

Risk Factors for Knee Osteoarthritis in Japanese Women: Heavy Weight, Previous Joint Injuries, and Occupational Activities

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ABSTRACT. *Objective.* Risk of knee osteoarthritis (OA) associated with constitutional factors, history of joint injuries, and occupational factors was assessed in a case-control study among women in Japan. Results were contrasted with a comparable study in Britain.

Methods. The study covered 3 health districts in Japan. Cases were women aged ≥ 45 years old, diagnosed with knee OA by orthopedic physicians utilizing radiography. No cases displayed established causes of secondary OA. Controls selected randomly from the general population were individually matched to each case for age, sex, and residential district. Subjects were interviewed using structured questionnaires to determine medical history, including history of joint injury, physical activity, socioeconomic factors, and occupation. Height and weight were measured.

Results. Interviews were obtained from 101 female cases and controls. The highest third of heaviest body weight in the past [high (> 62.0 kg) vs low (< 55 kg) odds ratio = 4.42, 95% confidence interval 1.17–16.64], previous injury to the knee (OR 7.11, 95% CI 2.40–21.09), sedentary work during initial employment (OR 0.35, 95% CI 0.15–0.84), and total working years (OR 1.05, 95% CI 1.01–1.08) represented independent factors associated with knee OA, after controlling for other potential risk factors.

Conclusion. Heavy weight in the past appears to represent a risk factor for knee OA among women in Japan, as reported in Britain. Constitutional factors may represent important determinants for knee OA, regardless of race. Previous injury to the knee and occupational factors are also associated with knee OA in both Britain and Japan, although characteristic activities for work vary. (J Rheumatol 2004;31:157–62)

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Knee osteoarthritis (OA) is a frequent cause of pain and disability in elderly individuals in Britain, accounting for some 9000 knee arthroplasties annually in England and Wales¹. Furthermore, the recent World Health Organization report on the global burden of disease indicated knee OA as an increasingly important cause of disability in the elderly, suggesting that strategies for preventing knee OA are urgently required².

To determine suitable preventive strategies, detailed knowledge of the risk factors associated with the disorder is essential. Several investigations of risk factors for knee OA have been undertaken^{3–10}. In these reports, important risk factors have included obesity, previous injury, and presence of Heberden's nodes. In addition, the disorder is more common in people who have performed heavy physical work, particularly those whose jobs have involved frequent kneeling or squatting^{3,11–14}. Case-control studies in Britain^{15,16} have also found significant associations between knee OA and obesity, knee injury, and kneeling/squatting, in both sexes.

Knee OA is similarly recognized as a major cause of disability in older individuals in Japan. Some cross-

sectional surveys have suggested that being female, obese, or engaged in agricultural work are factors associated with development of knee OA^{17,18}. However, no case-control studies have assessed risk factors for knee OA in Japan.

Our replication of a British case-control study of hip OA identified some variation in risk factors between Britain and Japan¹⁹⁻²¹. Differences in constitutional and mechanical risk factors for knee OA between Western and Oriental populations would imply potentially important differences in etiology and preventive strategies.

To address this issue, the present case-control study replicated another British study¹⁶, and compared and contrasted the findings with those of the original investigation.

MATERIALS AND METHODS

Methods of data collection in the Japanese study were essentially the same as those of the original case-control study in Britain¹⁶. Cases were identified from the registration systems of the 6 hospitals participating in the study, located in 3 cities in Japan (Wakayama City and Arita City in Wakayama Prefecture, and Sennan City in Osaka Prefecture).

Cases comprised female individuals ≥ 45 years old, who suffered knee pain and walking difficulties, and were first diagnosed by an orthopedic surgeon as displaying a tibiofemoral joint with radiographic grade ≥ 3 on the Kellgren and Lawrence scale²² within the year preceding the start of the study. Cases with a history of knee injury in the previous year, rheumatoid arthritis (RA), or ankylosing spondylitis (AS) were excluded by chart review. A minor difference existed in case criteria for the 2 studies. In the British study, cases were selected from waiting lists of patients awaiting knee surgery, while the Japanese study utilized new patients diagnosed using a radiographic scale. This was unavoidable because no system of waiting lists for surgical treatment is used by general practitioners in Japan.

For each case, we randomly selected a single control from women of the same age and district of residence on city registers of the local population, which are updated as residents move into or leave the city. Controls who had had knee OA were replaced, as were controls who declined to participate in the study. All cases and controls were initially approached using a letter to determine willingness to participate in the study. After providing informed consent, controls were interviewed by the same trained interviewer.

We utilized an identical questionnaire (translated and back-translated from Japanese to English) to that used in the British case-control study for ascertainment of risk factors. Subjects completed a structured questionnaire that requested details of medical history, socioeconomic status and education, cigarette smoking and alcohol consumption, functional status, and lifetime history of leisure activities. Lifetime history of leisure activities included participation in sports such as soccer, swimming, tennis, cricket, and golf, in addition to frequency and duration of less physical activities, such as gardening. Information about 8 types of occupational physical activity was obtained, namely: standing, sitting, climbing stairs, kneeling, squatting, driving, walking, and heavy lifting. Information on these activities was obtained for the initial job, defined as the earliest job reported, and for the principal job, defined as the job at which the subject had worked longest. For each job, the questionnaire enquired whether work entailed lifting weights ≥ 10 kg, ≥ 25 kg, and ≥ 50 kg, more than once during an average working week. Information regarding transport, including frequency and duration of cycling and motorcycling, was obtained. Information regarding the involvement of other joints, including hands, shoulders, and hips, was also obtained. Further, information about back pain and stiffness, which was not included in the British study, was obtained. After heaviest reported weight after age 25 years was obtained, height and weight were measured during the interview.

Data were analyzed initially using chi-squared univariate analysis.

Conditional logistic regression for matched sets was then applied. Results were summarized as odds ratios (OR) with 95% confidence intervals (CI). OR were calculated for categories of exposure, and tests of trend were performed across these categories. Statistical analyses were performed using SPSS statistical software (SPSS Inc., Chicago, IL, USA) and the Stata statistical package (Stata Corp., Collage Station, TX, USA).

RESULTS

We identified 120 female cases ≥ 45 years old who fulfilled the entry criteria for the study. Of the eligible cases, 101 (84.2%) women agreed to participate. Unilateral knee OA was 56 cases, although bilateral disease was common: 45 cases. The right side (28 women) was equally affected compared to the left (28 women).

For controls, we approached age, sex, and residence matched candidates for each case. In order to recruit 101 controls matched for age, sex, and area of residence, we needed to approach 170 subjects (overall response rate 59.4%).

Table 1 shows background characteristics for the 101 pairs of cases and controls at present. Mean body weight of cases was significantly greater than for controls (p < 0.01). Further, body mass index (BMI) of cases was significantly higher than BMI of controls (p < 0.001).

History of joint pain is also shown in Table 1. In total, cases suffered other joint pain more than controls. Joint pain in cases was more frequently reported as back and hip pain (p < 0.05).

The association between knee OA and heaviest reported body weight was analyzed. Mean heaviest reported body weights for cases and controls were 60.6 ± 10.6 kg and 56.5 ± 8.6 kg, respectively, displaying a significant difference (p < 0.01). To address the influence of heaviest reported weight on development of knee OA, cases were categorized into 3 groups according to the distribution of heaviest reported weight: high (> 62.0 kg), middle (55.0–62.0 kg), and low (< 55.0 kg). These categories were defined by dividing the total distribution into equal thirds. Cases in the high group displayed a more than 3-fold greater risk,

Table 1. Baseline characteristics and physical impairments of participants. Data are mean ± SD (%).

	Cases, n = 101	Controls, n = 101
Age, yrs	73.3 ± 9.8	73.3 ± 9.8
Weight, kg	53.8 ± 10.1*	49.7 ± 8.6
Height, cm	148.8 ± 6.3	149.6 ± 6.9
BMI, kg/m ²	24.3 ± 3.9**	22.1 ± 3.0
Current smoking, n (%)	9 (8.9)	5 (5.0)
Current drinking, ≥ 5 times/week, n (%)	10 (9.9)	5 (5.0)
Previous finger pain (%)	9 (8.9)	4 (4.0)
Previous shoulder pain (%)	16 (15.8)	12 (11.9)
Previous back pain (%)	25 (24.8)*	9 (8.9)
Previous hip pain (%)	10 (9.9)*	1 (1.0)

* p < 0.01; ** p < 0.001, cases vs controls.

compared with those in the low group (OR 3.10, 95% CI 1.26–7.58 for high vs low, $p < 0.05$; OR 1.68, 95% CI 0.74–3.84 for middle vs low, $p = 0.22$).

The association between knee OA and history of injury in other joints is shown in Table 2. Previous injury of the knee provided an OR of 5.0, representing a significant difference ($p < 0.001$). For previous injury of the hip, although OR exceeded a 2-fold increase, no significant difference was observed between cases and controls. This indicates a striking association between previous trauma in knee joints and risk of knee OA in women.

Most subjects in the study had held relatively few jobs over the course of their working lifetime (mean number of jobs in cases 2.7, controls 2.2). A total of 73% of cases and 53% of controls reported a principal job different from their initial job. The most frequent areas of employment for all subjects were factory/construction, shop assistant/manager, agriculture/fishery, and clerical/technical workers (Table 3). Distributions of initial occupations differed significantly between cases and controls. The proportion engaged in factory/construction work was significantly higher among cases than controls ($p < 0.01$), while the proportion of clerical workers was significantly higher among controls than cases ($p < 0.01$).

Two cases declined to report occupational physical activities, and 3 cases and 7 controls reported no history of employment. Analysis of the effects of workplace activity was therefore restricted to the 93 cases and matched controls who provided data on physical activity in the workplace.

Table 2. Association of knee OA with previous joint injuries.

Risk Factors	Numbers Exposed (n = 101)		OR (95% CI)
	Cases	Controls	
Previous injury of either hip	7	4	2.00 (0.50–8.00)
Previous injury of either knee	50	14	5.00 (2.44–10.23)*

* $p < 0.001$.

Mean age at commencement of the first job was 15.9 ± 7.6 years for cases and 16.4 ± 7.3 years for controls.

Occupational activities of sitting for > 2 hours each day during the initial job was associated with significantly reduced risk of knee OA ($p < 0.01$). No other activities displayed associations, although greater number of jobs experienced and longer total working period was associated with increased risk of knee OA ($p < 0.001$) (Table 4).

Although no relationship was observed between knee OA and frequency and duration of motorcycling, risk of knee OA was significantly elevated in female subjects who used bicycles regularly for more than 12 months in the course of their occupations (OR 1.9, 95% CI 1.0–3.4, $p < 0.05$).

Table 5 shows correlations between knee OA and the above potential risk factors. Correlations were determined using conditional regression analysis in which the following potential risk factors obtained by univariate analysis were mutually adjusted for: heaviest weight in the past, previous injury of either knee, bicycling, sedentary work, number of previous jobs, and total working period. Bicycling and number of jobs no longer represented significant risk factors. Heaviest weight in the past, previous injury of the knee, sedentary work, and longer total working period represented independent factors associated with knee OA after controlling for other factors.

DISCUSSION

The results of our case-control study performed in Japan indicate that heavy weight in the past, history of knee injury, and total working period increased risk of knee OA in women. In addition, among workplace activities, sedentary work was associated with decreased risk of knee OA.

A number of limitations apply to our study. For a start, it was based on a relatively small number of cases and controls. Cases were defined as those suffering knee pain and walking difficulties, who were first diagnosed by an orthopedic surgeon as displaying a tibiofemoral joint with a

Table 3. Occupations reported as the initial job and the principal job.

	Initial Job		Principal Job	
	Cases (%)	Controls (%)	Cases (%)	Controls (%)
Total	101 (100)	101 (100)	101 (100)	101 (100)
Factory/construction workers	35 (34.7)	17 (16.8)	28 (27.7)	23 (22.8)
Agricultural/fishery workers	21 (20.8)	19 (18.8)	14 (13.9)	16 (15.8)
Housekeepers	12 (11.9)	6 (5.9)	1 (1.0)	1 (1.0)
Clerical workers/technical experts	7 (6.9)	25 (24.8)	5 (5.0)	13 (12.9)
Clinical workers	7 (6.9)	3 (3.0)	5 (5.0)	4 (4.0)
Shop assistants and managers	6 (5.9)	10 (9.9)	27 (26.7)	19 (18.8)
Dressmakers	5 (5.0)	9 (8.9)	4 (4.0)	9 (8.9)
Teachers	2 (2.0)	2 (2.0)	2 (2.0)	6 (5.9)
Hairdressers	1 (1.0)	1 (1.0)	5 (5.0)	1 (1.0)
Other (soldier, taxi driver, etc)	0 (0.0)	2 (2.0)	5 (5.0)	2 (2.0)
No work, no answer	5 (5.0)	7 (6.9)	5 (5.0)	7 (6.9)

Table 4. Association of knee OA with occupational activities at the initial and the principal job.

Risk Factors		Numbers Exposed (n = 93)		OR (95% CI)
		Cases	Controls	
Occupational activities at the initial job	Sitting ≥ 2 h/day	38	58	0.43 (0.23–0.78)**
	Standing ≥ 2 h/day	76	73	1.17 (0.54–2.52)
	Kneeling ≥ 1 h/day	26	27	0.95 (0.52–1.76)
	Squatting ≥ 1 h/day	31	30	1.05 (0.57–1.94)
	Driving ≥ 4 h/day	0	1	—
	Walking ≥ 3 km/day	41	43	0.88 (0.50–1.56)
	Climbing ≥ 30 steps/day	13	15	0.87 (0.41–1.82)
	Lifting weights > 25 kg	19	19	1.00 (0.50–2.00)
Occupational activities at the principal job	Sitting ≥ 2 h/day	48	55	0.77 (0.45–1.32)
	Standing ≥ 2 h/day	81	74	1.64 (0.77–3.46)
	Kneeling ≥ 1 h/day	31	34	0.87 (0.48–1.58)
	Squatting ≥ 1 h/day	38	34	1.20 (0.66–2.17)
	Driving ≥ 4 h/day	1	2	0.50 (0.05–5.51)
	Walking ≥ 3 km/day	47	41	1.29 (0.73–2.27)
	Climbing ≥ 30 steps/day	23	20	1.19 (0.61–2.31)
	Lifting weights > 25 kg	26	16	1.91 (0.92–3.96)
Age at first job, yrs		15.9 (7.6)	16.4 (7.3)	0.99 (0.95–1.03)
Total number of jobs		2.7 (1.5)	2.2 (1.5)	1.24 (1.02–1.50)*
Total working period, yrs		37.4 (18.3)	23.8 (17.8)	1.05 (1.03–1.07)***

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

Table 5. Association of knee OA with the heaviest weight in the past, previous injury of either knee, transportation, and occupational factors.

Risk Factors		OR (95% CI)
Heaviest weight in the past [†]	Medium (vs low)	3.13 (0.94–10.48)
	High (vs low)	4.42 (1.17–16.64)*
Previous injury of either knee	Yes vs no	6.84 (2.35–19.94)***
Transportation	Bicycling almost every day ≥ 12 mo (vs less)	1.77 (0.66–4.78)
Occupational factors	Sitting ≥ 2 h/day at the initial job (vs less)	0.35 (0.15–0.84)*
	No. of jobs (one job)	0.92 (0.67–1.25)
	Total working period (one year)	1.05 (1.01–1.08)**

All risk estimates are mutually adjusted. [†] Lowest 3rd: < 55.0 kg, medium: 55.0–62.0 kg, highest 3rd: > 62.0 kg.

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

radiographic grade ≥ 3 on the Kellgren-Lawrence scale within the year preceding the start of the study. Only 120 female individuals in the 6 participating hospitals fulfilled these criteria during the study period. Clarification is required whether this low frequency represents lower prevalence or lower severity of radiographic knee OA in Japan. Our previous comparative study of OA in the lumbar spine indicated that OA in the general population tended to display a lower prevalence and severity in Japan than in Britain²³. As a second limitation, the response rate for controls (59.4%) in our study was lower than that for study cases (84.2%). Individuals from poorer or disadvantaged backgrounds may have been less willing to participate as controls. Morioka reported that participants in a health check survey performed in a general population displayed better lifestyle factors than nonresponders²⁴. These results

may therefore be subject to some degree of overestimation. However, OR obtained in this survey were little altered by adjusting for the social class (age at last schooling, education level) and lifestyle factors, such as smoking and drinking, suggesting that such factors did not represent a major source of bias. Finally, we did not include domestic work as an occupation. This is because the number of female subjects who reported no history of employment made up only 5 cases and 7 controls. Moreover, a useful index to distinguish the differing strength of domestic work between women with or without a history of employment was unavailable. However, multiple occupational factors were assessed, such as activities, total working period, and total number of jobs. These factors were considered to represent the strength of exposure to occupational factors.

Obesity has previously been shown to display a strong

association with risk of knee OA³⁻⁹. Epidemiological studies in Japan have confirmed an association between obesity and knee OA^{17,18}. In Japan, generalized predisposition is believed to play an important role in the pathogenesis of OA at all sites except the hip²¹. In our study, a history of heavy weight was shown to independently influence risk of knee OA, supporting the results of these previous studies. Obesity has also been identified as a significant risk factor for knee OA in Britain. These findings indicate that the influence of excessive weight on development of knee OA is consistent across ethnic groups.

The involvement of other joints is believed to play a role in increased risk of OA. Studies of knee OA in Western populations have revealed an association between hand involvement and generalized OA^{10,25,26}. In the British study paralleling this one, presence of Heberden's node and previous knee injury were both strongly and independently associated with knee OA. Although we obtained no information on the presence of Heberden's nodes, information about previous knee injury was obtained, and indicated an independent association between previous injury and knee OA. These findings indicate that the influence of previous injury on the development of knee OA is again consistent across ethnic groups. In addition, previous hip injury might increase risk of knee OA, although the relationship was not significant. Our findings might indicate that knee OA can occur as a part of generalized polyarticular OA. However, too few subjects displayed a history of hip injury, so further studies are required to clarify associations between knee OA and involvement of other joints.

Another factor believed to broadly account for the pathogenesis of OA in any joint site is mechanical stress. Mechanical stress has been linked with the development of OA in knee^{3,11,15,27}, finger²⁸, and hip joints^{21,27,29,30}. Although the British study identified repetitive kneeling and squatting as occupational activities representing risk factors for knee OA¹⁶, no workplace activities increased risk of knee OA in the present Japanese study. However, regular use of a bicycle was associated with increased risk of knee OA in women. After adjustment for other risk factors, this association was diluted, suggesting the influence of mechanical stress. Further, total years of work experience displayed a significant association with knee OA in this study, showing the influence of working activity on the development of knee OA.

Although our study did not identify any significant risk factors for knee OA among specific occupational activities, prolonged sitting at work was found to be associated with reduced prevalence of knee OA. This suggests that sitting is inversely associated with knee OA. Regarding the relationship between sedentary work and OA, our previous case-control study for hip OA in Japan found that subjects who had spent more than 2 hours each day sitting during their initial job were significantly protected from hip OA, after

adjusting for other potential risk factors²¹. The results of studies investigating the influence of sedentary work on knee OA are controversial. A case-control study in which cases were confirmed radiographically showed sitting at jobs tended to increase risk of knee OA, but not significantly¹⁵. By contrast, in our parallel case-control study in the UK, sedentary work tended to decrease risk in women, although again, no significant association was observed¹⁶. Although the sitting position clearly involves reduced load on many joints compared to other working activities, no other studies have reported a relationship between sedentary activity and knee OA. Sitting as a physical activity in the workplace might represent a characteristic protective factor for OA in Japan.

Despite controlling for weight in the analysis of occupational activities, we cannot exclude the effect of weight as a factor in mechanical stress on knees. In the British study, subjects in the highest BMI category (> 30) who reported kneeling/squatting activities displayed a 15-fold increase in risk of knee OA compared to subjects in the lowest BMI (< 25) category with no kneeling/squatting activities. Subjects in the lowest BMI category reporting occupational kneeling/squatting displayed only twice the risk of knee OA compared to subjects in the lowest BMI category and no occupational kneeling/squatting. Obesity, therefore, increases the contribution of kneeling/squatting to the development of knee OA. In the Japanese study, subjects in the high BMI category (> 25.8) largely overlapped the lowest third of the BMI distribution in the British study, although BMI in the Japanese study was obtained using measurements taken during the interview, not in the past. However, even if this time lag is taken into consideration, female subjects in the Japanese study were clearly shorter and lighter than those in the British study. The lighter build of Japanese women may protect against the adverse effects of occupational activities.

In summary, our analysis of individual risk factors for symptomatic knee OA in women in Japan confirms that obesity and previous knee injury represent independent risk factors for knee OA in both Oriental and Western populations. Moreover, occupational physical activities clearly influence the development of knee OA in Japan, as in Britain, although differences exist in the specific activities that exert influence.

Further studies of men and of conditions among populations in different regions are required to characterize variant risk profiles of knee OA.

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