A simple protocol for preventing falls and fractures in elderly individuals with musculoskeletal disease

Kiyoshi Kita, MD, PhD[1]; Keiji Hujino, MD, PhD[1]; Teruo Nasu, MD, PhD[1]; Kazuo Kawahara, MD, PhD[2]; Yoshihumi Sunami, MD, PhD[1]

Japanese Clinical Orthopaedic Association, Committee on Musculoskeletal Rehabilitation

1) Japanese Clinical Orthopaedic Association (JCOA), Okachimachi, Tokyo, Japan

2) Tokyo Medical and Dental University, Graduate School of Medical and Dental Science, Tokyo Medical and Dental University, Department of Health Policy Science Yushima, Bunkyo-ku, Tokyo, Japan

Correspondence: Kiyoshi Kita, M.D., Ph D.

Kita Orthopaedic Clinic

Asagiri KM Building 3F 165-5 Ookuradani-azakariguti Akasi City, Hyogo, Japan

Address reprints to: Dr Kita at Kita Orthopaedic Clinic

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Mini-abstract

Our protocol resulted in significant prevention of falls and fractures in addition to marked improvements in balance function. Intervention comprised a new balance exercise and quadriceps femoris exercise. Subjects were outpatients with musculoskeletal disorders who were ≥65-years-old and displayed results of ≤15 s for timed one-leg balance test.

ABSTRACT

Introduction and Hypothesis: A study investigating chronological changes in the level of required care showed that this level increases markedly for older patients requiring mild or severe long-term care. The present study aimed to identify frail elderly patients among older patients with chronic pain of the musculoskeletal system, and to assess the fracture prevention and fall prevention effects of exercise therapy using stratified analysis.

Methods: This prospective cohort study investigated 683 outpatients with chronic pain of the musculoskeletal system who were ≥65-years-old and displayed results of ≤15 s for timed one-leg balance test with eyes open. Intervention comprised a new balance exercise and quadriceps femoris exercise. The main outcome was fall rate, while secondary outcomes were the results of timed one-leg balance test with eyes open and fracture rate.

Results: Fall rate was decreased by 44% ($p<0.001$) and fracture rate was decreased by 47% ($p<0.05$) by 8 months after the start of intervention. Results of timed one-leg balance testing with eyes open improved 2- to 3-fold after intervention ($p<0.01$).

Conclusions: Our protocol has been safely implemented at a large number of clinics in Japan, and the reductions in frequency of falls and fractures suggest effective preventive care.

Keywords: balance; exercise; fall prevention; fracture prevention; musculoskeletal disease; rehabilitation

Figure 1a: Dynamic flamingo therapy

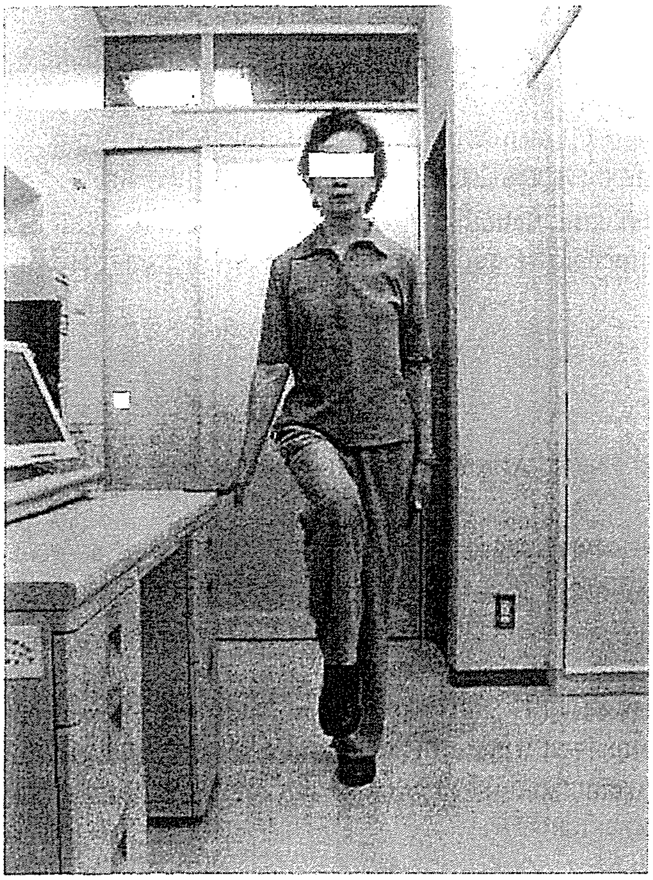


Figure 1b: Quadriceps femoris exercise

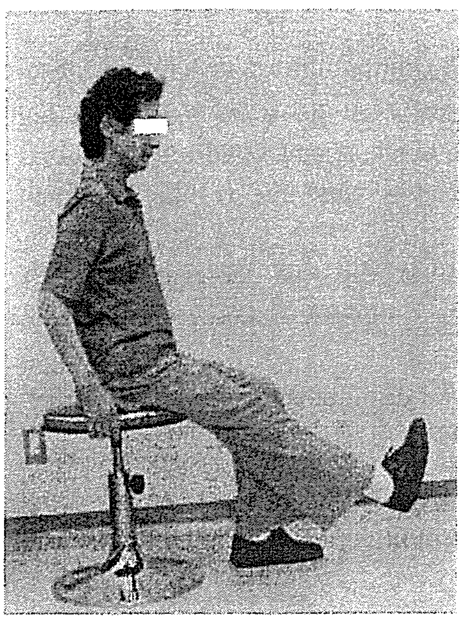
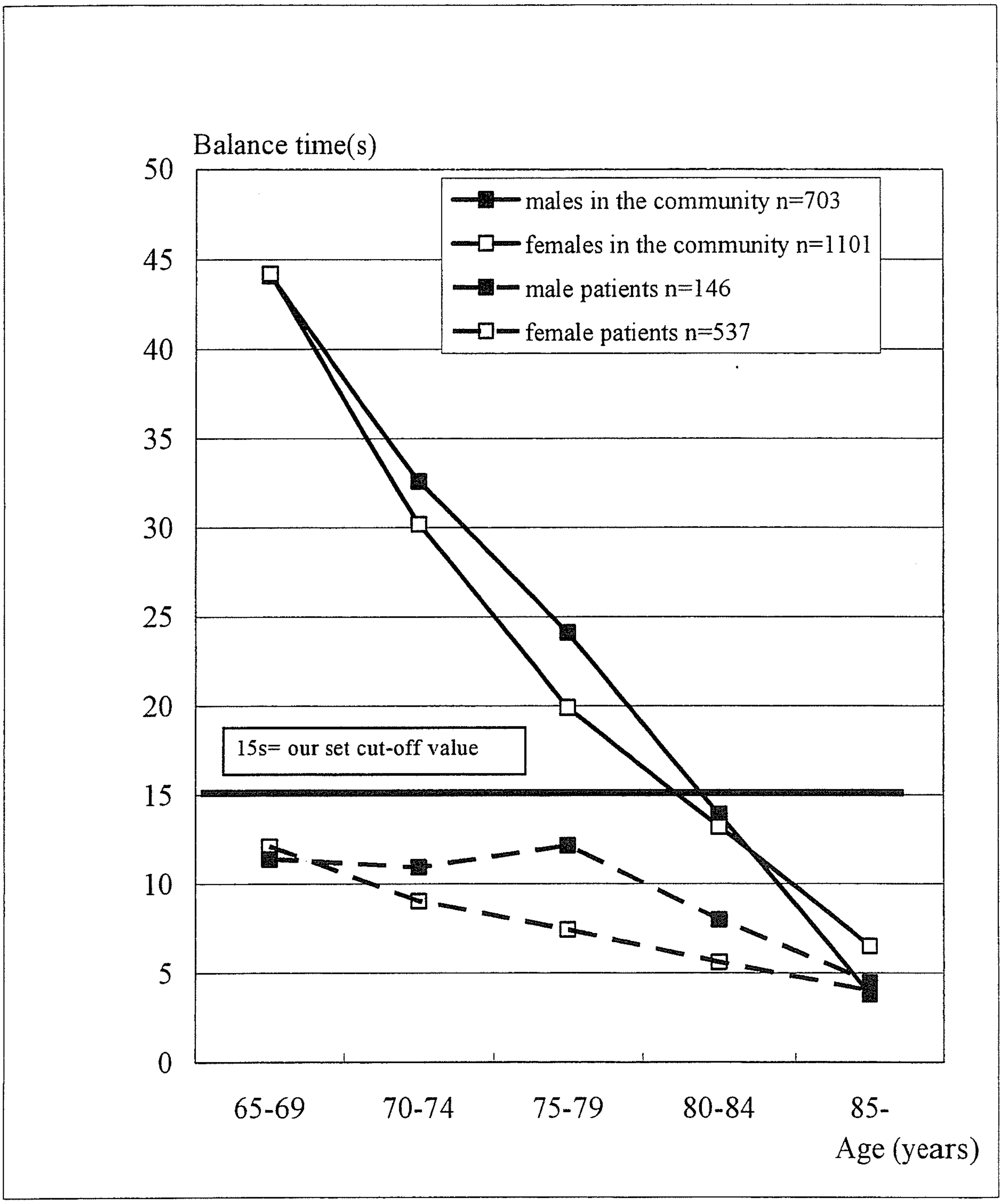


Figure 2: Results of timed one-leg balance test with eyes open for community-dwelling elderly individuals in Japan[11] and our patients.



INTRODUCTION

A long-term care insurance system was implemented in Japan in 2000. At the same time, long-term care prevention measures were specified, and community-based rehabilitation programs have subsequently been developed to improve physical strength in the elderly. A study investigating chronological changes in the level of required care has shown that the level of required care increases markedly for older patients requiring mild or severe long-term care [1]. In other words, community-based rehabilitation programs have proven ineffective in preventing older patients from requiring long-term care. Furthermore, the number of patients requiring mild long-term care has increased rapidly, and as the benefit expense for patients requiring severe care increases, costs for long-term nursing care also increase [1]. In addition, many patients requiring mild long-term care are diagnosed with disuse syndrome due to bone and joint diseases. Older patients thus need to seek medical help from orthopedists specializing in musculoskeletal diseases, to prevent the need for long-term care. One reason for this rapid increase in the number of patients requiring mild long-term care is reduced physical strength of the elderly, and falls markedly compromise activities of daily living in frail older patients and cause the need for long-term care.

Numerous randomized studies have analyzed fall-related risks and assessed fall prevention. However, past analyses of fall-related risks have mainly identified high-risk factors, and nearly all previous randomized studies have involved small numbers of patients. To the best of our knowledge, no studies have investigated the results of exercise therapy with proven efficacy using stratified analysis. The objectives of this prospective cohort study were to conduct a stratified analysis of the fall prevention effects of exercise therapy by increasing the number of cases, and to determine the fracture prevention effects of exercise therapy.

We have been developing cost-effective programs to prevent long-term nursing care as part of the "Bone and Joint Decade" campaign of the World Health Organization [2]. The Japanese Clinical Orthopedic Association prepared a safe, compact and cost-effective protocol that can be prescribed at clinics, and then conducted a study with two objectives: 1) early detection of frail older patients based on balance test findings; and 2) stratified analysis of the preventative effects of balance and muscle-strengthening exercises with proven efficacy against falls and fractures.

Given this background, we hypothesized that the combination of balance exercises and quadriceps femoris exercises that are effective for knee osteoarthritis may give rise to a fall prevention effect in frail patients with musculoskeletal disease.

MATERIALS AND METHODS

Design

The present prospective cohort study was approved by the administrative board of the Japanese Clinical Orthopedic Association. Study methods were mailed and e-mailed to recruit member orthopedists. For the first 2 months after the start of intervention, changes in timed one-leg balance test with eyes open were assessed, then participants were asked to participate in an investigation on fall prevention. Participants continued to perform the exercises, and fall prevention was monitored for 8 months after the start of intervention. Furthermore, fall prevention was assessed 12 months after the start of intervention. The survey period started in April 2003 and ended in March 2005.

Participants and setting

Subjects met the following criteria: 1) patients ≥65-years-old being treated at clinics; 2) patients with persistent chronic pain in a musculoskeletal organ (extremities or spine); and 3) patients with results of ≤15 s for the timed one-leg balance test with eyes open for either leg.

Patients excluded were: 1) those unable to walk due to complications; 2) those unable to perform one-leg standing balance exercise due to complications; 3) those for whom exercise was not recommended due to acute inflammation; 4) asymptomatic patients with osteoporosis or other conditions (i.e. patients with osteoporosis, etc, who are asymptomatic), and 5) those with infectious or neoplastic disease.

Fall prevention was assessed by excluding individuals who fell ≥5 times over the previous year or during the study period (chronic fallers) [3]. The following baseline values were ascertained: age; gender; numbers of falls and fractures over the previous year; and timed one-leg balance test with eyes open. Values were directly gathered or measured by orthopedists.

Intervention

The intervention program was explained by orthopedists, and participants were instructed to perform daily balance and quadriceps femoris exercises (Fig. 2). Subsequent clinical examinations were conducted by orthopedists once or twice a month. Balance exercise adopted a new exercise method called dynamic flamingo therapy [4]. In dynamic flamingo therapy, the patient stands on 1 leg for 1 min 3 times/day. Participants in the present study were all frail older patients, and so were instructed to firmly hold on to a desk or something stable during exercise. When holding up the right leg with the right hand, a greater mechanical load is applied to the left femoral head, thus facilitating increased bone mass in the femoral neck. In the quadriceps femoris exercise, participants were instructed to sit in a chair, and then to extend the knee fully, bend the hip until the heels were about 10 cm above the floor, and hold this position for 2-3 s. A single set consisted of 20 repetitions, and 2 sets/day were performed. The effectiveness of both exercises has been confirmed in randomized studies conducted in collaboration with the Japanese Orthopedic Association [5,6].

Outcome assessment

The main outcome was fall rate, while secondary outcomes were results for the timed one-leg balance test with eyes open and fracture rate. These parameters were assessed before the start of intervention and 8 and 12 months after the start of intervention. The timed one-leg balance test with eyes open was measured by instructing participants to put their hands on their hips and raise one leg, then measuring the amount of time until the raised leg touched the floor using a stopwatch measuring to the nearest tenth of a second. Subjects practiced the task once on each leg prior to measurement, then performed the task twice on each leg and the best of the two trials was recorded.

Training frequency, which was confirmed by an interview with the doctor, was classified into 4 levels as follows: Level 1 (exercise on an almost daily basis); Level 2 (exercise 3-4 days/week); Level 3 (exercise 1-2 days/week); and Level 4 (other).

Adverse events that occurred after the start of intervention were reported to collaborators via mail and e-mail. Missing data were gathered to the fullest extent possible by contacting orthopedists via mail, fax or telephone.

Statistical analysis

Statistical analysis was performed using SAS 9.1.3 software (SAS Institute, Cary, NC, USA), and all usable data were analyzed. At the start of intervention, a □^{2} test and Kruskal-Wallis test were used for intergroup comparisons. Fall rate was calculated by dividing total number of falls during the intervention period by total length of follow-up. Fall proportion was calculated by dividing total number of patients who fell during the intervention period by total participant population. Fracture rate and fracture proportion were calculated in the same manner. We compared fall rate, fracture rate and the timed one-leg balance test with eyes open before and after intervention using the Wilcoxon signed rank test. Chronic fallers who fell ≥5 times during the study period or over the previous year were excluded from all analyses of fall and fracture prevention [3]. Table 4 lists chronic fallers. Subgroup analysis was executed to compare fall and fracture status in different age group, numbers of fall over previous year and frequency of exercise. Among participants who were followed for 1 year, missing data for falls and fractures at 8 months after the start of intervention were handled by assuming the worst-case scenario. Values of $p<0.05$ were considered statistically significant.

RESULTS

A total of 68 institutions collaborated in this study. At the start of intervention, subjects included 146 men with a mean age of 77.0±5.9 years (range: 65.5-88.9 years) and 537 women with a mean age of 77.5±6.3 years (range: 65.0-98.0 years). Over the 1-year period before the start of intervention, fall proportion was 36.5% (exact binomial 95% confidence interval: 32.86-40.28%) and fracture proportion was 9.3% (6.1-12.1%). Over the 1-year period before the start of intervention, fall and fracture rates were 0.84 and 0.10, respectively. Since the mean number of falls was 0.84±2.13, based on the 95% critical interval, chronic fallers were defined as those patients who fell ≥5 times over the 1-year period before the start of intervention or during the study period.

At 8 months after the start of intervention, 565 of the 683 patients (83%) at the 68 participating institutions could be followed. Reasons that were reported for the 51 withdrawal cases included: "improved symptoms" (n=3); "stopped making scheduled visits" (n=21); "leg or lumbar pain" (n=6); "changed program" (n=6); "other complications" (n=8; including 1 death); and "reduced motivation" (n=10). Reasons for transient discontinuation or reduced frequency of exercises were: "leg and lumbar pain" (n=6); "complications" (n=8); and "reduced motivation" (n=4). At 12 months after the start of intervention, 377 of the 466 patients (81%) at 52 participating institutions could be followed.

First, while excluding chronic fallers, at 8 months after the start of intervention (main assessment period for fall and fracture prevention for the entire participant population), fall rate decreased by 44% from 0.597 to 0.334 ($p<0.01$, Wilcoxon signed rank test), and fracture rate decreased by 47% from 0.096 to 0.051 ($p<0.05$, Wilcoxon signed rank test).

Table 1 shows baseline values for each age group. While no significant intergroup differences were noted in gender or past history of fractures among different age groups, significant differences were seen in past history of falls, with higher age associated with increased number of falls.

Table 2 shows chronological changes in falls, fractures and timed one-leg balance test with eyes open for each age group. Exercises markedly decreased fall rate. For 70- to 84-year-old patients, intervention was significantly effective at 8 and 12 months after start of intervention. While a similar tendency was seen for fracture rate, only one stratum at 8 months was significantly different, due to the low incidence of fractures. Table 3 shows the numbers of falls and fractures in relation to the number of falls occurring over the 1-year period before the start of intervention. While no significant differences were seen in gender or left leg balance, significant differences in age or right leg balance were identified between groups. Fall rate decreased at 8 and 12 months after the start of intervention, and an investigation of fall rate by Kruskal-Wallis testing during follow-up showed that a greater number of falls over the previous year was significantly associated with a greater fall rate ($p<0.001$). Fall rate for chronic fallers did not decrease significantly (Wilcoxon signed rank test).

Prevalence of chronic fallers was 19 cases out of a total of 671 cases (2.8%) at the start of the study period, and 12 cases out of a total of 554 cases (2.2%) during follow-up. A total of 5 new cases (0.9%) of chronic fallers were identified. Among the 14 chronic fallers at the start of the study period for whom follow-up was possible, 5 patients remained chronic fallers during the follow-up period.

Table 4 shows fall and fracture prevention in relation to frequency of exercise. This data represents cases for which 1 year of follow-up was possible. Baseline values were comparable for all groups. Fall rate for participants who exercised (Levels 1-3) was significantly decreased by 48-59%. For participants who did not exercise (Level 4), fall and fracture rates did not decrease significantly. As the number of fractures decreased in all exercise groups (Level 1-3), these results may indicate a fracture prevention effect of the applied exercises.

Mean result for the timed one-leg balance test with eyes open was 6.3±7.8 s for the right leg and 5.8±5.4 s for the left leg. At 8 months after the start of intervention, results were significantly improved to 14.7±18.2 s and 15.0±20.6 s, respectively ($p<0.001$). This tendency was seen 12 months after the start of intervention. Among the 346 patients who could be followed at 12 months after the start of intervention, impaired one-leg standing balance at baseline as defined by Tinetti [7] normalized for both legs in 61% of cases.

DISCUSSION

In 1953, Hirshberg prescribed exercises to disabled persons and then proposed disuse syndrome [8]. In recent years, the number of frail older patients with disuse syndrome has been rapidly increasing. For orthopedists, this poses an important clinical challenge. Since the majority of patients with disuse syndrome display osteoarthrosis of the knee, interventions should be designed with this disease firmly in mind. Gardner et al. [9] reported that because orthopedists often treat patients with femoral neck fractures, primary care by orthopedists plays an important role. They prescribed instructive intervention for osteoporosis to inpatients with femoral neck fractures and proved the effectiveness of this approach in a randomized study. In this manner, in the field of orthopedics that treats numerous high-risk patients, properly identifying frail older patients and prescribing proper exercise programs is crucial.

The present study identified frail older patients based on balance test findings from among patients ≥65-years-old with chronic pain who saw orthopedists. As an indicator of balance function, we measured the timed one-leg balance test with eyes open, a parameter that is thought to be useful for measurements of relatively healthy individuals [10] and for early detection of declining physical strength in older individuals, as scores decrease rapidly with age. According to a study by Shimada et al. [11], the ratio of people who lead independent lives markedly decreases after 75-years-old and drops below 50% after 85-years-old. They reported that dysfunction markedly worsens around 75- to 80-years-old. Chronological changes in timed one-leg balance test with eyes open among elderly individuals living in the community have also been assessed in the United States [12], China [13] and Japan (Saitama Prefecture, Fig. 2) [14,15], and while measurement methods have varied, this parameter dropped below 15 s from around 75- to 85-years-old. Hence, in the present study, frail older patients were defined as those with a result of ≤15 s on the timed one-leg balance test with eyes open. Results for the timed one-leg balance test with eyes open for frail older patients ranged from 5.8 to 6.3 s, comparable to the upper limit of the one-leg balance test of 5 s as reported by Tinetti [7]. With regard to age group-stratified results for the timed one-leg balance test with eyes open, our cases uniformly showed markedly decreased balance function in comparison to community-dwelling elderly individuals capable of independent gait as reported by Sakata et al. (Fig. 2)[14]. In the present study, over the 1-year period before the start of intervention, fall proportion was 36.5%. Yasumura [16] reported that the fall proportion among the elderly living in the community was 18%. The figure obtained in the present study was about 18% higher. In other words, participants in the present study were more frail. From the perspective of early prevention of falls and fractures, setting the upper limit for the timed one-leg balance test with eyes open at 15 s is appropriate. As in the study by Vellas et al. [17], we identified frail older patients based solely on balance test findings. The present program was designed so that patients and doctors could easily understand assessments and exercises. Balance function is also easily measured in clinics, and the program can be safely prescribed for long periods of time [17,18].

The characteristics of the elderly individuals reported in the meta-analysis on fall prevention by Province et al. [3] were similar to those of patients in the present study, in terms of the proportion of women, which was 42-81% depending on the region in the meta-analysis, and mean age, which was 73-80 years among community-dwelling elderly individuals in the United States. In general, the majority of visitors to orthopedics clinics in Japan are women, but this may be attributable to the fact that the average life expectancy of women in Japan is 7 years longer than that of men, and prevalence is thus higher among women. A survey on underlying disease in our subjects (n=553) revealed osteoarthritis (knee, 61%; hip, 3%) in 64% of patients, spondylosis deformans (including spinal canal stenosis, radiculopathy and myelopathy) in 62% of patients, osteoporosis in 31% of patients and compression fractures in 9% of patients. Considering that subclinical osteoporosis also occurs frequently, most subjects appear likely to suffer from multiple musculoskeletal diseases.

In 1995, the Frailty and Injuries: Cooperative Studies of Intervention Technique (FICSIT) study found that the fall prevention effect of exercise intervention including balance exercise was particularly high [3]. Analysis of fall-related risks has shown that balance is an important factor. The fall prevention guidelines published by Moreland et al. in 2003 [19] state, "Balance exercises are recommended for all individuals who have had a fall and there is evidence for a program of home physiotherapy for women over 80 years of age regardless of risk factor status". In a 2004 review published by Gillespie et al. [20], a program consisting of muscle strengthening and balance retraining, individually prescribed at home by a trained health professional, was found to be effective, while group-delivered exercise and individual lower limb strengthening training were ineffective. In fact, Lathman et al. [21] prescribed only quadriceps femoris exercise to elderly individuals living at home and reported that such exercise exerted no beneficial effect on fall prevention. Means [22] prescribed balance and mobility exercises with higher intensity than a 1996 program and proved the efficacy of this in fall prevention.

Our intervention program comprised dynamic flamingo therapy and quadriceps femoris exercise. Prior to the present study, in collaboration with the Japanese Orthopedic Association, we conducted randomized studies to ascertain the preventative effects of dynamic flamingo therapy on falls [6] and the effects of quadriceps femoris exercise on osteoarthrosis of the knee [5] at elderly care facilities. Dynamic flamingo therapy decreased falls by 34% [6] (personal communication, July 6, 2006), while quadriceps femoris exercise improved function and alleviated pain to a degree comparable to non-steroidal anti-inflammatory drugs [5]. Our intervention program should thus alleviate pain and prevent falls in patients with disuse syndrome and chronic pain. In addition, the amount of dynamic load applied to the femoral neck by dynamic flamingo therapy is equivalent to approximately 54 min of walking [3], and since this therapy is easily accepted by patients with gait disorders, many patients can continue to perform the exercise.

The results of stratified analysis showed that although intervention prevented falls for patients with a past history of falls, fall rate during the follow-up period was high, and falls could not be prevented for chronic fallers and patients who did not exercise frequently. This indicates the limits to our intervention program, and designing new exercise programs and establishing comprehensive fall risk management for patients with a past history of fall will be important in future. To further improve compliance, patients need to understand the correlation between osteoporosis and falls. Fracture prevention was one of the secondary outcomes, and given that the intervention program lowered the frequency of fractures, these results can be considered the first to suggest a possible fracture prevention effect of exercise. However, number of fractures was not reported at the start of intervention for 165 patients (24%), and a study focusing solely on fracture prevention is thus necessary.

Few previous studies investigating the effects of exercise on the timed one-leg balance test with eyes open have documented improvements in this test [23,24,25,26,27]. Li et al [27] conducted a tai chi intervention, 12 months after which test results had improved from 6.8 s to 13.0 s for the right leg and from 7.0 to 12.5 s for the left leg, indicating a significant difference from the control group. In our study on exercise intervention, significant improvements were noted, and the results of timed one-leg balance test with eyes open for frail older patients improved to the level of healthy older individuals. Since the present study was not a randomized study, learning effects with exercise must be taken into account, but the degree of improvement was comparable to or better than that in the exercise group in the study by Li [27]. As our intervention program prevented falls, dynamic flamingo therapy appears to improve balance function to the same extent as tai chi.

In and outside of Japan, few studies.have examined withdrawal and adverse events related to exercise therapy. Latham et al. [21] conducted a randomized study on resistance exercise and clarified the frequency of musculoskeletal disorders at 8%. They found that reporting of adverse events had been poor in studies of elderly exercise therapy. In our study, 7 patients discontinued exercise due to pain. Pain management thus represents a key issue. Pain management by specialists is essential, and if exercise intensity is adjusted under the guidance of specialists, an intervention program consisting of dynamic flamingo therapy and quadriceps femoris exercise can be continued relatively safely for long periods of time.

Regarding points of caution, some patients may discontinue exercise due to physical ailments caused by exercises, fall if a supporting chair slips, or stand on one leg while having both hands on the hips during exercise .While the present study did not include such cases, safety must be ensured by preventing falls and physical ailments while exercising.

Finally, the most cost-effective and safe method of spreading this protocol may be implementation at clinics. This is because exercise must be performed with utmost caution with regard to fractures (which may occur simply from gait unsteadiness in patients with severe osteoporosis), and the individualized guidance indicated by Gillespie et al [20] is effective for the continuation of exercise under appropriate guidance, even in cases where pain may exacerbate during training. Large-scale implementation at clinics of this protocol may reduce the number of fractures by approximately 45%. The estimated number of patients with hip fractures in 2000 was 92,000. Mean medical expenses were $11,500 per patient, which amounts to $1.06 billion a year, in addition to the costs associated with fracture-related care, which is estimated to be $4.73 billion a year [28]. The total population of Japan was 120 million in 2005, and with the aging of society, the number of cases of hip fractures is estimated to have increased to 120,000 [29]. With the number of frail older individuals who are capable of walking at an estimated 2.5-3 million, fall and fracture prevention will become particularly effective in primary care clinics. Effective April 2006, frail elderly with musculoskeletal instability who take part in fall prevention are eligible for benefits under the Musculoskeletal Rehabilitation section of the National Health Insurance system. The accepted rehabilitation period is 150 days following diagnosis, with an estimated consultation frequency of 2-3 times weekly. For reference, the two most representative examples of medical costs for training 2-3 times weekly for 3 months (total, 30 times) are listed below:

1) Implementation of 20 min exercises in clinics administered by certified nurses using the present protocol under the direction of certified doctors: benefits of a total of about 380 dollars over 3 months. 2) Implementation of 20 min comprehensive rehabilitation consultations based on the present protocol administered by physical or occupational therapists under a comprehensive plan jointly developed by a certified doctor and a co-medical: benefits of a total of about 650 dollars over 3 months. Unfortunately, guidance for "home exercise" by doctors is currently included in general consultation fees in Japan, and is not covered by any special medical fees.

In conclusion, among chronic pain patients being treated by orthopedists, frail older patients with a result of ≤15 s on the timed one-leg balance test with eyes open were identified, and the effects of exercise therapy were ascertained by stratified analysis. Dynamic flamingo therapy and quadriceps femoris exercise were prescribed with pain management to these frail older patients, and the results confirmed improvement in balance function (p<0.01). At 8 months after the start of intervention, fall rate decreased by 44% (p<0.001) and fracture rate decreased by 47% (p<0.05). These findings suggest that exercise intervention can prevent frail older patients who are being treated at a large number of clinics from requiring long-term care.

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Table 1: Characteristics at baseline by age

Age (years)	65-69	70-74	75-79	80-84	85-
n	75	186	201	132	89
Sex (%)*					
male	20 (26.7)	36 (19.4)	41 (20.4)	33 (25.0)	16 (18.0)
female	55 (73.3)	150 (80.6)	160 (79.6)	99 (75.0)	73 (82.0)
History of falls (%)†					
history of falls	16 (21.9)	64 (35.0)	71 (36.2)	60 (45.8)	34 (38.6)
no history of falls	57 (78.1)	119 (65.0)	125 (63.8)	71 (54.2)	54 (61.4)
History of fractures (%)‡					
history of fractures	5 (10.0)	9 (6.9)	17 (10.2)	5 (5.0)	12 (17.4)
no history of fractures	45 (90.0)	122 (93.1)	150 (89.8)	96 (95.0)	57 (82.6)

* A χ^2 test for gender and age showed no significant difference between groups (p=0.484)

† All respondents. A χ^2 test showed a significant difference between groups (p=0.018).

‡ All respondents. A χ^2 test showed no significant difference between groups (p=0.677).

Table 2: Differences in fall and fracture prevention by age

Age (years)	65-69	70-74	75-79	80-84	85-
Falls					
in previous year	0.33	0.57	0.5	0.82	0.59
(n)	(73)	(173)	(188)	(128)	(85)
after 8 months	0.28	0.30*	0.27*	0.36*	0.50
(n, p value†)	(58, 0.216)	(136,	(166, 0.001)	(100, <0.001)	(75, 0.599)
after 1 year	0.24	0.33*	0.30*	0.47*	0.22
(n, p value†)	(42, 0.437)	(90, 0.003)	(118, 0.008)	(62, <0.001)	(46, 0.063)
Fractures					
in previous year	0.10	0.08	0.11	0.06	0.19
(n)	(50)	(131)	(167)	(101)	(69)
after 8 months	0.00	0.03	0.045*	0.06	0.10
(n, p value†)	(55, 0.125)	(132, 0.449)	(168, 0.023)	(98, 0.469)	(78, 0.169)
after 1year	0.02	0.06	0.03	0.05	0.09
(n, p value†)	(42, 0.250)	(96, 1.000)	(118, 0.109)	(62, 1.000)	(46, 0.148)

* p<0.05

† Wilcoxon signed rank test was used to compare fall rate and fracture rate among patients before and after intervention.

Table 3. Fall and fracture prevention in relation to past history of falls

History of falls	0 falls	1 fall	2-4 falls	≥5 chronic faller
Male:female†	92:333	23:100	12:87	8:16
Age (years)‡	77.0±6.4	77.9±6.1	78.6±5.7	77.5±25.3
Right-leg balance§	6.5±7.1	5.7±5.0	5.9±6.1	3.5±3.3
Left-leg balance‖	6.1±5.7	5.5±4.8	5.8±5.1	3.3±2.8
Fall rate				
in previous year	0	1	2.52	7.96
(n)	(425)	(123)	(90)	(24)
after 8 months	0.20*	0.38*	0.81*	6.16
(n, p value¶)	(340, <0.001)	(102, <0.001)	(83, <0.001)	(19, 0.268)
after 1 year	0.23*	0.36*	0.62*	13.31
(n, p value¶)	(215, <0.001)	(74, <0.001)	(60, <0.001)	(8, 0.398)
Fracture rate				
in previous year	0.03	0.20	0.23	0.35
(n)	(324)	(91)	(79)	(17)
after 8 months	0.04	0.06*	0.07	0.09
(n, p value¶)	(322, 0.272)	(100, 0.004)	(82, 0.234)	(17, 0.461)
after 1 year	0.03	0.10	0.07	0.14
(n, p value¶)	(214, 0.750)	(73, 0.405)	(61, 0.132)	(7, 0.317)

† A χ^2 test for gender and number of falls showed no significant difference between groups (p=0.671)

‡ Kruskal-Wallis test for age and past history of falls showed a significant difference between groups (p=0.046).

§ Kruskal-Wallis test for right-leg balance and number of falls showed a significant difference between groups (p=0.039)

‖ Kruskal-Wallis test for left-leg balance and the number of falls showed no significant difference between groups (p=0.064).

¶ A Wilcoxon signed rank test was used to compare fall rate and fracture rate before and after intervention among patients with data available for both before and after intervention.

Table 4: Prevention of falls and fractures by exercise frequency				
Exercise frequency	Level 1	Level 2	Level 3	Level 4
Baseline characteristics				
Male:female	15:58	16:81	14:62	16:46
Age	76.6±5.5	78.1±5.2	76.3±5.9	77.3±6.6
Right leg balance, s (mean ±SD)	6.8±7.2	5.9±5.2	5.3±4.2	8.1±10.4
Left leg balance, s (mean ±SD)	6.3±6.1	5.0±4.2	6.4±5.4	6.7±5.0
Rate of falls				
in previous year	0.64	0.79	0.65	0.58
(n)	(73)	(97)	(76)	(62)
after 8 months	0.27*	0.34*	0.30*	0.48
(n, p value¶)	(74, 0.003)	(97, <0.001)	(76, 0.004)	(62, 0.473)
after 1 year	0.33*	0.34*	0.26*	0.45
(n, p value¶)	(73, 0.009)	(97,<0.001)	(76, 0.006)	(62, 0.409)
Rate of fractures				
in previous year	0.13	0.10	0.09	0.07
(n)	(63)	(89)	(66)	(58)
after 8 months	0.02	0.05	0.02	0.03
(n, p value¶)	(63, 0.107)	(89, 0.125)	(66, 0.206)	(58, 0.285)
after 1 year	0.03	0.03	0.03	0.10
(n, p value¶)	(63, 0.083)	(89, 0.058)	(66, 0.157)	(58, 0.480)

This data represents cases for which 1 year of follow-up was possible.

† A χ^2 test for gender and number of falls showed no significant difference between groups (p=0.533)

‡ Kruskal-Wallis test for age and exercise-dosage showed no significant difference between groups (p=0.154).

§ Kruskal-Wallis test for right-leg balance and exercise-dosage showed no significant difference between groups (p=0.371)

|| Kruskal-Wallis test for left-leg balance and the number of falls showed no significant difference between groups (p=0.146).

¶ A Wilcoxon signed rank test was used to compare number of falls per person per year and number of fractures per person per year before and after intervention among patients with data available for both before and after intervention.* p<0.05.

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ORIGINAL ARTICLE

**Noriko Yoshimura · Hirofumi Kinoshita · Noriaki Hori
Taira Nishioka · Masahiko Ryujin · Yoshihiko Mantani
Mariko Miyake · Tatsuya Takeshita · Masao Ichinose
Munehito Yoshiida · Hiroyuki Oka · Hiroshi Kawaguchi
Kozo Nakamura · Cyrus Cooper**

Risk factors for knee osteoarthritis in Japanese men: a case-control study

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Abstract Risk of knee osteoarthritis (OA) was assessed in a population-based case-control study of Japanese men. The study covered three health districts in Wakayama and Osaka prefectures, Japan. Subjects were male individuals ≥45 years old diagnosed radiographically with knee OA, and who did not display any established causes of secondary OA. Controls selected randomly from the general population were individually matched to cases for age, sex, and residential district. Subjects were interviewed using structured questionnaires to determine medical history, physical activity, socio-economic factors, and occupation. Interviews were obtained from 37 cases and 37 controls. In univariate analysis, heaviest weight in the past and physical work such as factory, construction, agricultural, or fishery work as the principal occupation significantly raised the risk of male knee OA ($P < 0.05$). Odds ratios (OR) were determined using conditional logistic regression analysis mutually adjusted for potential risk factors using the results of univariate analysis. Heaviest weight in the past (OR 6.01, 95% confidence interval (CI) 1.18–30.5, $P < 0.05$), past knee injury (OR 6.25, 95% CI 1.13–34.5, $P < 0.05$), and physical work as the principal occupation (OR 6.20, 95% CI 1.40–27.5, $P < 0.05$) represented independent factors associated with knee OA after controlling for other risk factors. Physical work is associated with knee OA, demonstrating the influence of working activity on the development of OA. The present study suggests that risk factors for knee OA in men resemble those in women.

Key words Case control study · Heavy weight · Knee joint · Osteoarthritis (OA)· Physical work

N. Yoshimura (✉) · H. Oka
Department of Joint Disease Research, Graduate School of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8655, Japan
Tel. +81-3-5800-9178; Fax +81-3-5800-9179
e-mail: yoshimuran-ort@h.u-tokyo.ac.jp

H. Kinoshita
Department of Orthopaedic Surgery, Wakayama Medical University Kihoku Hospital, Wakayama, Japan

N. Hori
Hori Hospital, Sennan, Japan

T. Nishioka
Nishioka Orthopaedic Hospital, Arita, Japan

M. Ryujin
Ryujin Clinic, Wakayama, Japan

Y. Mantani
Tamai Orthopaedic Hospital, Hannan, Japan

M. Miyake
Yamomoto Clinic, Shimotsu, Japan

T. Takeshita
Department of Public Health, Wakayama Medical University School of Medicine, Wakayama, Japan

M. Ichinose
Second Department of Internal Medicine, Wakayama Medical University School of Medicine, Wakayama, Japan

M. Yoshiida
Department of Orthopaedic Surgery, Wakayama Medical University School of Medicine, Wakayama, Japan

H. Kawaguchi · K. Nakamura
Department of Orthopaedic Surgery, Faculty of Medicine, The University of Tokyo, Tokyo, Japan

C. Cooper
MRC Epidemiology Resource Centre, University of Southampton, Southampton General Hospital, Southampton, UK

Introduction

Since osteoarthritis (OA) is a frequent cause of pain and disability in elderly individuals, the recent World Health Organization report on the global burden of disease indicated knee OA as an increasingly important cause of disability in both men and women, suggesting that strategies for preventing OA are urgently required.[1] In Japan, knee OA seems to represent a frequent cause of pain and disability, but few epidemiological studies have examined associated factors.

Several investigations regarding risk factors for hip and knee OA performed in Western populations have suggested obesity, previous injury, polyarticular joint involvement, and occupational activities as important risk factors for the disorder.[2-8] However, few studies of risk factors for OA in Japanese populations have been performed. Our earlier case-control study of hip OA identified some variations in risk factors in Japan.[9] In the previous case-control study of hip OA, occupational lifting was identified as a risk factor and sedentary work as a protective factor for hip OA. In addition, obesity was not identified as a risk factor for Japanese hip OA. For contrast, an identical case-control study was performed for knee OA in women in a Japanese population.[10] In the female study, risk factors of obesity, previous knee injury, and period of total work were identified, and sedentary work as the initial occupation represented a preventive factor.[10] The results from these two investigations suggest various similarities and differences in risk factors between hip and knee OA in Japanese populations.

The present study sought to clarify risk factors for knee OA among men in Japan, by performing a survey identical to that used in the previous female knee OA study. Results for men were compared to those from the female study.[10] Risk factors were then compared between knee OA and hip OA to address differences in risk factors for constitutional and mechanical factors between OA at different sites. Finally, risk factors for knee and hip OA were compared to those identified in a British study[11,12] that used identical methods to the Japanese studies, to clarify differences in risk factors for OA between Japanese and Western populations.

Patients and methods

Methods of data collection in the present study were basically identical to those of the case-control studies for female knee OA and hip OA reported previously.[9,10] A brief summary is provided here. Cases were identified from the registration systems of the six hospitals participating in the study, which were located in three cities in Japan (Wakayama City and Arita City in Wakayama Prefecture, and Sennan City in Osaka Prefecture).

Cases comprised men ≥45 years old who suffered knee pain and walking difficulties, and who were first diagnosed by an orthopedic surgeon as displaying a tibiofemoral joint with radiographic grade of ≥3 on the Kellgren and Lawrence scale[13] within the year preceding the start of the study. Cases with a history of knee injury in the previous year, rheumatoid arthritis, or ankylosing spondylitis were excluded.

For each case, a single control was randomly selected from among men 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 suffered knee OA were excluded from the study.

All eligible cases and controls were initially approached using a letter to determine willingness to participate in the study. After providing informed consent, cases and controls were interviewed by the same trained interviewer.

An identical questionnaire to that used in the British case-control study was used to ascertain risk factors of knee OA.[11,12] The questionnaire was translated and back-translated from Japanese to English. Subjects completed a structured questionnaire that requested details of medical history, socio-economic 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 eight types of occupational physical activity was requested, 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, or ≥50 kg) more than once during an average working week. Information regarding use of transport, including frequency and duration of cycling and motorcycling was obtained. Information was also requested on the involvement of other joints, including hands, shoulders, and hips. Furthermore, questions were added about back pain and stiffness, which were not included in the British study. Once heaviest reported weight after 25 years old was obtained, height and weight of each subject was measured at the time of the interview.

After analysis to clarify risk for male knee OA, results were compared between men and published results for women.[10] Risk factors for knee OA and hip OA were also compared to address differences in constitutional and mechanical risk factors between OA at different sites. Finally, risk factors for knee and hip OA were compared to the findings of the British study, which used identical methods to the Japanese studies.

Data were calculated using McNemar's Chi-square test and conditional logistic regression tests for matched sets. Results were summarized as odds ratios (OR) with 95% confidence intervals (CI). Odds ratios were calculated for categories of exposure, and tests of trend were performed across these categories. Statistical analyses were performed using SPSS statistical software (SPSS, Chicago, IL, USA) and the STATA statistical package (STATA, College Station, TX, USA).

Results

A total of 40 men ≥45 years old fulfilled the entry criteria for the study. Among these eligible cases, 37 men (92.5%) agreed to participate after information was provided. Unilateral knee OA ($n = 21$) was more common than bilateral disease ($n = 16$). Among the 21 men with unilateral disease, OA tended to be right-sided ($n = 13$) more often than left-sided ($n = 8$), but no significant difference was identified.

For controls, we approached age-, sex-, and residence-matched candidates for each case. To recruit the 37 matched controls, we approached 70 subjects (overall response rate 52.9%).

Table 1 shows background characteristics for the 37 case-control pairs in the present study. Mean body weight was significantly greater for cases than for controls ($P < 0.05$). Furthermore, body mass index was significantly higher for cases than for controls ($P < 0.05$). No differences in personal habits such as smoking or drinking were noted between cases and controls.

The association between knee OA and heaviest reported body weight was analyzed. Under univariate analysis, mean heaviest reported body weight for cases was 72.1 kg (standard deviation (SD) = 13.0 kg), significantly higher than that for controls ($P < 0.01$) in men. Odds ratios for heaviest reported body weight were 1.07 (95% CI 1.02–1.13), suggesting that a 1-kg increase in heaviest reported body weight raised the risk of knee OA by 7%.

To more clearly address the influence of heaviest reported weight on development of knee OA, cases were categorized into the following three groups according to the distribution of heaviest reported weight: high, ≥72.0 kg; middle, 61.0–72.0 kg; and low, <61.0 kg. These categories were defined by dividing total distributions into equal thirds. Cases in the high group displayed a >4-fold elevation in risk compared with cases in the low group (OR 4.22, 95% CI 1.13–15.8 for high vs low, $P < 0.05$; OR 1.60, 95% CI 0.50–5.08 for middle vs low, $P = 0.43$) (Fig. 1).

The association between knee OA and history of injury in other joints was calculated. Under univariate analysis, although ORs exceeded a 2-fold increase, no significant difference was observed between cases and controls (OR 2.50, 95% CI 0.78–7.97 for yes vs no, $P = 0.12$).

The association between knee OA and methods of transportation was examined by comparing the frequency of regular bicycle use between cases and controls. Under univariate analysis, while OR was higher for men (OR 2.67, 95% CI 0.71–10.05), no significant differences were noted between cases and controls.

Associations between knee OA and occupational history were analyzed. The most frequent areas of employment for all subjects were factory/construction, agriculture/fishery, clerical/technical, and shop assistant/manager (Table 2). Distributions of initial and principal occupations differed

Table 1. Anthropometric and background characteristics of cases and controls for knee OA in men

	Men	
	Cases	Controls
No. of participants	37	37
Age (years)	70.0 ± 6.6	70.1 ± 7.0
Weight (kg)	64.1 ± 10.7*	59.3 ± 8.7
Height (cm)	162.5 ± 6.9	163.0 ± 6.7
Body mass index (kg/m^2)	24.2 ± 3.4*	22.4 ± 3.8
Heaviest weight in the past (kg)	72.1 ± 13.0**	64.0 ± 9.2
Age at the heaviest weight (years)	57.4 ± 15.1*	51.7 ± 17.8
Current smoking (%)	16 (43.2)	15 (40.5)
Current drinking (≥5 times/week, %)	20 (54.1)	22 (59.5)

Mean ± SD; percentage in parentheses
* $P < 0.05$, ** $P < 0.01$ cases vs controls

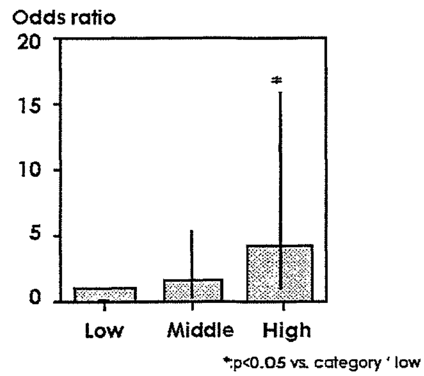

Fig. 1. Association of knee osteoarthritis with heaviest weight in the past. *Low*, lowest 3rd of the heaviest weight category, <61.0 kg; *Middle*, middle 3rd, ≥61.0 kg, <72.0 kg; *High*, highest 3rd, ≥72.0 kg. *Bar* represents 95% confidence interval

Table 2. Occupations reported as initial and principal jobs in men

	Initial occupation				Principal occupation			
	Cases	%	Controls	%	Cases	%	Controls	%
Total	37	100	37	100	37	100	37	100
Factory/construction workers	18	48.6	14	37.8	22	59.5	16	43.2
Agricultural/fishery workers	10	27.0	6	16.2	7	18.9	4	10.8
Clerical workers/technical experts	4	10.8	6	16.2	2	5.4	9	24.3
Shop assistants and managers	2	5.4	9	24.3	2	5.4	6	16.2
Clinical workers	2	5.4	0	0.0	1	2.7	0	0.0
Housekeepers	0	0.0	0	0.0	0	0.0	0	0.0
Hairdressers	0	0.0	0	0.0	0	0.0	0	0.0
Dressmakers	0	0.0	0	0.0	0	0.0	0	0.0
Teachers	0	0.0	0	0.0	2	5.4	0	0.0
Others (soldier, taxi driver, etc.)	1	2.7	2	5.4	1	2.7	2	5.4
No work, no answer	0	0.0	0	0.0	0	0.0	0	0.0

Table 3. Crude and adjusted odds ratios with risk factors for knee osteoarthritis in men

Men	Risk factors	Crude odds ratio (95% CI)	Adjusted odds ratio (95% CI)
Heaviest reported weight[a]	Middle vs Low	1.60 (0.50–5.08)	1.25 (0.29–5.35)
	High vs Low	4.22 (1.13–15.8)*	6.01 (1.18–30.5)*
Past injury of either knee	Yes vs No	2.50 (0.78–7.97)	6.25 (1.13–34.5)*
Occupational factors	Physical work[b] as principal occupation (vs Others)	2.80 (1.01–7.77)*	6.20 (1.40–27.5)*

Adjusted odds ratio refers to values after mutual adjustment for other potential risk estimates
95% CI, 95% confidence interval
[a]Lowest 3rd, <61.0 kg; middle 3rd, ≥61.0 kg, <72.0 kg; highest 3rd, ≥72.0 kg in men
[b]Physical work meaning factory, construction, agriculture or fishery work
*$P < 0.05$

Table 4. Crude and adjusted odds ratios with risk factors for knee osteoarthritis in women (cited from ref. 10)

Women	Risk factors	Crude odds ratio (95% CI)	Adjusted odds ratio (95% CI)
Heaviest reported weight[a]	Middle (vs Low)	1.68 (0.79–3.84)	3.33 (0.95–11.7)
	High (vs Low)	3.10 (1.26–7.98)*	3.92 (1.03–14.8)*
Past injury of either knee	Yes vs No	5.00 (2.44–10.2)*	7.51 (2.40–23.5)**
Transportation	Cycling almost every day for ≥12 months (vs Less)	1.88 (1.02–3.94)*	1.67 (0.61–4.57)
Occupational factors	Physical work[b] as initial occupation (vs Others)	2.54 (1.34–4.82)**	2.08 (0.88–5.61)
	Sitting ≥2 h/day at initial job (vs Less)	0.43 (0.23–0.78)**	0.44 (0.47–1.10)
	No. of jobs (1 job)	1.24 (1.02–1.50)*	0.91 (0.66–1.25)
	Total working period (1 year)	1.05 (1.03–1.07)***	1.05 (1.01–1.08)**

Adjusted odds ratio refers to values after mutual adjustment for other potential risk estimates
95% CI, 95% confidence interval
[a]Lowest 3rd, <55.0 kg; middle 3rd, ≥55.0 kg, <62.0 kg; highest 3rd, ≥62.0 kg in women
[b]Physical work meaning factory, construction, agriculture or fishery work
*$P < 0.05$; **$P < 0.01$; ***$P < 0.001$

significantly between cases and controls. Physical work (factory/construction or agriculture/fishery) at the principal job was significantly more common among cases than controls (OR 2.80, 95% CI 1.01–7.77 for yes vs no). Mean age at commencement of the first job was 16.3 years (SD 3.8 years) compared to 16.6 years (SD 4.1 years) for controls, indicating no significant difference between cases and controls. Occupational activities including standing, climbing stairs, kneeling, squatting, driving, walking, sitting, and heavy lifting were not associated with increased risk of knee OA in men.

Table 3 shows ORs determined using conditional logistic regression analysis mutually adjusted for potential risk factors. Various risk factors were entered into the conditional logistic model, comprising: heaviest reported weight; previous knee injury; and physical work at the principal occupation in men. Heaviest reported weight in the past (OR 6.01, 95% CI 1.18–30.5, $P < 0.05$), past injury of the knee (OR 6.25, 95% CI 1.13–34.5, $P < 0.05$), and physical work at the principal occupation (OR 6.20, 95% CI 1.40–27.5, $P < 0.05$) represented independent factors associated with knee OA after controlling for other risk factors (Table 3).

Discussion

The results of the present case-control study indicate that heavy weight in the past and previous knee injury are associated with knee OA in men. Also in men, the proportion engaged in physical work (factory, construction, agriculture, or fishery work) was significantly higher among cases than controls. These risk factors for male knee OA are similar to those seen for female OA knees. Although we have already reported the results elsewhere,[10] we briefly compared results for men and women. Table 4 shows ORs in women determined using conditional logistic regression analysis mutually adjusted for potential risk factors. Various risk factors were entered into the conditional logistic model, comprising: heaviest reported weight in the past; previous knee injury; regular bicycle use; physical work in initial occupation; sedentary work in initial occupation; number of jobs; and total working period, summarizing all years of all jobs that subjects worked. Heaviest reported weight in the past, past injury of the knee, and total working period in women represented independent factors associated with knee OA after controlling for other risk factors. The results of the present case-control study indicate that heavy weight in the past and previous knee injury are associated with knee OA in both men and women.

Several limitations apply to the present study. Firstly, this investigation was based on a relatively small number of male cases and controls. Before the start of the research, we had calculated the sample size. We accumulated 155 pairs of cases and controls based on assumed values of a 0.05 level of significance, 80% statistical power, 2.0 risk ratio, and the 30% prevalence of cases. As a result, we succeeded in identifying 160 cases (40 men, 120 women) >45 years old

Table 5. Comparison of risk factors for hip and knee osteoarthritis (OA) in Britain and Japan (combined results for men and women)

	Risk factors	Britain	Japan
Hip OA	Obesity	Yes	No
	Past joint disturbance	Yes	No
	Occupational factors	Yes (lifting)	Yes (lifting)
Knee OA	Obesity	Yes	Yes
	Past joint disturbance	Yes	Yes
	Occupational factors	Yes (kneeling/squatting)	Yes (physical work, working period)

who fulfilled the entry criteria for the study. Of the eligible cases, 138 (86.3%; 37 men, 101 women) agreed to participate. However, the lack of gender balance for cases resulted in a small number of male subjects, which might reduce statistical power, and thus might not have detected other risk factors among lifestyle variables. This could be due to the use of identical case definitions for subject selection as the case-control hip OA and British studies. 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 radiographic grade of ≥3 on the Kellgren and Lawrence scale. Our previous comparative study of OA in the lumbar spine indicated that OA in the general population tends to display lower prevalence and severity in Japan than in Britain.[14] In addition, the small number of male cases reflects gender differences in prevalence of knee OA in Japan. As a second limitation in the present study, the response rate for controls (52.8%) was lower than that for cases (92.0%). The present results may therefore be subject to some degree of overestimation.

Obesity has previously been shown to display strong associations with risk of knee OA,[2–8] and epidemiological studies performed in Japan have confirmed associations between obesity and knee OA.[15,16] In the present study, a history of heavy weight was shown to exert significant influences on risk of knee OA among men, resembling the results of women,[10] and consistent with previous studies. These findings indicate that the influence of heavy weight on knee OA is consistent across gender in both Japanese and Western populations.

The involvement of other joints is believed to play a role in increased risk of OA. In the British study paralleling the present study, presence of Heberden's node and previous knee injury were both strongly and independently associated with knee OA.[11,12] Although the present study did not seek information regarding the presence of Heberden's node, information was obtained about past history of the involvement of other joints and areas, as diagnosed by a medical doctor, indicating an independent association between previous knee injury and knee OA. In particular, site of knee OA was basically in accordance with the injured site among cases with previous knee injured (right side 91.7%, left side 100%). These findings were again consistent among men and women across Japanese and Western populations.

Mechanical stress represents another factor in the pathogenesis of OA at any joint site. In the present study, although occupational activities of standing, climbing stairs, kneeling, squatting, driving, walking, and heavy lifting were not associated with increased risk of knee OA in men, physical work at the principal occupation raised the risk of knee OA. Physical work represented by factory, construction, agricultural, or fishery work for long periods involved mechanical stress on the knee joints. The previous report utilized conditional logistic regression analysis without physical work, and identified sedentary work as a preventive factor in women.[10] These occupational activities influencing the risk of knee OA suggest that excess stress at the joint raises the risk, while reduced load on the joint decreases risk.

The present case-control study of knee OA paralleled our previous study of hip OA,[9] and was identical in format to some British studies.[17,18] Table 5 summarizes the results of studies using the same methods, indicating differences in risk factors between hip OA and knee OA, and between populations in Britain and Japan. Occupational factors clearly influence the development of both of hip and knee OA in Japan, as in Britain, although differences exist in specific activities exerting influence. Moreover, previous joint injury represented a risk factor for knee OA in Japan, as in the British studies. Conversely, obesity did not represent an independent risk factor for hip OA in Japan, but was a risk factor for both hip and knee OA in the British studies. This may be because local mechanical factors such as acetabular dysplasia might exert stronger influences on hip OA in Japan than other general mechanical factors such as adiposity. However, these results suggest that the pathogenesis of knee OA is similar in Japan and Western countries. Further studies of OA in other sites are required to characterize the risk profile in Japan.

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