strength (worse side) (kg)	26.0 (9.4)	22.5 (7.9)	<0.0001***	34.6 (8.8)	30.1 (8.7)	<0.0001***	21.1 (5.3)	19.6 (5.2)	0.0003***
Percentage of selected characteristics (%)									
Residing in a coastal area	57.9	42.1	<0.001***	53.8	44.2	0.110	60.4	41.3	<0.001***
Current smoking habit (more than once a month)	14.1	8.6	0.013*	31.2	24.4	0.220	4.1	2.3	0.222
Current alcohol consumption (more than once a month)	44.4	32.5	<0.001***	72.1	57.0	0.006**	28.6	23.1	0.114
Regular exercise after graduation from school	18.1	8.0	<0.001***	39.6	23.3	0.005**	5.8	2.2	0.034*
Past injury of either knee	2.0	3.2	0.226	1.1	3.5	0.112	2.6	3.1	0.660

*p<0.05, **p<0.01, ***p<0.001.

KOA, knee osteoarthritis; progression(-), no progression of the Kellgren-Lawrence grade; progression(+), progression of the Kellgren-Lawrence grade.

BMI, body mass index; n, number of subjects.

Table 5 OR for the progression of the Kellgren-Lawrence grade for either knee during the 3-year follow-up period versus mild cognitive impairment (MCI)

MMSE summary score		Univariate analysis			Logistic regression model 1			Logistic regression model 2		
Explanatory variables	Reference	OR	95% CI	p Value	OR	95% CI	p Value	OR	95% CI	p Value
MMSE summary score	+1 score	0.84	0.79 to 0.90	<0.001***	0.95	0.88 to 1.02	0.131	0.96	0.89 to 1.03	0.232
Other potential risk actors										
Age (year)	+1 year				1.06	1.05 to 1.08	<0.001***	1.06	1.04 to 1.07	<0.001***
Gender	0: men, 1: women				1.89	1.40 to 2.55	<0.001***	1.29	0.798 to 2.11	0.308
Region	0: mountainous area, coastal 1: area				0.75	0.57 to 1.00	0.048*	0.69	0.52 to 0.92	0.011*
BMI (kg/m ²)	+ 1 kg/m ²				1.12	1.07 to 1.17	<0.001***	1.13	1.08 to 1.18	<0.001***
Grip strength (worse side) (kg)	+1 kg							0.99	0.97 to 1.02	0.572
Smoking	0: exsmoker or never smoker, 1: current smoker							0.99	0.59 to 1.64	0.964
Alcohol consumption	0: exdrinker or never drinker, 1: current drinker							0.84	0.61 to 1.15	0.274
Regular exercise after graduation from school	0: no, 1: yes							0.55	0.33 to 0.91	0.021*
History of knee injuries	0: no, 1: yes							2.27	0.99 to 5.22	0.053
MCI										
Explanatory variables			Univariate analysis		Logistic regression model 1			Logistic regression model 2		
MCI	0: absence, 1: presence	2.54	1.25 to 5.16	0.010*	1.56	0.74 to 3.30	0.242	1.38	0.63 to 3.03	0.416
Other potential risk actors										
Age (year)	+1 year				1.07	1.05 to 1.08	<0.001***	1.06	1.04 to 1.08	<0.001***
Gender	0: men, 1: women				1.89	1.40 to 2.54	<0.001***	1.26	0.77 to 2.05	0.353
Region	0: mountainous area, coastal 1: area				0.75	0.56 to 0.99	0.041*	0.68	0.51 to 0.91	0.010*
BMI (kg/m ²)	+ 1 kg/m ²				1.13	1.08 to 1.17	<0.001***	1.13	1.08 to 1.18	<0.001***
Grip strength (worse side) (kg)	+1 kg							0.99	0.97 to 1.02	0.484
Smoking	0: exsmoker or never smoker, 1: current smoker							0.99	0.60 to 1.65	0.974
Alcohol consumption	0: exdrinker or never drinker, 1: current drinker							0.83	0.61 to 1.15	0.264
Regular exercise after graduation from school	0: no, 1: yes							0.55	0.33 to 0.91	0.021*
History of knee injuries	0: no, 1: yes							2.27	0.99 to 5.21	0.053

*p<0.05, **p<0.01, ***p<0.001

BMI, body mass index; ; MMSE, mini mental state examination; n, number of subjects.

Mild cognitive impairment influences in onset of KOA

0.97 for +1 MMSE score; $p=0.019$) or to the presence of MCI (OR 4.78; 95% CI, 1.15 to 19.9 for the presence of MCI; $p=0.032$) remained significant, and hypertension was also significantly associated with the occurrence of KOA in relation to MMSE summary score (OR 2.23; 95% CI, 1.04 to 4.79 for the presence of hypertension; $p=0.039$) or to the presence of MCI (OR 2.26; 95% CI, 1.06 to 4.85; $p=0.036$). However, there was no significant association between the occurrence of KOA and overweight, dyslipidaemia and impaired glucose tolerance after adjustment for the factors used in model 2.

DISCUSSION

We studied a population-based cohort with a high participation rate (81.9%) over a period of 3 years, and observed a significant association between the baseline presence of MCI and incident radiographic KOA identified at 3-year follow-up. This association persisted after adjustment for potential confounding factors.

In contrast, we did not observe an association between MCI and further progression of radiographic KOA identified at baseline. We identified progression of KOA when the KL grade was higher at follow-up than at baseline; MCI might have had less influence in patients with an increase of at least one KL grade compared to baseline. We reanalysed the influence of the MMSE score or the presence of MCI on rapid progression of OA, which was defined as an increase of at least two KL grades at either knee at follow-up. The results were similar after adjustment for confounders as in model 2; that is, we identified a significant association between MMSE score and rapid progression of OA (OR 0.84; 95% CI, 0.73 to 0.98, for +1 MMSE score; $p=0.026$). The OR for rapid progression of OA was increased in the presence of MCI, but not significantly so (OR 2.73; 95% CI, 0.71 to 10.5; $p=0.144$). Then we concluded that the influence of cognitive decline in the future KOA was more pronounced in occurrence of radiographic KOA than in progression.

Links between musculoskeletal disease and dementia have been reported previously; osteoporosis at the femoral neck, for example, is more common in patients with Alzheimer's disease than in healthy volunteers,¹⁹ but the relationship between KOA and dementia has not been examined. In the current analysis, we showed that the occurrence of KOA was influenced not only by the MMSE scores but also by the presence of MCI. We think that this may be the effect of subclinical inflammation in both MCI and KOA, as inflammatory mechanisms could be involved in the pathogenesis of MCI^{19 20} as well as OA.²¹ Therefore, we performed logistic regression analysis similar to that performed in model 2, with the addition of the CRP values. The adjusted ORs for the occurrence of OA in relation to the MMSE summary score or to the presence of MCI remained unchanged, and serum CRP level was not significantly associated with occurrence or progression of OA. However, we used

a standard method to measure CRP levels, and further studies using a more sensitive measurement method are required to assess the effect of systemic inflammation on cognitive impairment and KOA.

Another hypothesis is that there are hidden confounding factors that might affect both MCI and the onset of KOA. We considered risk factors for metabolic syndrome as potential confounders. Metabolic risk factors such as hypertension and diabetes have been suggested to play a role in the pathogenesis of Alzheimer's disease as well as in the development of vascular dementia.²²⁻²⁴ We have also already reported the presence of hypertension and impaired glucose tolerance, and shown that accumulation of metabolic risk factors may cause the occurrence of KOA.²⁵ These findings may indicate that the MCI is a candidate surrogate index for metabolic risk factors as a predictor of KOA occurrence. Therefore, we performed logistic regression analysis similar to that performed for model 2, with the addition of metabolic risk factors. The adjusted ORs for the occurrence of KOA in relation to the MMSE summary score or to the presence of MCI remained significant. In addition, hypertension was also significantly associated with the occurrence of KOA in relation to the MMSE summary score and the occurrence of KOA in relation to MCI, but there was no significant association between the occurrence of KOA and overweight, dyslipidaemia and impaired glucose tolerance. This result shows that components of metabolic syndrome, such as hypertension and MCI, coexist as risk factors for onset of KOA, and MCI might not be a surrogate index for metabolic risk factors for indicating the occurrence of KOA. There might be a direct or an indirect pathway between cognitive impairment and onset of KOA, but based on the information currently available, a causal relationship between MCI and onset of KOA seems to be biologically improbable.

Besides inflammation and metabolic risk factors, there might be other hidden confounders, which could influence both MCI and OA, for example, nutritional factors. Further investigation would be needed to clarify whether the causal relationship still remains after careful consideration with analysis of other possible confounders.

There were several limitations to our study. First, although we used a standard measure of global cognitive function, we used only the MMSE to diagnose MCI, and were unable to perform additional examinations such as MRI to improve the accuracy of the diagnosis. Consequently, we may have underdiagnosed MCI. Second, we used KL grade ≥ 2 for diagnosis of KOA. However, the KL scale is a categorical index, and it is impossible to separately evaluate osteophytosis and the minimum joint space. A computer-assisted diagnostic system for the measurement of minimum joint space width and area of osteophytosis is currently under development,²⁶ this will help measure the severity of KOA using quantitative parameters, and allow us to establish a more accurate assessment of the association between MCI and the development of OA, and facilitate early

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prevention of disability. Further, the small proportion of the population with MCI at risk for KOA onset detection might raise the bias in the results of the study.

On the contrary, the strengths of the present study include a population-based design of a cohort, large number of participants with KOA, and a 3-year follow-up with a high participation rate of 81.9%. Substantial amount of detailed information, including an interviewer-administered questionnaire, dietary assessment, anthropometric measurements, neuromuscular function assessment, biochemical measurements, medical history, radiographic assessment and bone mineral density measurement, was collected at both the baseline and the second visit.

CONCLUSION

Our results indicated that MCI significantly influences the occurrence of radiographic KOA, and that KOA occurs more frequently with an decrease in the summary score of the MMSE and the presence of MCI. Prevention of MCI may be useful in preventing the occurrence of KOA and subsequent disability, while further investigation is needed to clarify whether such causalities were caused by direct or indirect associations.

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Acknowledgements The authors wish to thank Dr Takako Nojiri and Mr Kazuhiro Hatanaka of the Gobo Public Health Centre; Dr Naoki Hirabayashi of the Kawakami Clinic, Hidakagawa Town; Mrs Tomoko Takijiri, Mrs Kumiko Shinou, Mrs Rie Takiguchi, Mrs Kyoko Maeda, Ms Ikuyo Ueyama, Mrs Michiko Mori, Mrs Hisayo Sugimoto, and other members of the public office in Hidakagawa Town; Dr Shinji Matsuda of the Shingu Public Health Centre; and Mrs Tamako Tsutsumi, Mrs Kanami Maeda, Mr Shoichi Shimoichi, Mrs Megumi Takino, Mrs Shuko Okada, Mrs Kazuyo Setoh, Mrs Chise Ryouno, Mrs Miki Shimosaki, Mrs Chika Yamaguchi, Mrs Yuki Shimoji, and other members of the public office in Taiji Town for their assistance in locating and scheduling participants for examinations. We also thank Ms Kyoko Yoshimura, Mrs Toki Sakurai and Mrs Saeko Sahara for their assistance with data reduction and administration.

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

Funding This work was supported by Grants-in-Aid for Scientific Research B23390172 and B20390182 to NY, B23390357 and C20591737 to TA, B23390356 and C20591774 to SM, for Young Scientists A18689031 to HO, and Collaborating Research with NSF 08033011-00262 (Director, NY) from the Ministry of Education, Culture, Sports, Science, and Technology; and H17-Men-eki-009 (Director, KN), H18-Choujyu-037 (Director, Toshitaka Nakamura), H20-Choujyu-009 (Director, NY), and H23-Choujyu-002 (Director, TA) from the Ministry of Health, Labour and Welfare in Japan. This study was

also supported by grants from the Japan Osteoporosis Society (NY, SM, HO, and TA), and research aid from the Japanese Orthopaedic Association (JOA-Subsidized Science Project Research 2006-1 & 2010-2, Director, HK).

Competing interests None.

Ethics approval Ethics approval was provided by the institutional review board at the University of Tokyo (approval number 1264).

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement No additional data are available.

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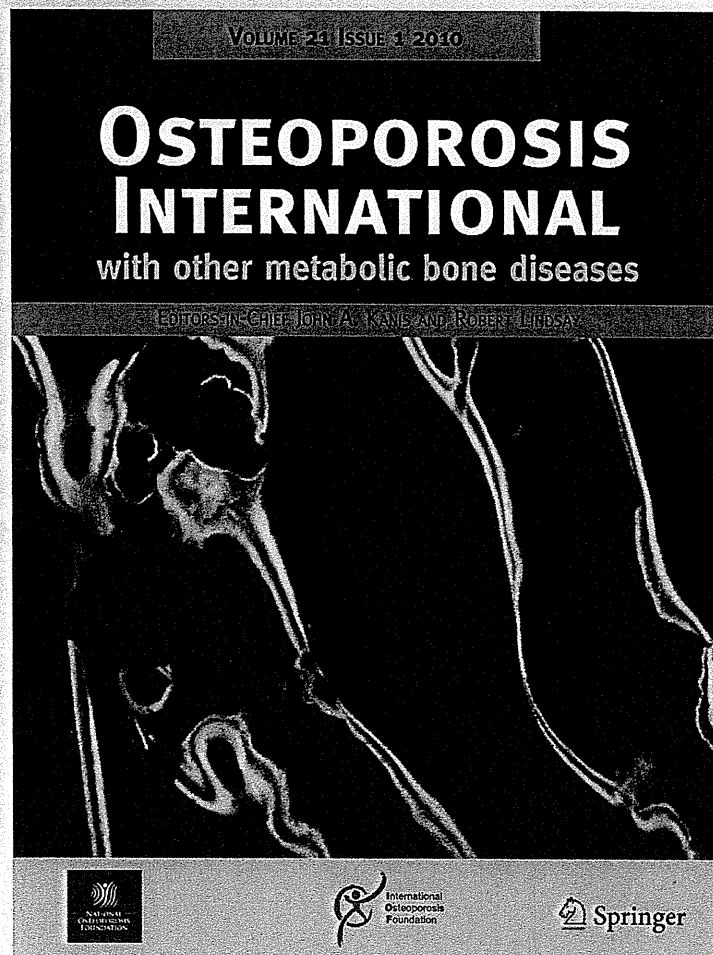
Physical performance, bone and joint diseases, and incidence of falls in Japanese men and women: a longitudinal cohort study

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Osteoporosis International
With other metabolic bone diseases

ISSN 0937-941X

Osteoporos Int
DOI 10.1007/s00198-012-1967-0



 Springer

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

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Received: 20 October 2011 / Accepted: 27 February 2012
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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.

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Introduction The objective of the present study was to clarify the incidence of falls by sex and age and to determine whether physical performance and bone and joint diseases are risk factors for falls in men and women using a large-scale population-based cohort of the ROAD.

Methods A total of 745 men and 1,470 women were analyzed in the present study (mean age, 68.5 years). A questionnaire assessed the number of falls during 3 years of follow-up. Grip strength and walking speed were measured at baseline. Knee and lumbar spine radiographs were read by Kellgren–Lawrence (KL) grade; radiographic knee osteoarthritis and lumbar spondylosis were defined as KL=3 or 4. Knee and lower back pain were estimated by an interview.

Results During a mean follow-up of 3 years, 141 (18.9 %) men and 362 (24.6 %) women reported at least one fall. Slower walking speed was a risk factor for falls in men (0.1 m/s decrease; odds ratio [OR], 1.15; 95 % confidence interval [CI], 1.09–1.23) and women (0.1 m/s decrease; OR, 1.05; 95 % CI, 1.01–1.10). Knee pain was also a risk factor for falls (OR, 1.38; 95 % CI, 1.03–1.84) in women, but lower back pain was not.

Conclusion We examined the incidence and risk factors for falls in men and women. Slower walking speed was a risk factor for falls in men and women. Knee pain was a risk factor for falls in women.

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

Introduction

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

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]/height² [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 \pm 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 \pm 11.3	69.4 \pm 11.1	68.1 \pm 11.4*
Height (cm)	154.7 \pm 8.8	163.2 \pm 6.6	150.4 \pm 6.3*
Weight (kg)	55.5 \pm 10.2	62.2 \pm 9.9	52.0 \pm 8.5*
BMI (kg/m ²)	23.1 \pm 3.3	23.3 \pm 3.0	23.0 \pm 3.4*
Grip strength (kg)	26.3 \pm 9.3	34.5 \pm 8.8	22.1 \pm 6.2*
Walking speed (m/s)	1.24 \pm 0.34	1.26 \pm 0.35	1.23 \pm 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 \pm 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

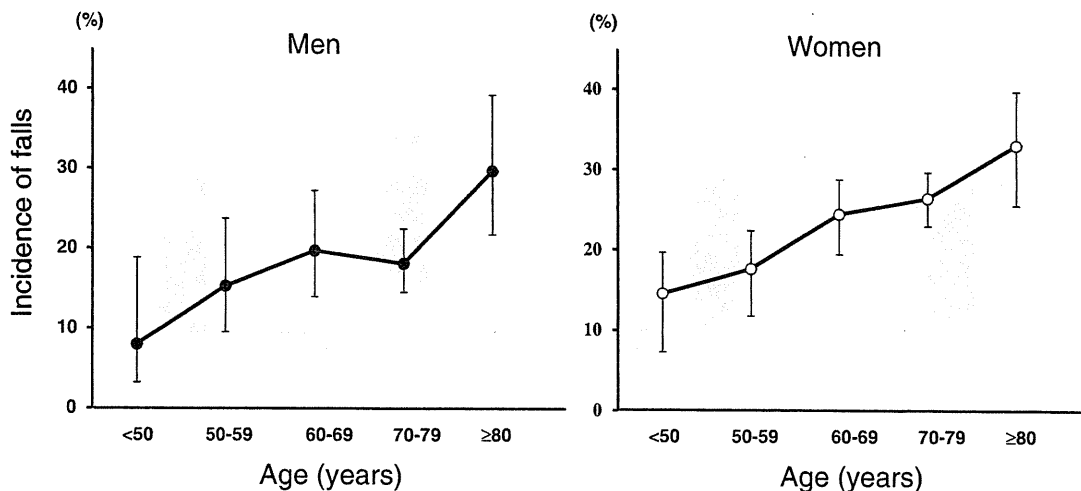


Fig. 1 Incidence rate of falls (95 % CI) by gender and age

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	<i>p</i> value	Nonfallers	Fallers	<i>p</i> 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

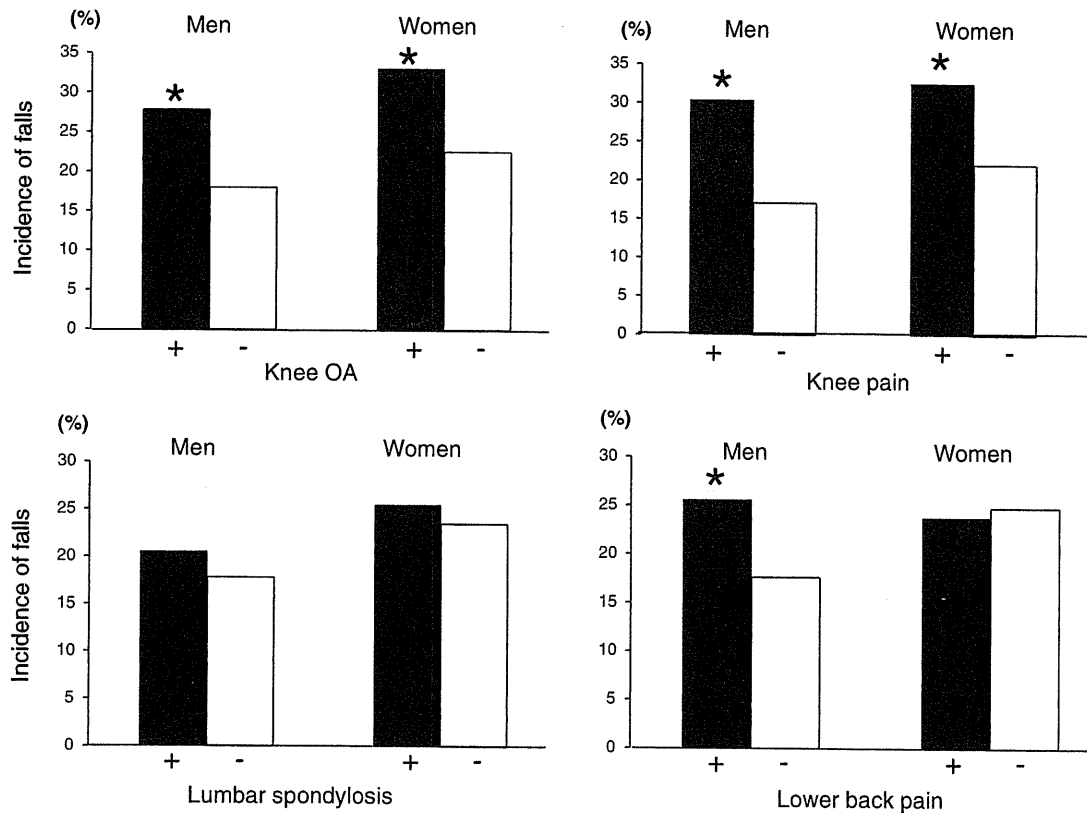


Fig. 2 Incidence of falls by knee OA, knee pain, LS, and lower back pain. * $p < 0.05$ vs. subjects without knee OA, LS, knee pain, and lower back pain, respectively, by chi-square test

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 OR₁ was calculated using multiple logistic regression analysis after adjustment for age and BMI. Adjusted OR₂ was calculated using multiple logistic regression analysis with age, BMI, walking speed, radiographic knee OA, and knee pain as independent variables. Radiographic knee OA and LS were defined as KL grade 3 or 4

OA osteoarthritis

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

Acknowledgments This work was supported by Grants-in-Aid for Scientific Research (S19109007, B20390182, C20591737, and C20591774), for Young Scientists (A18689031), and for Exploratory Research (19659305) from the Japanese Ministry of Education, Culture, Sports, Science and Technology; H17-Men-eki-009, H18-Chouju-037, H20-Chouju-009, H21-Chouju-Wakate-011, and H22-Chouju-Wakate-007 from the Ministry of Health, Labor and Welfare; Research Aid from the Japanese Orthopaedic Association (JOA-Subsidized Science Project Research 2006-1); and Grant No. 166 from the Japan Orthopaedics and Traumatology Foundation. The authors thank Dr. Yamamoto, Dr. Ishibashi, Dr. Anamizu, and members of the Department of Orthopaedics and Mr. Kutsuma and other members of the Department of Radiology at Tokyo Metropolitan Geriatric Medical Center; 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.

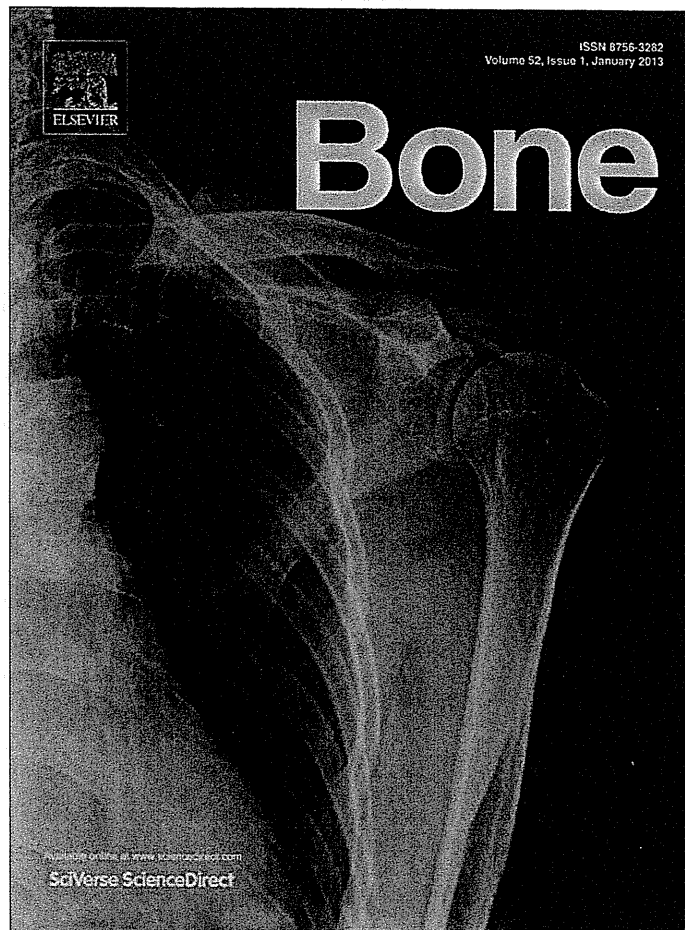
Conflicts of interest None.

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