

## 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  $62 \pm 8.2$  years for women and  $68 \pm 10.3$  years for men. The average duration of follow-up was  $4.0 \pm 2.8$  (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 preva-

lence 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<sup>®</sup>) 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<sup>®</sup> 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

osteomalacia, Paget's disease, Scheuermann's disease, hyperparathyroidism, renal bone disease and malignancy with bone metastasis, were excluded. Information on symptoms associated with vertebral fractures was also collected, including difficulty in bending forward, kyphosis (occiput-to-wall >0 cm and/or gap between the costal margin and iliac crest <3 fingerbreadths), low back pain and height loss more than 2 cm since the age of 25 years. These data were collected from interviews conducted by a trained research assistant.

All subjects were followed annually via telephone interviews using a structured questionnaire for assessment of the clinical outcome of incident fractures, falls, hospitalization, use of anti-osteoporotic medications, living status and functional status. Subjects who commenced anti-osteoporosis medication prior to the occurrence of a primary fracture were excluded. Medical history and incident fractures were verified with the computerized patient information system of the Hospital Authority of the Hong Kong Government. For this study, only non-traumatic incident hip fractures and clinical vertebral fractures were included in the analysis. Hip fractures were defined as having a diagnosis coded as International Classification of Disease, Tenth Revision (ICD-10) S72.0–S72.2 (fracture of the femoral neck, intertrochanteric, trochanteric, or subtrochanteric), and clinical vertebral fractures were identified in subjects who received medical attention from a physician with a diagnosis coded as ICD-10S22.0–S22.1 (fracture of the thoracic vertebra/multiple thoracic vertebrae), S32.0 or S32.7 (fracture of the lumbar vertebra/multiple lumbar vertebrae). Pathological fractures or fractures caused by traffic accidents or falls from standing heights were excluded. The study was approved by the Institutional Review Board of the University of Hong Kong and the Hong Kong West Clusters Hospital of the Hospital Authority.

#### Japan

The hip and clinical vertebral fracture incidence rates for the Japanese were obtained from previously published data used to develop the Japanese version of FRAX<sup>®</sup> [24]. The hip fracture incidence rate was based on data from a census study in Tottori Prefecture, Japan, in 1994 [25]. The incidence of vertebral fracture was based on data obtained from the Adult Health Study in Hiroshima, Japan [26]. Participants were followed through biennial medical examination including radiology assessments since the establishment of the study in 1958. A total of 2,613 subjects (763 men and 1,593 women) who attended at least two follow-up examinations in 1994 to 2000 were included in the analysis. An incident morphometric vertebral fracture was diagnosed by lateral and posterior–anterior chest and spinal

X-rays using the semi-quantitative assessment [12], in which a decrease of at least 20% in height of any vertebral body from initial reading to the end of the study was defined as a morphometric vertebral fracture. Since the incidence of clinical vertebral fracture was not known in Japan, the ratio of clinical fracture to morphometric fracture incidence was assumed to be the same in Japan as it was for Sweden when the Japanese version of FRAX<sup>®</sup> was developed, i.e. 30% of morphometric vertebral fractures were assumed as clinical fractures [24, 27].

#### Sweden

The incidence rates of hip and clinical vertebral fractures for Swedish Caucasians were also obtained from a previously published study by Kanis et al., in which all incident fractures, including hip fractures (1991) and clinical vertebral fractures (1993 and 1994) were identified from files at the Department of Diagnostic Radiology in Malmö, Sweden, for the relevant year. Only vertebral fractures that came to clinical attention were captured, and subjects who previously sustained a fracture of the same type were excluded from analysis. The annual incidences of hip and clinical vertebral fractures were calculated for men and women by age [28].

#### Statistical analyses

Baseline characteristics of the Chinese subjects are expressed in means±SD for continuous variables and in percentage for categorical variables. Time to incident hip or vertebral fractures was calculated according to the date of X-ray reports or physician's consultations when the diagnosis was made. The average follow-up period for all subjects was 4.0±2.8 (range, 1 to 14) years, with a total follow-up of 14,733 patient-years. Subjects who had received anti-osteoporosis medication after sustaining a fracture during the follow-up period or those who deceased at the time of analysis were analysed up to their time of treatment initiation or last contact time point. Incidence rates were reported as rate per 100,000 person-years. The incidence rates of vertebral and hip fractures were compared to the published data from Japan and Sweden. Vertebral-to-hip fracture ratios were used to demonstrate the proportion of vertebral fractures in relation to hip fractures in different populations.

#### Results

A total of 4,116 Southern Chinese subjects (2,302 women and 1,810 men) aged 50 or above were included in the analysis. The mean age at baseline was 62±8.2 years for

women and  $68 \pm 10.3$  years for men. Of the women, 37.2% and 63.4% of men were above the age of 65 years. Baseline demographic information and characteristics are shown in Table 1. Of the men, 55.5% and 72.1% of women reported having difficulty bending forward, kyphosis, low back pain and/or height loss  $>2$  cm since the age of 25. However, only 2.7% of men and 5.5% of women reported a history of past clinical vertebral fracture.

Two hundred and sixty-seven subjects had died at the time of analysis (77 women and 190 men), and 353 patients (333 women and 19 men) received anti-osteoporosis medication after sustaining a fracture during the follow-up period. The data for these subjects were analysed up to their last contact time point or time of treatment initiation, respectively. During the follow-up period, 57 clinical vertebral fractures and 34 incident hip fractures were reported (11 vertebral fractures and 10 new hip fractures in men; 46 vertebral fractures and 24 new hip fractures in women). The incidence for vertebral fractures was 194 per 100,000 person-years in men and 508 per 100,000 in women (overall female/male ratio=2.6:1), and the incidence for hip fractures was 176 per 100,000 person-years in men and 265 per 100,000 person-years in women (female/male ratio=1.5:1). Table 2 shows the incidence rates of clinical vertebral and hip fractures according to sex and age groups. Both clinical vertebral and hip fracture incidences increased exponentially with increasing age in both sexes. Men aged 50–55 years had a fracture incidence of 50 per 100,000 person-years for the vertebra and 10 per 100,000 for the hip versus men aged 85 years and above who have a

vertebral fracture incidence of 954 per 100,000 person-years and a hip fracture incidence of 477 per 100,000 person-years. Similarly, incidences of vertebral and hip fracture increase from 219 and 16 per 100,000 person-years in women 50 years of age to 2,689 and 1,377 per 100,000 person-years, respectively, at age 85. Overall, men older than 65 years have a vertebral fracture incidence of 299 per 100,000 person-years and hip fracture incidence of 332 per 100,000 person-years, and the overall incidence of vertebral and hip fractures for women older than 65 years were 594 per 100,000 person-years and 379 per 100,000 person-years, respectively.

The fracture incidence of Chinese subjects was compared to those of the Swedish and Japanese populations. The incidence rates of hip fractures in Caucasian men and women rose exponentially with age, whereas the rise was near linear for vertebral fractures. In contrast, for Asian women in Hong Kong and Japan, the incidence rate for vertebral fractures rose exponentially with age, whereas the rise was near linear for hip fractures. In Asian men, both the incidence rates of vertebral and hip fractures rose near linearly with age. The hip fracture incidences in Hong Kong men and women were similar to those of Japan but much lower than those of the Caucasian population in Sweden. For example, the hip fracture rates for Hong Kong men and women aged 65 to 69 years old were only 49% and 33%, respectively, of those of the Caucasian men and women in the same age group. However, the incidence of vertebral fractures in Asian men was similar to that of Caucasian men; and Asian women have a much higher

**Table 1** Clinical characteristic of the study population (Mean $\pm$ SD)

	Men ( $n=1,810$ )	Women ( $n=2,302$ )
Years of follow-up (mean $\pm$ SD (range))	3.5 $\pm$ 2.9 (1–14)	4.7 $\pm$ 2.6 (1–14)
Age (year)	68 $\pm$ 10.3 (50–99)	62 $\pm$ 8.2 (50–91)
Height (cm)	164.6 $\pm$ 6.5	152.7 $\pm$ 6.0
Weight (kg)	62.9 $\pm$ 10.3	55.3 $\pm$ 9.1
Body mass index (kg/m <sup>2</sup> )	28.1 $\pm$ 8.4	23.7 $\pm$ 3.7
Number of postmenopausal women	–	2,229 (96%)
Age at menopause (year)	–	49.5 $\pm$ 4.0
Current or history of hormone replacement therapy	–	217 (9.4%)
Difficulty bending forward	185 (10.2%)	365 (15.8%)
Kyphosis	78 (4.3%)	126 (5.5%)
Low back pain	510 (28.2%)	1,336 (58.0%)
Height loss $>2$ cm since 25 years old	442 (24.4%)	854 (37.1%)
Have at least one of the above symptoms	1,004 (55.5%)	1,660 (72.1%)
History of clinical vertebral fracture	48 (2.7%)	126 (5.5%)
History of hip fracture	24 (1.7%)	31 (1.3%)
Incident clinical vertebral fracture at follow-up	11 (0.6%)	46 (2.0%)
Incident hip fracture at follow-up	10 (0.6%)	24 (1.0%)

**Table 2** Incidence (per 100,000 person-years) of hip and clinical vertebral fracture according to sex and age groups

Fracture site and age group	Men	Women	F/M
<b>Hip</b>			
50–54	10	16	1.6
55–59	21	31	1.5
60–64	46	57	1.2
65–69	99	103	1.0
70–74	215	273	1.3
75–79	348	527	1.5
80–84	602	1,059	1.8
85+	477	1,377	2.9
<b>Vertebral</b>			
50–54	50	219	4.4
55–59	111	313	2.8
60–64	165	516	3.1
65–69	95	564	5.9
70–74	226	874	3.9
75–79	450	1,205	2.7
80–84	594	2,119	3.6
85+	954	2,689	2.8

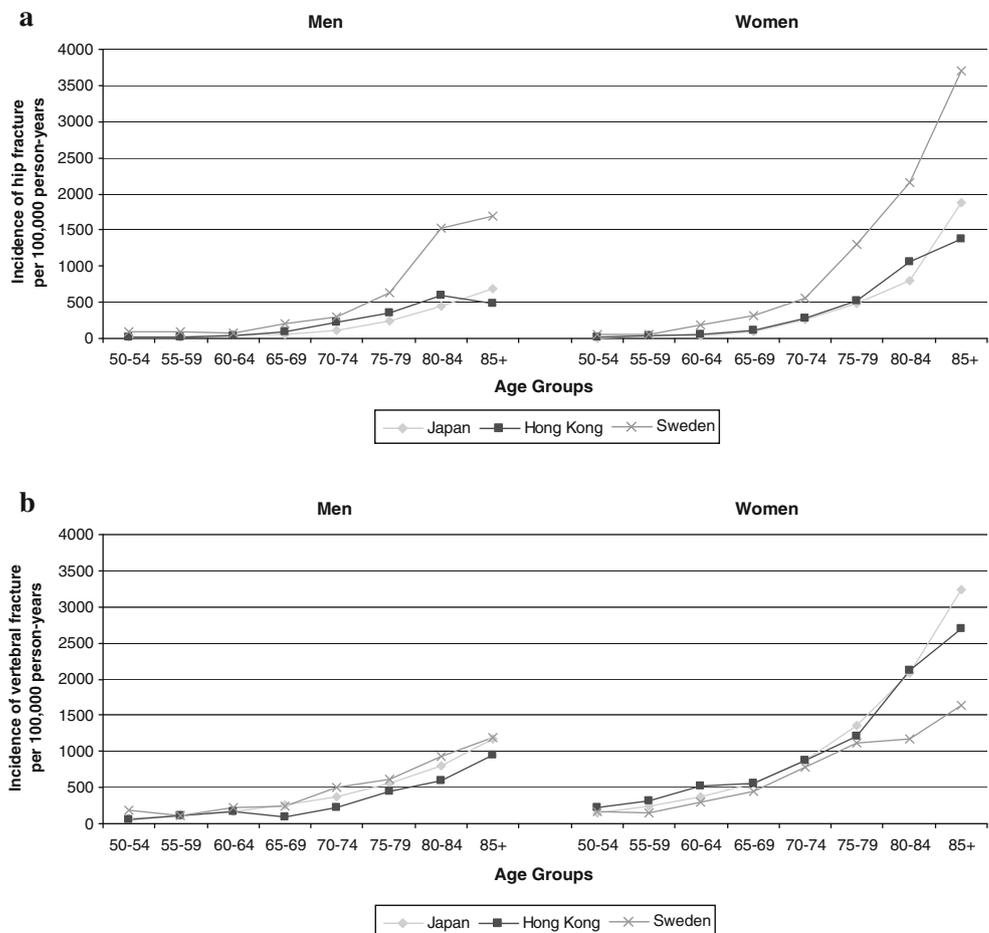
vertebral fracture incidence than Caucasian women (Fig. 1a and b). Among older women aged 80 or above, the incidence of vertebral fracture in Asians almost doubled to that of Swedish Caucasian women.

The spine-to-hip fracture ratios also differed between different Asians and Caucasians. Although vertebral fractures occur with a higher incidence earlier in life than hip fractures in both Asians and Caucasians, Asians have a much higher spine-to-hip fracture ratio than Caucasians, meaning vertebral fractures have a higher proportion to hip fractures in Asians than in Caucasians, especially among subjects younger than 65 years (Table 3).

**Discussion**

Vertebral fractures are the most common type of osteoporotic fractures, and they are well known as an independent predictor of future osteoporotic fractures, including both vertebral and non-vertebral fractures [22]. However, reports about the incidence of vertebral fracture are scant because of the discrepancies in the definition of vertebral fracture and the difficulties in recognizing them clinically. A

**Fig. 1** Age-specific incidence rates (per 100,000 person-years) in Hong Kong compared to Japanese and Swedish Caucasians for hip fracture (a) and clinical vertebral fracture (b)



**Table 3** Age- and sex-specific clinical vertebral-to-hip fracture ratio in Hong Kong compared to Japanese and Swedish Caucasians

Age group	Men			Women		
	Japan [24]	Hong Kong	Sweden [28]	Japan [24]	Hong Kong	Sweden [28]
50–54	3.9	5.0	2.2	N/A <sup>a</sup>	13.7	2.6
55–59	7.1	5.3	1.4	4.7	10.1	2.9
60–64	2.8	3.6	3.2	8.9	9.1	1.6
65–69	4.1	1.0	1.2	6.3	5.5	1.4
70–74	3.5	1.1	1.7	3.4	3.2	1.4
75–79	2.3	1.3	1.0	2.8	2.3	0.8
80–84	1.8	1.0	0.6	2.6	2.0	0.5
85+	1.7	2.0	0.7	1.7	1.1	0.4

<sup>a</sup> Clinical vertebral-to-hip fracture ratio for Japanese women aged 50–54 was not available since the hip fracture incidence for this group was zero

previous study has shown that the postmenopausal women in Hong Kong, Beijing and Taiwan have a similar prevalence of morphometric vertebral fracture as Caucasian women in the USA and Europe (about 25% in all regions), in contrast to the marked worldwide variations in the prevalence of hip fractures [21]. The present study further confirmed that, although the risk of hip fractures in Asians was low, Asian men do have a vertebral fracture risk similar to Caucasian men, and Asian women have an even higher clinical vertebral fracture risk than Caucasian women.

The observed ethnic differences in fracture incidences may be due to the fact that hip fracture risk was affected by fall risk, whereas the risk of vertebral fracture mostly depends on bone strength [13]. Despite the low hip fracture rate in our population, Hong Kong women had a higher prevalence of osteoporosis (bone mineral density T-score  $\leq -2.5$  at any one site in reference to ethnic-specific peak young mean according to the ISCD recommendation) than US Caucasian women (35.8% vs. 20%, respectively) [29, 30] and a similar prevalence of about 6% in Hong Kong and US Caucasian men [31]. In view of the ethnic differences, it is important to obtain accurate information on population fracture risk to characterize the absolute fracture risk of individual subjects. At present, information on the risk of clinical vertebral fracture in Asians is lacking, and the WHO fracture risk assessment algorithms (FRAX<sup>®</sup>) estimated population-specific absolute major osteoporotic fracture risks based on the assumption that the ratio of hip-to-vertebral fracture is the same as that observed in Swedish populations to provide. However, our study demonstrated the variations of the spine-to-hip fracture ratios between ethnic groups; thus, a fracture prediction model that assumes a universal spine-to-hip fracture ratio may be biased.

Our previous prospective study on Southern Chinese men over 50 years old has shown that the FRAX<sup>®</sup> algorithm seemed to overestimate the 10-year major osteoporotic fracture risk in subjects with low fracture risk, but under-

estimated the risk for high-risk groups [29]. Results from the current study raise a concern that a model that presumes a ratio of vertebral fractures to hip fractures in a Swedish population might underestimate the risk of vertebral fractures in Asians, resulting in a general underestimation of the absolute risk of major osteoporotic fracture.

Strengths of this study include the use of a community-based population to investigate the incidence rate of clinical vertebral fractures. All clinical vertebral fractures and hip fractures were confirmed by the medical record. A major limitation of the present study is that the comparisons to incidence rate of clinical vertebral fracture to other ethnic groups were based on published literatures, and the data among Asian countries are scanty. Japan is the only country in Asia that reported the incidence rate on morphometric vertebral fractures based on a radiographic survey in a community-based population. Also, the Japanese data used for comparison came from the early 1990s, and there has been some evidence that hip fracture rates are increasing in Asians [20]. The impact on the change in epidemiology of fracture in Asians has not been evaluated. Another drawback of the present study is that only the incidences of clinical vertebral fractures were reported due to the lack of a common definition of morphometric vertebral fractures in other publications. Furthermore, the sample size and the number of fractures recorded in the men's cohort were small, and this study may have underestimated the fracture rates in the general male population.

In conclusion, this study demonstrated that while the hip fracture incidence in Asians is lower than in Caucasians, the incidence of clinical vertebral fractures was at least as high in Asians as in Caucasians.

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**Conflicts of interest** None.

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