TABLE 4. Age, Body Mass Index, Myelopathic Signs, and Physical Performance Measures With and Without Cervical Cord Compression in Men and Women

	No Compression (<Grade 2)	Compression (≥Grade 2)
Men		
N	229	95
Age (yr)	65.5 ± 14.2	71.4 ± 12.1*
Body mass index (kg/m²)	23.8 ± 3.6	23.5 ± 3.0
Myelopathic signs and physical performance measures		
Hyper-reflexia of patellar tendon reflex, N (%)	7 (3.1)	2 (2.1)
Hoffmann reflex positive, N (%)	1 (0.4)	1 (1.1)
Babinski reflex positive, N (%)	2 (0.9)	1 (1.1)
Grip and release test, number of times	25.7 ± 6.0	22.9 ± 5.0*
Grip strength (kg)	39.1 ± 9.1	35.4 ± 8.7†
6-m walking time at a usual pace (s)	5.4 ± 1.5	5.7 ± 1.5
Step length at a usual pace (cm)	59.8 ± 8.9	55.8 ± 9.3*
6-m walking time at a maximal pace (s)	3.5 ± 1.0	3.9 ± 1.2†
Step length at a maximal pace (cm)	71.9 ± 10.1	67.6 ± 11.6†
Chair-stand time (s)	8.5 ± 3.3	9.3 ± 3.5
One-leg standing time (s)	39.0 ± 23.2	28.5 ± 24.6*
Women		
N	510	143
Age (yr)	64.3 ± 13.4	71.9 ± 11.5*
Body mass index (kg/m²)	22.9 ± 3.7	23.6 ± 3.5‡
Myelopathic signs and physical performance measures		
Hyper-reflexia of patellar tendon reflex, N (%)	42 (8.2)	18 (12.6)
Hoffmann reflex positive, N (%)	10 (2.0)	5 (3.5)
Babinski reflex positive, N (%)	8 (1.6)	7 (4.9)‡
Grip and release test, number of times	22.8 ± 5.3	21.3 ± 5.4†
Grip strength (kg)	24.5 ± 5.7	21.9 ± 5.8*
6-m walking time at a usual pace (s)	5.5 ± 2.3	6.7 ± 2.7*
Step length at a usual pace (cm)	55.7 ± 8.8	50.8 ± 13.2*
6-m walking time at a maximal pace (s)	3.8 ± 1.4	4.8 ± 1.9*
Step length at a maximal pace (cm)	62.5 ± 10.7	56.0 ± 11.7*
Chair-stand time (s)	8.4 ± 3.5	11.0 ± 5.8*

Values are mean ± SD except where otherwise indicated.

*Significantly different from values of the group of no compression (*P < 0.001, †P < 0.01, ‡P < 0.05).*

For continuous outcomes, comparison was by the Student t test. For categorical outcomes, comparison was by the χ^2 test.

In addition, multiple logistic regression analysis was performed to estimate the association of physical performance with CCC after adjustment for age, sex, and BMI (Table 5). As an overall result, GRT, step length at a usual and a maximal pace, 6-m walking time at a maximal pace, and CST were found to be significantly associated with CCC. The same logistic regression analysis was performed in participants older than 50 years, and the results remained the same.

TABLE 5. Association Between Cervical Cord Compression (≥Grade 2) and Physical Performance Measures

	OR	95% CI	*P*
*Overall**			
Grip and release test, N (+1SD)	0.26	0.08–0.79	0.02
Grip strength, kg (+1 SD)	0.22	0.03–1.37	0.11
6-m walking time at a usual pace, s (+1 SD)	4.88	0.81–31.1	0.09
Step length at a usual pace, cm (+1 SD)	0.04	0.03–0.45	0.01
6-m walking time at a maximal pace, s (+1 SD)	14.1	2.51–85.0	0.003
Step length at a maximal pace, cm (+1 SD)	0.13	0.03–0.46	0.002
Chair-stand time, s (+1 SD)	11.1	2.00–64.5	0.006
One-leg standing time, s (+1 SD)	0.87	0.51–1.50	0.62

**OR was calculated by multiple logistic regression analysis after adjustment for age, sex, and body mass index in the overall study population.*

OR indicates odds ratio; CI, confidence interval.

DISCUSSION

This study is the first population-based study to use MRI to clarify the prevalence of CCC and its association with myelopathic signs and physical performance measures in Japanese men and women. The prevalence of CCC was higher with increasing age in both sexes. There was no significant association between CCC and myelopathic signs. Regarding physical performance measures, GRT, step length at a usual and a maximal pace, 6-m walking time at a maximal pace, and CST were significantly associated with CCC.

Regarding the prevalence of CCC, Matsumoto *et al*[8] reported that CCC caused by disc protrusion beyond the vertebral body was found in 7.6% of all intervertebral discs using MRI in asymptomatic subjects. This study was the first to clarify the prevalence of CCC, age, and sex differences using MRI in a population-based cohort study.

Previous studies have shown that the prevalence of cervical spondylotic myelopathy was higher in men than in women.[2,26] However, as has been described earlier, and to the best of our knowledge, there have been no previous population-based studies regarding sex differences with CCC. Irvine *et al*[27] reported that the prevalence of cervical spondylosis was higher in men than in women, but the study was not population-based and diagnosis was made with x-ray films. This study is the first to clarify that the prevalence of CCC is more frequent in men than in women.

This study also used multiple logistic regression to examine the association of CCC with myelopathic signs and found that there was no significant association between CCC and hyper-reflexia of patellar tendon, Hoffman reflex, and the Babinski reflex. It is well recognized that, among the elderly, exaggerated reflexes are uncommon, whether they be caused by peripheral neuropathy or other causes. Therefore, diagnosis of early-stage CM using myelopathic signs is often difficult, especially among the elderly. In addition, the prevalence of severe CCC (> grade 3) was only 5.9% in men and 2.6% in women, and most of the participants with CCC had slight to moderate spinal compression. These findings may affect the results of this study, which found no significant association between CCC and myelopathic signs. With regard to physical performance measures, many were significantly associated with CCC in this study. The GRT, 6-m walking time at a maximal pace, and CST, all of which required agility, were significantly associated with CCC. This indicates that a decrease in agility may be observed early in the course of CM, and these kinds of physical performance measures may be useful indices for diagnosis of early-stage CM.

Limitations of the Study

There are several limitations in this study. First, although this study included more than 1000 participants, these participants may not represent the general population because they were recruited from only 2 areas of Japan. However, anthropometric measurements were compared between the participants of this study and the general Japanese population,[28] and no significant differences in BMI were found between participants in this study and the Japanese population at large in both sexes (BMI [SD] in men: 23.71 [3.41] and 23.95 [2.64], $P = 0.33$, respectively, and in women: 23.06 [3.42] and 23.50 [3.69], $P = 0.07$, respectively). In addition, the proportion of current smokers and current drinkers (those who regularly smoked or drank more than 1 drink per mo) in the general Japanese population was compared with the study population. Proportions of current smokers and drinkers in men and that of current drinkers in women were significantly higher in the general Japanese population than in the study population, and there was no significant difference in current smokers in women (male smokers, 32.6% in the Japanese population and 25.2% in study participants, $P = 0.015$; female smokers, 4.9% in the Japanese population and 4.1% in study participants, $P = 0.50$; male drinkers, 73.9% in the Japanese population and 56.8% in study participants, $P < 0.0001$; female drinkers, 28.1% in the Japanese population and 18.8% in study participants, $P < 0.0001$). These results suggest that it is likely that in this study, participants had healthier lifestyles than the general Japanese population. Second, the prevalence only applies to a portion of the Japanese population and cannot be extrapolated beyond that. Third, ossification of the posterior longitudinal ligament (OPLL) and spondylotic changes were included in CCC. There were a total of 21 participants with OPLL, which was examined by x-ray in the same population. Associations of physical performance between spondylotic changes and OPLL may be different; however, only 14 (1.4% in total) OPLL participants had CCC and therefore would not strongly affect the results of this study.

CONCLUSION

This cross-sectional population-based study revealed a high prevalence of CCC in the elderly. The prevalence of CCC was more frequent in men than in women. The highest prevalence of intervertebral lesions was at the C5–C6 level. The GRT, 6-m walking time at a maximal pace, and CST may be useful tools for diagnosis of the early stages of CM.

➢ Key Points

- ❑ This is the first study to reveal the prevalence of CCC, using a population-based study.
- ❑ The prevalence of CCC was 24.4% in this cohort.
- ❑ CCC was associated with physical performance both from an early stage of the disease and before signs of myelopathy.

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Prevalence of symptomatic lumbar spinal stenosis and its association with physical performance in a population-based cohort in Japan: the Wakayama Spine Study

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SUMMARY

Objective: The purpose of this study was to investigate the prevalence of symptomatic lumbar spinal stenosis (LSS) and to clarify the association between symptomatic LSS and physical performance using magnetic resonance imaging (MRI) in a population-based cohort.
Design: This cross-sectional study was performed as a part of the Research on Osteoarthritis/osteoporosis Against Disability (ROAD) in Japan and 1,009 subjects (335 men, 674 women, mean age 66.3 years, age range 21–97 years) were analyzed. An experienced orthopedic surgeon obtained the medical history and performed the physical testing for all participants. Symptomatic LSS diagnostic criteria required the presence of both symptoms and radiographic LSS findings. A 6-m walking time, chair standing time, and one-leg standing time were obtained from all participants.
Results: The prevalence of symptomatic LSS was 9.3% (95% confidence interval [CI]: 7.7–11.3) overall, 10.1% (CI: 7.4–13.8) in men and 8.9% (CI: 7.0–11.3) in women. There was a difference in the prevalence with increasing age by gender. The LSS prevalence showed little difference with age greater than 70 years for men, but the LSS prevalence for women was higher with increasing age. Among physical performance measures, 6-m walking time at a maximal pace was significantly associated with symptomatic LSS ($P = 0.03$).
Conclusion: The prevalence of symptomatic LSS was approximately 10% in a cohort resembling the general Japanese population. A 6-m walking time at a maximal pace was a more sensitive index than walking at a usual pace in assessing decreased physical performance associated with symptomatic LSS.

Introduction

Symptomatic lumbar spinal stenosis (LSS) is usually associated with impaired walking and other disabilities in the elderly. Symptomatic LSS has been shown to be the most frequent indication for spinal surgery in patients more than 65 years old[1,2]. However, little is known about the prevalence of symptomatic LSS in the general population. This is because the subjects in previous symptomatic LSS studies were limited to patients who visited the hospital[3,4]. Hence, people with minor symptomatic LSS who did not visit the hospital were not included in those studies. Furthermore, an examination that can capture minute changes of the intervertebral discs and ligaments using a tool like magnetic resonance imaging (MRI) is essential for the diagnosis of symptomatic LSS. This is because the definition of stenosis includes a morphological element. Many previous studies have reported the utility of MRI[5,6], but, to our knowledge, there have been no population-based cohort studies of symptomatic LSS using MRI.

It is well-known that the principal symptoms for LSS are sciatica and intermittent claudication (IC)[1,2]. Although most patients with MRI evidence of radiographic LSS are asymptomatic[7,8], when symptoms are present, severe symptoms are probably associated with poor physical performance. There have been few reports concerning physical performance of patients with symptomatic LSS[9,10]. According to a previous report concerning walking ability of

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subjects with three different degenerative musculoskeletal disorders (knee osteoarthritis, hip osteoarthritis, and symptomatic LSS) who were scheduled for either joint replacement or spinal decompression surgery, walking ability was limited in all three groups compared to healthy controls[9]. However, patients with symptomatic LSS showed the greatest restrictions in walking ability. In another report regarding subjects with symptomatic LSS in an orthopedic clinical practice, subjects in the healthy group showed greater functional mobility than those in the symptomatic LSS group[10]. The subjects included in the previous studies had enough symptoms to have visited the hospital, however, the association of physical performance measures with symptomatic LSS in subjects with minor symptoms who do not visit the hospital has not been well characterized. Although there may be a latent diminished physical functioning in symptomatic LSS with even minor radiographic changes and symptoms, there have been no population-based studies on symptomatic LSS that have included people with minor signs and symptoms of LSS.

Symptomatic LSS in this study was diagnosed by the presence of both clinical symptoms and radiographic LSS findings consistent with the clinical presentation. The aim of the present study was to clarify the prevalence of symptomatic LSS by gender and age strata using a population-based cohort. In addition, the association of symptomatic LSS with physical performance measures (walking speed, chair standing time, and one-leg standing time) was evaluated.

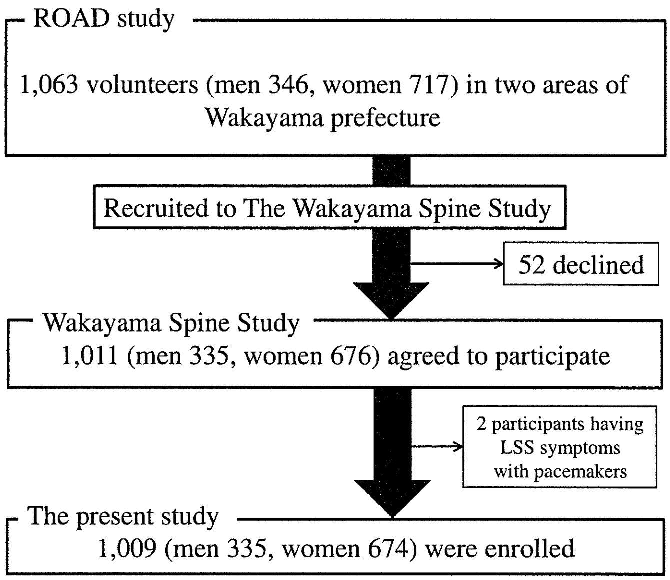

Fig. 1. Flow diagram depicting participants recruited to the Wakayama Spine Study from the ROAD study.

Methods

Participants

The present study, entitled "the Wakayama Spine Study: population-based cohort", was a population-based study for degenerative spinal disease and performed in a subcohort of the large-scale population-based cohort study called Research on Osteoarthritis/osteoporosis Against Disability (ROAD). ROAD is a nationwide, prospective study of bone and joint diseases consisting of population-based cohorts established in several communities in Japan. As a detailed profile of the ROAD study has already been described elsewhere, only a brief summary is provided here[11–14]. To date, creation of a baseline database including clinical and genetic information for 3,040 inhabitants (1,061 men, 1,979 women) in the age range of 23–95 years (mean, 70.6 years) has been completed. Participants were recruited from listings of resident registrations in three communities: an urban region in Itabashi, Tokyo; a mountainous region in Hidakagawa, Wakayama; and a coastal region in Taiji, Wakayama. All participants provided written informed consent, and the study was conducted with the approval of ethical committees of the University of Tokyo and the Tokyo Metropolitan Institute of Gerontology. Participants completed an interviewer-administered questionnaire of 400 items that included lifestyle information, underwent anthropometric measurements, and physical performance measures were recorded. A second visit of the ROAD study to the mountainous region of Hidakagawa and the seacoast region of Taiji was performed between 2008 and 2010. From inhabitants participating in the second visit of the ROAD study, 1,063 volunteers were recruited to undergo MRI examinations. Fifty-two of the 1,063 volunteers declined the MRI examination, therefore, 1,011 were registered in the present study. All participants provided another written informed consent for the MRI examination. Among those 1,011 participants, two participants with LSS symptoms for whom MRI was contraindicated (due to presence of a pacemaker) were excluded, because a final diagnosis of symptomatic LSS could not be made (Fig. 1). Thus, 1,009 participants (335 men and 674 women, mean age 66.3 years, age range of 21–97 years) were analyzed in the present study. Similar to the baseline study, participants in the second visit of the ROAD study completed an interviewer-administered questionnaire of 400 items that included lifestyle information such as smoking habits, alcohol consumption, family history, past history, physical activity, reproductive variables, and health-related quality of life (QOL). Anthropometric measurements included height, weight, bilateral grip strength, and body mass index (BMI) (weight [kg]/height^2 [m^2]). The ankle-brachial index (ABI) was measured using PWV/ABI (OMRON Co., Kyoto, Japan) for all participants. A timed 6-m walk at the participant's usual pace in a hallway was recorded to measure physical performance. Similarly, 6-m walking time at a maximal pace was measured[15–18]. The time taken for five consecutive chair rises without the use of hands was also recorded[18–20]. One-leg standing time with each leg was measured using a stopwatch (upper limit, 60 s) and the time adopted was the mean value of both legs[21,22].

MRI

A mobile MRI (Excelart 1.5 T, Toshiba, Tokyo, Japan) unit was used in the present study, and total spinal MRI was performed for all participants on the same day as the examination. MRI exclusion criteria included presence of a cardiac pacemaker, claustrophobia, or other contraindications. The participants were positioned in supine during the MRI, and those with rounded backs used triangular pillows under their head and knees. The imaging protocol included sagittal T2-weighted fast spin echo (FSE) (repetition time (TR): 4,000 ms/echo, echo time (TE): 120 ms, field of view (FOV): 300 × 320 mm), and axial T2-weighted FSE (TR: 4,000 ms/echo, TE: 120 ms, FOV: 180 × 180 mm). Sagittal images were taken for the entire spine, but axial images were done at each lumbar intervertebral level (L1/2–L5/S1) parallel to the vertebral endplates.

Symptomatic LSS diagnosis

An experienced orthopedic surgeon (YI) consistently took the medical history and performed the physical testing for all the participants in this study. The history included information on the presence of low back, buttock and leg pain, the area of pain or other discomfort, the presence of IC and its distance, and a modified Zurich Claudication Questionnaire[23] (excepting six items about satisfaction and a history of lumbar surgery for symptomatic LSS). Physical examinations included symptoms induced by lumbar extension, symptoms improved or induced with lumbar flexion, floor finger distance (cm), peripheral circulation (good or poor), a straight leg raising test, manual muscle testing of both upper and lower extremities, tendon reflex testing for both upper and lower extremities, and Babinski reflex testing. In addition, the MRI study of the entire spine was performed on all participants on the same day as the physical examination.

The diagnostic criteria for symptomatic LSS used in the present study were based on the LSS definition from the North American Spine Society (NASS) guideline, which requires presentation of both LSS symptoms and radiographic signs of LSS[24]. The orthopedic surgeon (YI) made the diagnosis of symptomatic LSS using this definition. The diagnosis for LSS symptoms required one or more of the following symptoms: pain, numbness and neurological deficits in the lower extremities and buttocks, and bladder/bowel dysfunction. The symptom characteristics should be induced or exacerbated with walking or prolonged standing and relieved with lumbar flexion, sitting and recumbency. The severity of radiographic LSS was assessed by qualitative measurements, which were performed by a well-experienced orthopedic surgeon (YI) and images were provided on films. The features assessed for LSS included severity of central, lateral recess, and foraminal stenosis, rated as four grades: none, mild, moderate and severe. The lateral recess was defined, as per Fardon and Millette[25], as extending from the medial edge of the facet to the edge of the neural foramen. We applied the general guideline classification of a[26] mild stenosis as narrowing of the normal area by one-third or less, moderate stenosis as narrowing between one-third and two-thirds, and severe stenosis as narrowing of more than two-thirds. Central and lateral recess stenosis was rated on the axial images and foraminal stenosis on the sagittal images. We used the most severe side for the rating of lateral and foraminal stenosis at each level. The same observer scored 50 randomly selected lumbar MRI films more than 1 month after the first reading to evaluate the intraobserver variability of the severity rating. Two experienced orthopedic surgeons also scored 50 different lumbar MRI films (YI & KN) for interobserver variability. The intraobserver variability was confirmed by a kappa analysis which dichotomized radiographic LSS severity as no/mild stenosis vs moderate/severe stenosis, and showed sufficient reliability for assessment of central, lateral and foraminal stenosis (0.77, 0.70 and 0.65, respectively). Interobserver variability was also sufficient for assessment using the kappa analysis (0.71, 0.65 and 0.65, respectively).

Radiographic LSS also required the severity to be more than moderate and the radiographic finding needs to be consistent with the symptoms as outlined above. An experienced orthopedic surgeon (YI) made the final diagnosis of symptomatic LSS using this definition, which requires presentation of both LSS symptoms and radiographic LSS findings. There were no participants with LSS symptoms due to tumor, inflammatory, or traumatic pathologies.

Statistical analysis

All statistical analyses were performed using JMP version 8 (SAS Institute Japan, Tokyo, Japan). Differences in age, height, weight, BMI, 6-m walking time at a usual pace, 6-m walking time at a maximal pace, chair standing time, and one-leg standing time between men and women were examined by the non-paired Student's *t*-test. The non-paired Student's *t*-test was also used to compare age between participants with and without symptomatic LSS. The prevalence of symptomatic LSS was also compared between men and women by the chi-square test. Differences in physical performance measures (6-m walking time at a usual pace, 6-m walking time at a maximal pace, chair standing time, and one-leg standing time) between participants with and without symptomatic LSS were examined by the non-paired Student's *t*-test. Furthermore, logistic regression analysis was used to estimate the odds ratios (ORs) of physical performance measures (6-m walking time at a usual pace, 6-m walking time at a maximal pace, chair standing time, and one-leg standing time) for symptomatic LSS after adjustment for age, gender and BMI.

Results

Table I shows the characteristics of 1,009 participants (335 men and 674 women, mean age 66.3 years, age range of 21–97 years) including age, anthropometric measurements, and physical performance in the present study. Two-thirds of the 1,009 participants were women. Mean age was not significantly different between men and women. BMI was significantly lower in women than in men ($P = 0.005$). Physical performance measures of the 6-m walking time at a usual pace and at a maximal pace were significantly shorter in men than in women ($P < 0.05$ for both), while chair standing time and one-leg standing time were not significantly different between men and women.

The prevalence of radiographic LSS findings was much greater than the prevalence of symptomatic LSS for the participants in this study. The percentage of participants with moderate or severe radiographic central stenosis was 76.5% (95% confidence interval [CI]: 73.7–79.0) in total, while the prevalence of symptomatic LSS was 9.3% (95% CI: 7.7–11.3) in total, 10.1% (CI: 7.4–13.8) in men, and 8.9% (CI: 7.0–11.3) in women. There was no significant difference between men and women ($P = 0.52$). The prevalence in men less than 39 years, 40–49, 50–59, 60–69, 70–79, and 80 years and older was 0%, 3.8% (CI: 0.7–18.9), 9.8% (CI: 4.6–19.8), 11.8% (CI: 6.1–21.5), 11.7% (CI: 6.7–19.8), and 10.7% (CI: 5.6–19.7), respectively, while that in women was 0%, 1.4% (CI: 0.2–7.3), 5.7% (CI: 2.8–11.3), 9.3% (5.7–14.8), 11.9% (CI: 7.9–17.5), and 13.3% (CI: 8.4–20.6), respectively (Fig. 2). The prevalence of both genders

Table I
Characteristics of participants

	Total	Men	Women	P value for gender
No. of participants	1009	335	674	
Age group (years)				
≦39	30	11	19	–
40–49	100	26	74	–
50–59	184	61	123	–
60–69	229	68	161	–
70–79	271	94	177	–
≧80	195	75	120	–
Demographic characteristics				
Age, years	66.3 ± 13.6	67.3 ± 13.8	65.9 ± 13.4	0.11
Height, cm	155.9 ± 9.4	164.5 ± 7.1	151.6 ± 7.2	<0.0001
Weight, kg	56.8 ± 11.5	64.4 ± 11.7	53.1 ± 9.4	<0.0001
BMI, kg/m^2	23.3 ± 3.6	23.7 ± 3.5	23.1 ± 3.6	0.005
Physical performance				
Six-meter walking time at a usual pace, s	5.7 ± 2.2	5.5 ± 1.5	5.8 ± 2.4	0.04
Six-meter walking time at a maximal pace, s	3.9 ± 1.4	3.6 ± 1.1	4.0 ± 1.6	<0.0001
Chair standing time, s	8.9 ± 4.0	8.8 ± 3.4	8.9 ± 4.2	0.61
One-leg standing time, s	36.0 ± 23.7	35.7 ± 24.0	36.1 ± 23.6	0.82

Non-paired *t*-test was used to determine differences in demographic characteristics and measurements of physical performance between men and women. Values are the means ± standard deviation.

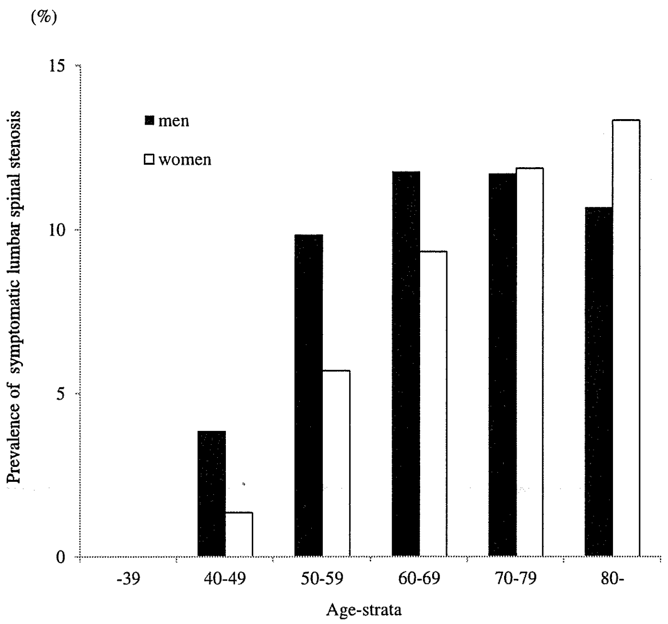

Fig. 2. Prevalence of symptomatic LSS classified by age and gender among 1,009 participants from a community cohort in Japan.

increased until reaching the 60–69 year old age group in which the prevalence in men was higher than that of women. However, the prevalence for women was higher than that of men after age 70. The prevalence of symptomatic LSS in men demonstrated little difference between age groups 60–69 years to over 80 years, but the prevalence for women became significantly higher with increasing aging ($P = 0.036$).

Fifty-five (58.5%) of 94 participants defined as having symptomatic LSS had IC. Five of these 55 participants presented with an ABI < 0.9. However, these five participants also had symptomatic LSS and their leg symptoms were positionally dependent. In this study, there were fifty neurogenic IC cases. There were five cases of unspecified IC, which was caused by both neurogenic and vascular claudication.

Table II shows the physical performance measures in participants with and without symptomatic LSS. In the overall population, 6-m walking time at a usual pace, 6-m walking time at a maximal pace, chair standing time, and one-leg standing time were significantly worse in participants with symptomatic LSS than those without symptomatic LSS ($P < 0.01$ for all). When analyzed in men and women separately, the results were similar to those overall, although the significant differences disappeared in some physical performance measures in men. The significant differences of 6-m walking time at a usual pace in both genders and one-leg standing time in men disappeared after a Bonferroni adjustment. Logistic regression analysis after adjustment for age, gender and BMI showed that 6-m walking time at a maximal pace was significantly associated with symptomatic LSS (OR: 1.17, 95% CI: 1.01–1.34). The physical performance measures of 6-m walking time at a usual pace, chair standing time, and one-leg standing time were not significantly associated with symptomatic LSS (OR: 1.04, 95% CI: 0.94–1.13, OR: 1.03, 95% CI: 0.97–1.09 and OR: 1.00, 95% CI: 0.98–1.01, respectively).

Discussion

The present study is the first to clarify the prevalence of symptomatic LSS by gender and age strata and the association of symptomatic LSS with physical performance measures using a population-based cohort. The prevalence of symptomatic LSS was found to be 9.3% in the general Japanese population, 10.1% in men, 8.9% in women, and there were no significant differences between genders. Interestingly, although the prevalence in women was higher with increasing age, the prevalence in men was the highest at 60–69 years, and little difference in prevalence was seen in men aged 60–69 years to 80 years or older. The prevalence of radiographic LSS was much greater than the prevalence of symptomatic LSS, with only a small proportion of participants with radiographic LSS actually showing symptoms suggestive of the clinical syndrome. The 6-m walking time at a maximal pace was significantly associated with symptomatic LSS, while the 6-m walking time at a usual pace was not.

We have identified no previous studies of symptomatic LSS prevalence. Johnsson[4] reported that the incidence of symptomatic LSS was 50/million person-years in southern Sweden in a study of patients who consulted the orthopedic department in two cities. However, as the author of that report described, the incidence of symptomatic LSS could be underestimated, because the studies did not include patients with minor symptoms who did not visit the hospital. This study is the first to clarify the prevalence of symptomatic LSS using a population-based cohort study.

Reported differences in prevalence of symptomatic LSS between men and women are mixed[27–29]. Verbiest reported a preponderance of symptomatic LSS in men as compared to women among his patients diagnosed by clinical symptoms and myelography[28]. However, Getty reported an equal gender distribution of symptomatic LSS prevalence in a series in which subjects were treated surgically for symptomatic LSS[29]. It is important to note that the subjects in those studies were patients who visited hospitals. In the present study, differences in the prevalence of symptomatic LSS between men and women in the general population were clarified. The prevalence of symptomatic LSS in men was slightly higher than in women, but there was no significant difference between genders. There was a difference in distribution of symptomatic LSS between men and women. The prevalence in women was higher with increasing age, but that in men was the highest at 60–69 years and

Table II
Measurements of each physical performance in participants with and without symptomatic LSS

	Total			Men			Women		
	LSS	Non-LSS	*P* value	LSS	Non-LSS	*P* value	LSS	Non-LSS	*P* value
Number of participants	94	915		34	301		60	614	
Physical performance									
Six-meter walking time at a usual pace, s	6.3 ± 2.7	5.6 ± 2.1	0.003	6.0 ± 1.6	5.4 ± 1.5	0.03	6.5 ± 3.1	5.7 ± 2.3	0.02
Six-meter walking time at a maximal pace, s	4.5 ± 2.1	3.8 ± 1.3	<0.0001	3.9 ± 1.1	3.6 ± 1.1	0.09	4.8 ± 2.4	3.9 ± 1.5	<0.0001
Chair standing time, s	10.1 ± 4.0	8.8 ± 3.9	0.002	9.7 ± 2.8	8.7 ± 3.4	0.10	10.3 ± 4.6	8.8 ± 4.1	0.008
One-leg standing time, s	27.9 ± 23.5	36.8 ± 23.6	0.0005	27.7 ± 25.4	36.7 ± 23.7	0.04	28.0 ± 22.6	36.9 ± 23.5	0.006

Values are the means ± standard deviation.
Non-paired *t*-test was used to determine differences in measurements of physical performance between LSS and non-LSS.

little different in men aged 60–69 years to 80 years and older. The prevalence of lumbar spondylosis (LS) diagnosed as Kellgren/Lawrence (KL) grade two or greater (defined as osteophyte formation with and without disc space narrowing) was found to be significantly higher in men than in women[30]. The prevalence of LS in women was found to be higher with increasing age, while that in men found little difference over 60 years[13]. Interestingly, these distribution patterns are similar to the prevalence of symptomatic LSS in the present study. Anatomical LSS arises from degenerative LS, and facet osteoarthritis and/or hypertrophy, which is associated with narrowing of the space available for the neural elements[1]. This may be one reason for the similarity between LS and symptomatic LSS prevalence.

The present study was the first to show that, among the general population, 6-m walking time at a maximal pace was significantly associated with symptomatic LSS, while 6-m walking time at a usual pace was not. This may mean that participants with symptomatic LSS appeared to have no disadvantage concerning activities of daily living compared to those without symptomatic LSS. However, when requiring greater functional reserve, such as 6-m walking time at a maximal pace, differences between participants with and without symptomatic LSS appeared. This is also the first study to indicate that tasks requiring greater functional reserve, such as walking at a maximal speed, could be a more sensitive index in assessment of decreased physical performance due to symptomatic LSS.

There are several limitations in the present study. First, although the present study included more than 1,000 participants, these participants may not represent the general population as they were recruited from only two areas. However, anthropometric measurements were compared between participants and the general Japanese population, and no significant differences were found in BMI (men: 23.71 (3.41) and 23.95 (2.64), $P = 0.33$, women: 23.06 (3.42) and 23.50 (3.69), $P = 0.07$)[31]. In addition, the proportion of current smokers and current drinkers (those who regularly smoked or drank more than one drink/month) in the general Japanese population was compared with that in the study population. Proportions of current smokers and drinkers in men and that of current drinkers in women were significantly higher in the general Japanese population than in the study population, but there were no significant differences in that of current smokers in women (smokers: men, 32.6% in the Japanese population, 25.2% in study participants, $P = 0.015$; women, 4.9% in the Japanese population, 4.1% in study participants, $P = 0.50$; drinkers: men, 73.9% in the Japanese population, 56.8% in study participants, $P < 0.0001$; women, 28.1% in the Japanese population, 18.8% in study participants, $P < 0.0001$), suggesting that it is likely that the participants (both men and women) had healthier lifestyles than the general Japanese population. Second, this is a cross-sectional study, so any causal relationship between symptomatic LSS and physical performance cannot be clarified. The Wakayama Spine Study is a longitudinal survey, so further progress will help to elucidate any causal relationships. Thirds, total walking distance/duration was not measured, and this metric for walking would likely have been of greater relevance to symptomatic LSS than speed of walking. In addition, this study only represents the Japanese population, hence, prevalence in other countries may be quite different.

In conclusion, the present study clarified that the prevalence of symptomatic LSS was about 10% in a cohort resembling the Japanese general population. There was a difference in the prevalence of symptomatic LSS distribution by age strata between men and women. The 6-m walking time at a maximal pace was a more sensitive index for assessing decreased physical performance due to LSS than the 6-m walking time at a usual pace. Further longitudinal surveys of the Wakayama Spine Study will help to further clarify the incidence and risk factors for symptomatic LSS.

Author contributions

All authors worked collectively to develop the protocols and methods described in this paper. YI, SM, KN, NO, HO, TA, and NY were principal investigators responsible for the fieldwork in the Wakayama Spine Study. YI and SM performed the statistical analysis. YI, HY, SM, KN, HH, HO, TA, MY, and NY contributed to the analysis and interpretation of results. YI wrote the report. All authors read and approved the final report.

Role of the funding source

The study sponsors played no role in the study design, the collection, analysis, and interpretation of data, writing of the report, or the decision to submit the paper for publication. The corresponding author had full access to all the data and had the final decision to submit for publication.

Conflict of interest

The authors declare that we have no conflicts of interest.

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Original Research

Prevalence of vertebral fracture in Asian men and women: Comparison between Hong Kong, Thailand, Indonesia and Japan

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SUMMARY

Objectives: Little is known about the prevalence of vertebral fracture among Asians. This study investigated the prevalence of radiographically defined vertebral fracture, and identified associated risk factors in the aged population of four Asian countries.
Study design: In total, 1588 males and females aged ≥65 years were recruited from Hong Kong, Thailand, Indonesia and Japan.
Methods: Standard X-rays for the spine were taken and vertebral heights were measured. Vertebral fracture was defined as a reduction of >3 standard deviations in vertebral height ratio. Bone mineral density (BMD) of the hip was measured by dual energy X-ray absorptiometry, and anthropometric measurements were taken in Hong Kong and Japan. Other relevant data were entered in a standard questionnaire.
Results: The prevalence of vertebral fracture for both males and females was highest in Japan for younger (65–74 years) and older (≥75 years) age groups (36.6% and 37.6% for males; 18.8% and 28.7% for females). Lower hip BMD was associated with vertebral fracture in both sexes. Older age, lower quality of life score on Short Form-12 (physical), past longest occupation as a farmer, and history of cataract were significantly associated with vertebral fracture in females. However, smoking did not appear to be an important risk factor for vertebral fracture.
Conclusions: Radiographic assessments for vertebral fracture were performed in all four Asian countries. The prevalence of vertebral fracture was highest in Japan. Lower hip BMD, poorer physical condition and past longest occupation as a farmer were associated with vertebral fracture.

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Introduction

Osteoporosis is a condition characterized by low bone mass and micro-architectural deterioration of bone tissues causing increased bone fragility and susceptibility to fracture. The disease is becoming a major health problem in Asia where a rapidly increasing aged population will be accompanied by increasing incidence of hip fracture.[1] In Hong Kong, for instance, over the last two decades, the number of cases of hip fracture has increased two-fold due to the increase in the ageing population. Of every 1000 people who are aged ≥80 years, one man and two women will have a fractured hip each year.[2] The age-adjusted rate in Hong Kong is comparable to that in Singapore and higher than that in Japan. It has been projected that over half of all hip fractures in the world will occur in Asia by 2050.[1]

While there are many data on the prevalence and risk factors for hip fracture, little is known of the prevalence and risk factors for vertebral fracture in Asia. In a study by Lau *et al.*, the prevalence of vertebral fracture was estimated to be 29% in women in Hong Kong.[3] Vertebral deformity, back pain and psychological problems were associated symptoms in elderly Chinese women, and the use of analgesics was common in men. Overseas studies have demonstrated associations between vertebral fracture and back pain, disability and the need for healthcare support.[4–6] The survival rate of elderly people who had experienced a clinical vertebral fracture was found to be lower than that of elderly people who had not experienced a fracture.[7] Women with severe vertebral deformities were found to have a consistently higher risk of back pain and height loss. In addition, genetic and lifestyle factors may influence vertebral fracture. However, the risk factors for Asian men are still unclear.

The aim of this study was to investigate the prevalence of radiographically defined vertebral fracture, and to identify underlying risk factors associated with vertebral fracture in the aged population in four Asian countries (Hong Kong, Thailand, Indonesia and Japan). Existing data from Beijing, China were used for comparison.

Methods

Subjects

In total, 1588 subjects were recruited from Hong Kong, Thailand, Indonesia and Japan. Each country was required to recruit 400 ambulatory community-dwelling subjects (200 males and 200 females), half of whom were aged 65–74 years and the other half were aged ≥75 years. They all were ethnic Asians. Subjects were recruited in community centres (recreation centres for group activities, social support and public information) for the elderly. Recruitment notices were placed at these centres explaining the purpose and procedures of this study in different districts, including urban and rural areas. Moreover, community activities and community advertisements were used to enhance the representativeness of the whole region.

Radiographs and digitization

Radiographic films of the lateral thoracic and lumbar spine were taken with a tube-to-film distance of 100 cm, with thoracic films centred at T8 and lumbar films centred at L3. The radiographs were evaluated by morphometry using a backlight translucent digitizing table (GTCO, Rockville, MD, USA) and cursor. Six points were marked on the radiographs with a wax pencil for each vertebral body T4–L4, and the X,Y co-ordinates for each point were recorded on an electronic grid with a resolution of 0.1 mm. In total, 120 and 68 subjects lacked T4 and T5, respectively. Standardized procedures were adopted. The six points corresponded to the four corners of the vertebral body and the midpoints of the end plates[8] (Fig. 1). Vertebral height ratios (VHR) were calculated [anterior to posterior (Ha/Hp), middle to posterior (Hm/Hp) and posterior above to posterior below (Hp/Hp−1 and Hp/Hp+1)]. Prevalent vertebral fracture was defined as a reduction of >3 standard deviations (SD) among any one of the VHRs.[6,8] Mean (SD) VHRs are shown in Table 1. X-ray films for Hong Kong, Thailand and Indonesia were measured in Hong Kong by three trained members of staff, all with >10 years of experience and trained by the radiologist-in-charge with standardized procedures. Fifteen films were selected at random for reliability analysis. Whereas X-ray films from Japan were measured in Japan, 30 were selected at random and sent to Hong Kong for reliability analysis. The analysis was performed by two members of staff (one from Hong Kong and one from Japan).

Questionnaire

Subjects were interviewed using a standardized and structured questionnaire in Hong Kong, Thailand and Indonesia by trained staff. Data collected included demographic information, Mini-Mental Status Examination score, medical history, fall history, smoking habit, alcohol consumption, Physical Activity Screening for Elderly score, quality of life,

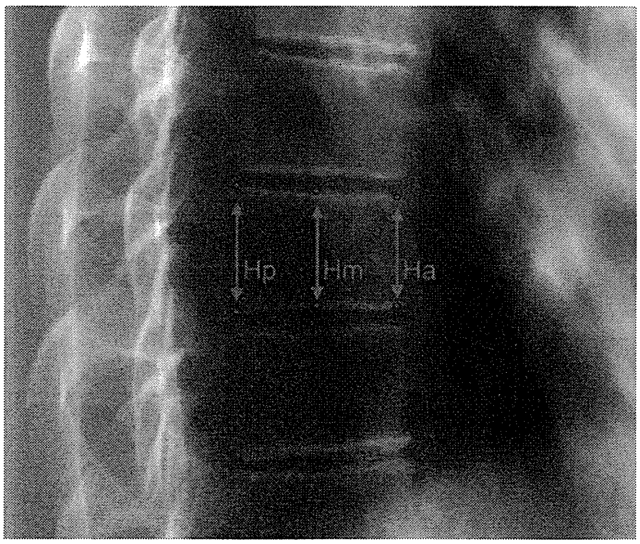

Fig. 1 – Measurement of vertebral height. Hp, posterior height; Hm, mid-body height; Ha, anterior height.

Table 1 – Adjusted means[a] and standard deviations (SD) of vertebral height ratios in Chinese male and female subjects.

Level	Ha/Hp		Hm/Hp		Hp/Hp−1		Hp/Hp+1	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Male[b]								
T4	0.87	0.06	0.91	0.04	–	–	1.00	0.06
T5	0.87	0.07	0.92	0.04	1.00	0.06	0.98	0.06
T6	0.87	0.07	0.92	0.04	1.03	0.06	0.98	0.06
T7	0.86	0.07	0.92	0.04	1.02	0.06	1.00	0.06
T8	0.89	0.07	0.93	0.04	1.00	0.06	0.98	0.06
T9	0.91	0.07	0.94	0.04	1.02	0.06	0.95	0.06
T10	0.92	0.07	0.94	0.04	1.05	0.06	0.91	0.06
T11	0.86	0.08	0.91	0.05	1.10	0.07	0.93	0.05
T12	0.84	0.07	0.90	0.04	1.08	0.06	0.95	0.05
L1	0.84	0.06	0.89	0.04	1.06	0.05	1.01	0.04
L2	0.88	0.06	0.91	0.03	1.00	0.04	1.01	0.04
L3	0.92	0.06	0.94	0.04	0.99	0.04	1.06	0.05
L4	0.97	0.07	1.00	0.05	0.95	0.04	–	–
Female[c]								
T4	0.90	0.08	0.92	0.06	–	–	0.99	0.09
T5	0.88	0.08	0.91	0.06	1.03	0.09	0.99	0.07
T6	0.86	0.07	0.91	0.05	1.03	0.07	0.99	0.07
T7	0.86	0.08	0.91	0.05	1.02	0.07	0.99	0.06
T8	0.88	0.07	0.92	0.05	1.01	0.06	0.99	0.06
T9	0.92	0.08	0.94	0.05	1.01	0.06	0.97	0.06
T10	0.92	0.08	0.94	0.05	1.04	0.07	0.95	0.06
T11	0.87	0.08	0.91	0.05	1.06	0.07	0.94	0.06
T12	0.86	0.09	0.90	0.06	1.07	0.07	0.96	0.07
L1	0.87	0.08	0.89	0.05	1.05	0.08	1.00	0.05
L2	0.93	0.08	0.91	0.05	1.01	0.06	1.01	0.06
L3	0.98	0.08	0.95	0.06	0.99	0.06	1.04	0.07
L4	1.02	0.10	1.01	0.07	0.96	0.07	–	–

Ha/Hp, anterior height of vertebrae/posterior height of vertebrae; Hm/Hp, middle height of vertebrae/posterior height of vertebrae; Hp/Hp−1, posterior height of vertebrae/posterior height of vertebrae above; Hp/Hp+1, posterior height of vertebrae/posterior height of vertebrae below.
a Adjusted means were estimated as the mode on the log-frequency curve after trimming 5% of the values from each end of the distribution. The adjusted SDs were estimated by quantile–quantile plot after 10% of values were trimmed from each end of the distribution.
b Data used by Lau *et al.*[30]
c Data published by Lau *et al.*[3]

fracture history, back pain and musculoskeletal symptoms, medications, diet history, Geriatric Depression Scale score, and past longest occupation in their life.

Dual X-ray densitometry and anthropometric measurement

Bone mineral density (BMD), height and weight were measured in Hong Kong and Japan. Hip and spine BMD were measured by dual energy X-ray absorptiometry (DXA) using a Hologic QDR-4500W densitometer (Hologic, Waltham, MA, USA). The same type of DXA machine was used in both Hong Kong and Japan. The coefficient of variation (CV) in the laboratory was 0.7% and 0.9% for hip and spine, respectively. Height was measured using a Holtain Harpenden stadiometer (Holtain Ltd., Crosswell, UK), and weight was measured using the Physician Beam Balance Scale (Healthometer, IL, USA) with subjects wearing a light gown.

Study flow

The study started in Hong Kong, Indonesia and Thailand. Radiographs and questionnaires were performed in these three countries. Japan joined the study at a later date; radiographs, BMD and anthropometric measurements were conducted but no questionnaire was used. As different information was collected from the four countries, the results are shown in three parts. First, the prevalence of vertebral fracture was compared between the four countries. Second, lifestyle and medical risk factors for vertebral fracture were analysed for Hong Kong, Indonesia and Thailand. Finally, anthropometric factors in Japan were compared with those for Hong Kong.

Statistical analysis

Inter-rater reliability of each parameter was assessed using the intraclass correlation coefficient (ICC). The prevalence of deformity was calculated based on the number of individuals with at least one vertebral deformity, and this was compared between countries using Chi-squared test. Data were analysed separately by sex. Continuous variables were compared between the countries using t-test or analysis of variance, while categorical variables were compared using Chi-squared test. Logistic regression (with adjustment for age) was used to calculate odds ratios (OR) and 95% confidence intervals (CI) of various lifestyle and anthropometric factors for definite vertebral deformity. Significant factors were collated to form the final models. All statistical analyses were performed using SAS Version 9.1 (SAS Institute, Inc., Cary, NC, USA). An α level of 5% was used as the level of significance.

Results

Inter-rater reliabilities of vertebral measurements were fair to good. ICC (3,1) ranged from 0.54 to 0.94 for anterior heights, from 0.70 to 0.96 for middle heights, and from 0.60 to 0.92 for posterior heights among 15 randomly selected subjects from Hong Kong, Thailand and Indonesia. ICC (3,1) ranged from 0.73 to 0.93 for anterior heights, from 0.69 to 0.93 for middle heights, and from 0.76 to 0.95 for posterior heights among 30 Japanese subjects.

Part 1: prevalence of vertebral fracture in four Asian countries

Seven hundred and seventy males (mean age 72.9 years) and 818 females (mean age 72.4 years) were recruited. The prevalence of vertebral fracture in Hong Kong, Indonesia, Thailand and Japan is shown in Table 2. Among males, the prevalence of fracture was highest in Japan (36.6% for age 65–74 years, 37.6% for age ≥75 years); the difference between Japan and the other three countries was significant. The prevalence of fracture was lowest in Hong Kong males (9.2%

Table 2 – Prevalence of vertebral fracture.

	Prevalence of vertebral fracture (%)				P-value of Chi-square
	Hong Kong (H)	Indonesia (I)	Thailand (T)	Japan (J)	
Male					
Age 65–74 years	(n = 98)	(n = 127)	(n = 105)	(n = 101)	
Radiological fracture					
Definite vertebral deformity, <mean − 3 SD	9.2	15.0	17.1	36.6[a,b,c]	<0.0001
Severe vertebral deformity, <mean − 4 SD	3.1	7.1	13.3[a]	20.8[a,b]	0.0003
Reported fracture	0.0	0.0	2.9	–	0.0402
Age ≥75 years	(n = 100)	(n = 40)	(n = 98)	(n = 101)	
Radiological fracture					
Definite vertebral deformity, <mean − 3 SD	18.0	20.0	24.5	37.6[a,b,c]	0.0102
Severe vertebral deformity, <mean − 4 SD	9.0	17.5	20.4[a]	20.8[a]	0.0926
Reported fracture	2.0	0.0	1.0	–	0.6125
Female					
Age 65–74 years	(n = 99)	(n = 170)	(n = 98)	(n = 101)	
Radiological fracture					
Definite vertebral deformity, <mean − 3 SD	2.0	7.6	8.2[a]	18.8[a,b,c]	0.0010
Severe vertebral deformity, <mean − 4 SD	1.0	5.9	6.1	10.9[a]	0.0338
Reported fracture	1.0	0.0	3.0	–	0.2930
Age ≥75 years	(n = 98)	(n = 54)	(n = 97)	(n = 101)	
Radiological fracture					
Definite vertebral deformity, <mean − 3 SD	15.3	13.0	17.5	28.7[a,b]	0.0727
Severe vertebral deformity, <mean − 4 SD	10.2	9.3	15.5	18.8	0.2312
Reported fracture	1.0	0.0	3.0	–	0.2930

SD, standard deviation.
Note: a higher number of reported fractures was significantly associated with a higher number of radiological fractures (Chi-squared = 7.078, P-value = 0.0078).
a P-value < 0.05 comparing Indonesia (I), Thailand (T) or Japan (J) with Hong Kong (H), by Chi-squared test.
b P-value < 0.05 comparing Thailand (T) or Japan (J) with Indonesia (I), by Chi-squared test.
c P-value < 0.05 comparing Japan (J) with Thailand (T), by Chi-squared test.

for age 65–74 years; 18% for age ≥75 years). In females, the prevalence of fracture was also highest in Japan (18.8% for age 65–74 years; 28.7% for age ≥75 years), and was lowest in Hong Kong and Indonesia (2% for age 65–74 years; 13% for age ≥75 years). The reported fracture rates ranged from 0 to 2.97%, which were much lower than radiological fracture rates (0–24.5%) (Table 2). More reported fractures were significantly associated with more radiological fractures (Chi-squared = 7.078, P-value = 0.0078).

Part 2: lifestyle and medical factors of vertebral fracture in Hong Kong, Indonesia and Thailand

Results for Hong Kong, Indonesia and Thailand are shown in Tables 3 and 4. Subjects' characteristics are shown in Table 3. Males and females in Hong Kong had significantly higher quality of life {Short Form[SF]-12 (mental)}; higher prevalence of hypertension, heart disease and myocardial infarction/angina; and lower levels of education compared with Indonesia and Thailand. The percentage of respondents who stated that their longest occupation had been as a farmer was highest in Thailand.

Risk factors of vertebral fracture are shown in Table 4. For males, older age, lower SF-12 (physical) score, and history of stroke were significantly associated with vertebral fracture. For females, older age, lower SF-12 (physical) score, history of cataract, and past longest occupation as a farmer were significantly associated with vertebral fracture. In logistic regression, a lower SF-12 (physical) score (OR 0.68, 95% CI 0.55–0.84) was associated with vertebral fracture among the males. Older age (OR 1.33, 95% CI 1.03–1.71), lower SF-12 (physical) score (OR 0.73, 95% CI 0.56–0.95), history of cataract (OR 2.86, 95% CI 1.48–5.53), and past longest occupation as a farmer (OR 2.47, 95% CI 1.07–5.72) were associated with vertebral fracture in females.

Part 3: anthropometric factors of vertebral fracture in Hong Kong and Japan

To investigate the difference in fracture rate between Japan and Hong Kong, 25 males and 27 females in Japan were selected at random as subsamples to obtain anthropometric factors: weight and height and bone density. Results are shown in Tables 5 and 6. Differences in characteristics between Hong Kong and Japan are shown in Table 5. Subjects in Hong Kong were heavier and taller (marginally in males but significantly in females). The body mass index of Hong Kong females was also significantly higher. Logistic regressions of vertebral fractures are shown in Table 6. Lower hip BMD (OR 1.47, 95% CI 1.001–2.17 per SD reduction) was associated with vertebral fracture in males, while in females, older age (OR 1.9, 95% CI 1.13–3.2), heavier weight (OR 1.6, 95% CI 1.1–2.3) and lower hip BMD (OR 3.23, 95% CI 1.72–6.25 per SD reduction) were associated with vertebral fracture.

Table 3 – Characteristics of subjects by country.

Variable	Male			P-value[a]	Female			P-value[a]
	Mean (SD)/%				Mean (SD)/%			
	Hong Kong ($n = 198$)	Indonesia ($n = 167$)	Thailand ($n = 203$)		Hong Kong ($n = 197$)	Indonesia ($n = 224$)	Thailand ($n = 195$)	
Age	73.7 (5.4)	70.3 (5.1)	73.8 (6.0)	0.9610	73.8 (5.5)	70.3 (5.8)	73.7 (5.5)	0.9078
SF-12 (physical)	49.7 (9.0)	47.2 (10.4)	46.0 (10.9)	**0.0003**	45.3 (9.0)	41.8 (11.6)	43.6 (11.6)	0.1085
SF-12 (mental)	56.4 (5.9)	52.1 (8.1)	53.1 (8.7)	**<0.0001**	55.7 (8.1)	52.3 (8.3)	52.7 (9.1)	**0.0005**
Physical activity (PASE score)	104.8 (49.8)	102.7 (67.9)	93.0 (80.8)	0.0880	81.3 (30.7)	70.8 (42.7)	70.5 (47.6)	**0.0081**
Marital status: married	84.1%	82.4%	81.3%	0.7564	57.7%	62.3%	50.5%	**0.0456**
Education				**<0.0001**				**<0.0001**
Primary or below	53.2%	41.9%	64.5%		76.6%	55.1%	72.9%	
Secondary	33.8%	43.8%	14.2%		18.9%	34.8%	15.1%	
Tertiary or above	12.9%	14.4%	21.3%		4.5%	10.1%	12.0%	
Demented (MMSE < 24)	11.0%	13.4%	15.8%	0.3634	36.3%	22.9%	25.0%	**0.0046**
Diabetes	14.9%	10.5%	11.3%	0.3690	9.0%	14.2%	13.0%	0.2243
Reported osteoporosis	5.0%	1.7%	3.5%	0.2361	9.0%	11.6%	10.0%	0.6492
Stroke	6.0%	2.3%	4.4%	0.2263	3.5%	2.2%	2.0%	0.5768
Hypertension	39.3%	19.2%	22.7%	**<0.0001**	42.3%	26.7%	25.0%	**0.0002**
Heart disease	19.9%	2.3%	4.9%	**<0.0001**	14.4%	3.5%	4.5%	**<0.0001**
Myocardial infarction/ angina	18.4%	1.2%	4.9%	**<0.0001**	11.4%	4.3%	3.5%	**0.0014**
Congestive heart failure	2.5%	0.6%	2.5%	0.3150	3.5%	1.3%	1.0%	0.1328
Chronic obstructive pulmonary disease	15.9%	5.2%	3.0%	**<0.0001**	6.5%	4.3%	1.5%	**0.0424**
Cataracts	33.3%	18.6%	22.2%	**0.0024**	44.8%	23.3%	27.0%	**<0.0001**
Gastrectomy	9.0%	8.1%	11.3%	0.5425	4.0%	14.2%	7.0%	**0.0005**
Cancer	4.5%	0.6%	1.5%	**0.0268**	3.5%	2.2%	1.5%	0.4115
Fall in past 12 months	22.9%	4.1%	21.7%	**<0.0001**	20.9%	14.2%	31.5%	**<0.0001**
Smoker	9.5%	29.2%	19.4%	**<0.0001**	0.5%	1.4%	1.0%	0.6472
Use of alcohol at least 12 times in past 12 months	22.9%	5.5%	36.1%	**<0.0001**	0.5%	0.5%	6.5%	**<0.0001**
Fracture after 50 years of age	6.0%	5.5%	9.4%	0.2739	16.9%	5.6%	7.6%	**0.0002**
Past longest occupation as a farmer	1.0%	14.3%	44.8%	**<0.0001**	3.1%	5.7%	40.0%	**<0.0001**

SF-12, Short Form-12; PASE, physical activity screening for elderly; MMSE, Mini-Mental State Examination.
Bold: P-value < 0.05.
a P-value of Chi-squared for categorical variables or analysis of variance for continuous variables where appropriate.

Discussion

The occurrence of osteoporotic vertebral fracture is particularly common in older postmenopausal Asian women. The common sites involved are T12 and L1 as these levels are, biomechanically, the most vulnerable regiments of the thoracolumbar spine.[9] The first vertebral fracture is an important indicator for subsequent vertebral fracture, and possibly non-vertebral fracture including hip fracture.[10,11] Understanding the prevalence of vertebral fracture and deformity is critical for prevention.

Fracture identification can easily be affected by differences in radiographic methods. Fracture definition and methods of morphological assessment also affect the determination of fracture rates. Degenerative spondylosis and old asymptomatic spinal fractures may lead to spuriously high BMD at the site of involvement, thus diminishing the sensitivity in the prediction of fracture. In this study, all the radiographs were taken according a standardized protocol, and were analysed by trained and experienced assessors to minimize possible observer bias and to acquire more precise and accurate results. The number of reported vertebral fractures was generally lower in both males and females than the number of radiologically determined vertebral fractures in all four countries. As elsewhere, vertebral fractures were often under-reported. Vertebral fractures could also be overlooked when patients present with back pain arising from various spinal conditions.

This study found that the prevalence of vertebral fracture was significantly higher in Japan compared with Hong Kong, Thailand and Indonesia for both sexes. BMD is an important factor,[12,13] but in this study, no difference was noted between Hong Kong and Japan. This may be explained by the smaller body size of Japanese subjects. In a systematic review, Ruyssen-Witrand *et al.*[14] showed that vertebral size was an independent risk factor for vertebral fracture. After controlling for well-known confounding factors such as age, height,

Table 4 – Characteristics in subjects with vertebral fracture and control.

Variable	Unit	Male		Female	
		Age-adjusted model OR (95% CI)	Multivariate model OR (95% CI)	Age-adjusted model OR (95% CI)	Multivariate model OR (95% CI)
Age	5	**1.24 (1.03–1.49)[a]**	1.17 (0.96–1.44)	**1.48 (1.20–1.84)[a]**	**1.33 (1.03–1.71)**
Country					
Hong Kong	–	1	1	1	1
Indonesia	Indonesia/Hong Kong	1.44 (0.79–2.62)	1.28 (0.68–2.40)	1.36 (0.67–2.72)	1.20 (0.53–2.73)
Thailand	Thailand/Hong Kong	1.66 (0.97–2.82)	1.45 (0.84–2.51)	1.58 (0.82–3.05)	1.36 (0.61–2.99)
SF-12 – Physical	10	**0.65 (0.53–0.80)**	**0.68 (0.55–0.84)**	**0.67 (0.53–0.85)**	**0.73 (0.56–0.95)**
SF-12 – Mental	10	0.99 (0.75–1.32)		0.86 (0.64–1.17)	
Physical activity (PASE score)	50	1.00 (0.84–1.19)		0.72 (0.50–1.03)	
Marital status – married	Yes/no	1.78 (0.91–3.46)		0.68 (0.40–1.18)	
Education					
Primary or below	–	1		1	
Secondary	Secondary/primary	0.63 (0.36–1.11)		0.96 (0.48–1.91)	
Tertiary or above	Tertiary/primary	1.02 (0.55–1.90)		0.37 (0.09–1.57)	
Demented (MMSE<24)	Yes/no	1.36 (0.74–2.49)		1.34 (0.76–2.37)	
Diabetes	Yes/no	1.09 (0.56–2.14)		0.67 (0.26–1.75)	
Reported osteoporosis	Yes/no	1.26 (0.41–3.91)		2.01 (0.95–4.24)	
Stroke	Yes/no	**2.61 (1.08–6.31)**	2.32 (0.94–5.71)	1.43 (0.31–6.60)	
Hypertension	Yes/no	1.08 (0.66–1.77)		0.72 (0.39–1.31)	
Heart disease	Yes/no	0.80 (0.36–1.77)		0.94 (0.35–2.53)	
Myocardial infarction/angina	Yes/no	0.94 (0.42–2.08)		0.88 (0.29–2.60)	
Congestive heart failure	Yes/no	1.67 (0.43–6.47)		1.74 (0.37–8.26)	
Chronic obstructive pulmonary disease	Yes/no	1.02 (0.46–2.27)		–	
Cataracts	Yes/no	1.21 (0.73–1.98)		**1.80 (1.05–3.10)**	**2.86 (1.48–5.53)**
Gastrectomy	Yes/no	0.83 (0.38–1.83)		0.72 (0.25–2.09)	
Cancer	Yes/no	–		0.64 (0.08–5.04)	
Fall in past 12 months	Yes/no	0.90 (0.49–1.63)		1.39 (0.76–2.51)	
Smoker	Yes/no	0.62 (0.33–1.20)		–	
Use of alcohol at least 12 times in past 12 months	Yes/no	1.30 (0.78–2.17)		2.12 (0.45–9.95)	
Fracture after 50 years of age	Yes/no	2.00 (0.93–4.31)		1.36 (0.62–2.98)	
Past longest occupation as a farmer	Yes/no	1.19 (0.68–2.08)		2.14 (1.13–4.05)	**2.47 (1.07–5.72)**

SF-12, Short Form-12; PASE, Physical Activity Screening for Elderly; MMSE, Mini-Mental State Examination; OR, odds ratio; CI, confidence interval.
Bold: P-value < 0.05.
a Crude OR.

weight and BMD, small vertebral dimensions including area, cross-sectional area and volume were associated with vertebral fracture.[14–16] Moreover, there is a difference in the nutrient intake of these two populations; dietary calcium intake in the Japanese population is less than that of the Hong Kong population (550 mg/day in men and 519 mg/day in women vs 628 mg/day and 569 mg/day for people aged ≥65 years).[17,18] Kobayashi reported that the calcium content of river water in Japan was lower than that in most European countries.[19]

For Asian women, a review of vertebral fracture revealed that the prevalence of vertebral fracture increases steeply with age in Beijing: the prevalence of vertebral fracture in Chinese women aged 50–59 years was 3.9%, compared with 10.5%, 15% and 31.2% at ages 60–69, 70–79 and ≥80 years.[6,20,21] A similar trend has also been observed among Japanese women residing in Japan and Hawaii[22,23]; the rates were slightly higher for those living in Japan (8%, 25%, 38% and 43% for ages 65–70, 70–75, 75–80 and 80–85 years, compared with 5%, 15%, 25% and 27% for those living in Hawaii in 1996), suggesting that environmental factors are more influential than genetic factors.[24] Horikawa *et al.* reported a prevalence of 22.6% for Japanese women aged 65–92 years living in a fishing/farming village located in Nansei-cho in 2001.[25] Data for Japan in the present study showed similar rates. These data are similar to findings among Caucasian women in the USA, where the prevalence of vertebral fracture was 22% for women aged 70–79 years, and 34% for women aged ≥80 years. Hence, observations from the present study suggest that vertebral fracture is as prevalent in Asian women as in Caucasian women.[20]

The prevalence of vertebral fracture among Chinese women in 1996 in Hong Kong was 29% at age 70–79 years.[1,3] The current study found a prevalence of vertebral fracture of 2% at age 65–74 years and 15% at age ≥75 years among Hong Kong Chinese women. The prevalence of vertebral fracture appears to have decreased significantly over the years between these studies. This may reflect a proper

Table 5 – Comparison of characteristics between Hong Kong and Japan.

Variable	Mean (SD)		P-value[a]
	Hong Kong	Japan	
Male	n = 198	n = 25	
Age (years)	73.75 (5.40)	73.28 (4.31)	0.6784
Weight (kg)	61.86 (9.35)	58.34 (6.66)	0.0692
Height (cm)	162.64 (5.75)	160.50 (7.70)	0.0925
Body mass index (kg/m^2)	23.35 (3.13)	22.72 (2.73)	0.3315
Hip BMD (g/cm^2)	0.851 (0.129)	0.823 (0.105)	0.2956
Spine BMD (g/cm^2)	0.950 (0.183)	0.961 (0.151)	0.7742
Female	n = 197	n = 27	
Age (years)	73.76 (5.51)	72.33 (4.67)	0.2012
Weight (kg)	55.01 (9.01)	48.62 (7.98)	0.0006
Height (cm)	151.48 (4.99)	148.61 (6.23)	0.0072
Body mass index (kg/m^2)	23.93 (3.44)	21.98 (3.05)	0.0056
Hip BMD (g/cm^2)	0.697 (0.113)	0.691 (0.112)	0.7654
Spine BMD (g/cm^2)	0.757 (0.141)	0.787 (0.137)	0.3028

BMD, bone mineral density; SD, standard deviation.
a P-value of t-test for continuous or Chi-squared test for categorical variables.

osteoporosis prevention regime, health promotion and raised public awareness of osteoporosis in Hong Kong since 2001. The Hong Kong experience may set an example to other Asian countries for reference in combating osteoporosis.

Lau *et al.*[13] reported that the prevalence of vertebral fracture among Chinese men aged 70–79 years in 1998 in Hong Kong was 16%. The present study shows a similar result; 9.2% and 18% for men aged 65–74 and ≥75 years, respectively.

This study found that both male and female subjects aged ≥75 years with a lower hip BMD have more vertebral fractures. Most vertebral fractures are not caused by direct trauma[26] but are linked with low BMD.[10,12] Previous studies have shown that US women of African descent have the highest bone mass in the spine, while Caucasian women have intermediate values, and Asian women have the lowest values (unadjusted BMD values). An analysis and comparison of different ethnic populations residing in the USA suggested that the BMD of Asian women differed little from that of Caucasian women after adjustment for body size.[27] Unadjusted lumbar spine and femoral neck BMDs were 7–12% and 14–24% higher in African-American women compared with Caucasian, Japanese or Chinese women. Among women of comparable weight of <70 kg, there were no differences in lumbar spine BMD among African-American, Chinese and Japanese women, all of whom have higher BMDs than Caucasians.[20] This study also noted that there were no differences in lumbar spine and hip BMDs between Hong Kong and Japanese women or men. Kung reported that the pattern and magnitude of age-related bone loss in the lumbar spine was similar between female Asian and Caucasian populations.[20] Subjects with a spinal fracture had a spine or hip BMD that was 20–30% lower compared with normal healthy controls. After adjusting for age and body size, each SD reduction in bone density in the Hong Kong Chinese women increased the risk of vertebral fracture approximately two-fold for both spine and femoral neck measurements, whereas in Beijing Chinese women, each SD reduction in BMD at the spine or hip was associated with a 2.5-fold increased risk of vertebral fracture.[20] In the present study, among Hong Kong and Japanese women, each SD reduction in hip BMD was associated with a 3.2-fold increased risk of vertebral fracture after adjustment for age and body size, which is consistent with the previous finding. In men, each SD reduction had a 1.5-fold increased risk, showing less

Table 6 – Logistic regression of vertebral fracture.

Variable	Mean (SD)/frequency (%)		Unit	Adjusted OR (95% CI)
	Control	Vertebral fracture		
Male	n = 187	n = 36		
Age	73.57 (5.27)	74.61 (5.29)	5	1.15 (0.81–1.65)
Country				
Hong Kong	171 (91.4%)	27 (75.0%)	–	1
Japan	16 (8.6%)	9 (25.0%)	Japan/Hong Kong	**3.67 (1.42–9.49)**
Weight (kg)	61.48 (9.17)	60.94 (9.21)	5	1.27 (0.95–1.69)
Height (cm)	162.59 (5.77)	161.07 (7.14)	5	0.77 (0.55–1.09)
Hip BMD (g/cm^2)	0.855 (0.126)	0.816 (0.125)	−0.1	**1.47 (1.001–2.17)**
Female	n = 201	n = 23		
Age	73.09 (5.31)	77.43 (4.81)	5	**1.90 (1.13–3.20)**
Country				
Hong Kong	180 (89.6%)	17 (73.9%)	–	1
Japan	21 (10.5%)	6 (26.1%)	Japan/Hong Kong	**5.99 (1.58–22.68)**
Weight (kg)	54.45 (9.10)	53.42 (9.69)	5	**1.61 (1.11–2.33)**
Height (cm)	151.51 (5.01)	148.55 (6.39)	5	0.68 (0.39–1.17)
Hip BMD (g/cm^2)	0.707 (0.109)	0.608 (0.115)	−0.1	**3.23 (1.72–6.25)**

BMD, bone mineral density; SD, standard deviation; OR, odds ratio; CI, confidence interval.
Bold: P-value < 0.05.

influence than that in women. However, low BMD is still a causal factor of vertebral fracture.[12]

Lifestyle and medical factors are other important determinants of vertebral fracture. Women who had jobs involving heavy physical labour had a lower prevalence of vertebral fracture than women who had had more sedentary jobs. This suggests that strenuous physical activity during young adulthood is protective against vertebral fracture.[6] Gregg *et al.*[28] found that physical activity reduced the risk of hip fracture but not vertebral or wrist fractures. However, in this study, subjects with vertebral fracture had significantly lower SF-12 (physical) scores, which implies that poor physical strength may lead to more vertebral fractures. Stroke is another risk factor for vertebral fracture. Kim *et al.* reported that in the acute stages of stroke, bone loss progressed rapidly. Risks of osteoporosis and vertebral fracture were higher among subjects who had experienced a stroke.[29] People with cataracts were more likely to fall, which increases the risk of fracture.[30] The prevalence of vertebral fracture was higher in farmers. This may be explained by the lower intake of calcium. Kamiyama *et al.* performed a survey in various areas in Japan, and found that calcium intake in three farm villages was lower than that in the city (512, 532 and 601 mg vs 633 mg). The prevalence of osteoporosis was also higher in farm villages.[31]

Subjects from Hong Kong had the highest prevalence of hypertension, heart disease and myocardial infarction/angina, but the association with vertebral fracture was insignificant. This implies that hypertension, heart disease and myocardial infarction/angina are not direct risk factors for vertebral fracture. However, Lau *et al.*[32] reported that hypertension was associated with higher BMD; this may explain the fact that the lowest prevalence of vertebral fracture was seen in Hong Kong.

There were more male smokers in Indonesia. However, smoking in Indonesia did not appear to lead to adverse effects resulting in vertebral fracture. Grazio *et al.*[33] found that current smoking was a risk factor for vertebral fracture, but a study by Bensen *et al.*[34] did not. Similarly, the rate of falls was lowest in Indonesia, but this did not reflect on the prevalence of vertebral fracture, implying that falls are not a strong risk factor for vertebral fracture. This differed from hip fracture, which was always associated with falls and trauma[20] and 90% of cases resulted from falls.[35]

This study was a joint venture between Hong Kong, Thailand, Indonesia and Japan. Radiographic assessments of vertebral fractures were completed carefully in all four countries using the same methodology. As subjects were recruited using community activities and community advertisements, the subjects were members of the general population and hence the results are representative. The percentages of people who worked as farmers in Hong Kong, Indonesia and Thailand were 2.1%, 9.3% and 42.4% in this study, which is close to the population figures: 0.9%, 12.4% and 39%, respectively.[36–38] Unfortunately, the Indonesian and Thai collaborators in this study did not possess a DXA machine; otherwise data correlation between the groups could be more comprehensive. Likewise, the questionnaire was not used in Japan, which influenced the completeness of this study. Moreover, it would be more convincing if a study with a larger sample size was conducted. Despite the obvious limitations, this study provides useful data for prevention planning. Some of these data are similar to the results of previous studies, but some are unique (e.g. strong association between low SF-12 (physical) score and vertebral fracture among Asians; smoking habit was not an important risk factor for vertebral fracture).

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Ethical approval

The institutional review board at each centre approved the study protocol, and written informed consent was obtained from all participants.

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Conflict of interest

None declared.

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ORIGINAL ARTICLE

Ethnic difference of clinical vertebral fracture risk

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Abstract
Summary Vertebral fractures are the most common osteoporotic fractures. Data on the vertebral fracture risk in Asia remain sparse. This study observed that Hong Kong Chinese and Japanese populations have a less dramatic increase in hip fracture rates associated with age than Caucasians, but the vertebral fracture rates were higher, resulting in a high vertebral-to-hip fracture ratio. As a result, estimation of the absolute fracture risk for Asians may need to be readjusted for the higher clinical vertebral fracture rate.
Introduction Vertebral fractures are the most common osteoporotic fractures. Data on the vertebral fracture risk in Asia remain sparse. The aim of this study was to report the incidence of clinical vertebral fractures among the Chinese and to compare the vertebral-to-hip fracture risk to other ethnic groups.
Methods Four thousand, three hundred eighty-six community-dwelling Southern Chinese subjects (2,302 women and 1,810 men) aged 50 or above were recruited in the Hong Kong Osteoporosis Study since 1995. Baseline demographic characteristics and medical history were obtained. Subjects were followed annually for fracture outcomes with a structured questionnaire and verified by the computerized patient information system of the Hospital Authority of the Hong Kong Government. Only non-traumatic incident hip fractures and clinical vertebral fractures that received medical attention were included in the analysis. The incidence rates of clinical vertebral fractures and hip fractures were determined and compared to the published data of Swedish Caucasian and Japanese populations.
Results The mean age at baseline was 62±8.2 years for women and 68±10.3 years for men. The average duration of follow-up was 4.0±2.8 (range, 1 to 14) years for a total of 14,733 person-years for the whole cohort. The incidence rate for vertebral fracture was 194/100,000 person-years in men and 508/100,000 person-years in women, respectively. For subjects above the age of 65, the clinical vertebral fracture and hip fracture rates were 299/100,000 and 332/100,000 person-years, respectively, in men, and 594/100,000 and 379/100,000 person-years, respectively, in women. Hong Kong Chinese and Japanese populations

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have a less dramatic increase in hip fracture rates associated with age than Caucasians. At the age of 65 or above, the hip fracture rates for Asian (Hong Kong Chinese and Japanese) men and women were less than half of that in Caucasians, but the vertebral fracture rate was higher in Asians, resulting in a high vertebral-to-hip fracture ratio.
Conclusions The incidences of vertebral and hip fractures, as well as the vertebral-to-hip fracture ratios vary in Asians and Caucasians. Estimation of the absolute fracture risk for Asians may need to be readjusted for the higher clinical vertebral fracture rate.

Keywords Asian · Chinese · Fracture incidence · Osteoporosis · Vertebral fracture

Introduction

Osteoporosis is a disease associated with decreased bone mass and bone strength and leads to increased fracture risk. Osteoporosis has become a major public health concern in the past decade due to the high prevalence and health care costs associated with it. Vertebral fractures, despite being the most common osteoporotic fracture, accounting for nearly 50% of all osteoporotic fractures, have received little attention compared to hip fractures. Data on the epidemiology of vertebral fractures in Asia remain sparse [1]. It has been shown that both symptomatic and asymptomatic vertebral fractures are predictors of future osteoporotic fractures [2] and are associated with physical deformity, as well as reduced mobility and quality of life [3, 4], and increased mortality [5, 6].

Unfortunately, obtaining accurate information on vertebral fracture is made difficult by the variable presentation of symptoms and the lack of a gold standard for the definition of vertebral fracture. Although vertebral fractures typically present with back pain, height loss and kyphosis, up to 75% of vertebral fractures were not diagnosed clinically due to the absence of specific symptoms in some cases and the difficulty in determining the cause of these physical symptoms [7]. Numerous methods were developed to help objectively identify morphometric vertebral fractures. The more important ones include the quantitative methods of measuring vertebral body height on radiographs [8, 9], as well as the semi-quantitative method proposed by Genant et al. [10]. These assessments use different cut-offs to define the presence of a vertebral fracture, and the reference for comparison of vertebral height could either be the individual's adjacent vertebral body or the mean of a reference population. These variations affected the sensitivity and specificity of the assessments resulting in high false-negative and false-positive rates and also created a considerable discordance of results in assessing the prevalence and incidence of vertebral fractures [11–13]. Also, vertebral fractures can also be confused with normal variants in vertebral shape or other end-plate deformities caused by other diseases Therefore, the exclusion of other vertebral deformities in order to make a correct diagnosis of vertebral fracture can only be accomplished by visual inspection and expert interpretation of the radiograph [14].

The lack of a gold standard for a definition of vertebral fracture makes it difficult to assess the true incidence of vertebral fractures. Previous cross-sectional and retrospective studies have suggested a similar prevalence of vertebral fracture in Asians and Caucasians [15–19] despite their lower hip fracture rates [20]. The World Health Organization (WHO) developed fracture risk assessment algorithms (FRAX®) to provide 10-year probabilities of hip fracture and major osteoporotic fracture (clinical spine, hip, humerus and forearm) based on a clinical risk factor profile and country-specific fracture and death incidence. The most complete models available are from the UK, Sweden, Japan and the US since the epidemiology of the relevant fractures is established [21]. However, the FRAX® models for some other countries (France, Spain, Italy, Turkey, Mainland China Hong Kong, etc.) are based on hip fracture risk alone due to the lack of ethnic-specific data and use assumptions, i.e. the site of fracture ratios observed from the Swedish population, to derive the relevant risk functions for other major fractures including vertebral fractures [22]. The objectives of this study were (1) to report the incidence rates of clinical vertebral and hip fractures in a prospective cohort of Chinese men and women, (2) to compare the clinical vertebral and hip fracture rates with those of other ethnic groups, and (3) to evaluate whether a fracture prediction model that assumes a universal spine-to-hip fracture ratio may be biased.

Methods

Hong Kong

This is the first prospective study of clinical vertebral fracture in an Asian population and is a part of the prospective Hong Kong Osteoporosis Study in which community-dwelling Southern Chinese men and women aged 50 or above were recruited from health fairs held in various districts in Hong Kong since 1995 [19, 23]. Baseline demographic data including anthropometric measurements, low-trauma fracture history after the age of 45 years, age at menopause and the use of hormone replacement therapy, medical history and symptoms associated with clinical vertebral fractures were obtained using a structured questionnaire at baseline. Subjects with conditions associated with vertebral deformity, including