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Review article

Epidemiology and diagnostic approaches to vertebral fractures in Asia

Annie W.C. Kung

Department of Medicine, University of Hong Kong, Queen Mary Hospital, 102 Pokfulam Road, Hong Kong, PR China

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Introduction

Osteoporosis represents a major public health problem worldwide, due mainly to the complications of fracture. Osteoporotic fractures, especially those of the hip and spine, cause considerable mortality and morbidity, and represent a tremendous socioeconomic burden. Currently, the Western nations have the highest incidence rates for hip fracture among women. However, it is expected that, over the next 50 years, there will be dramatic demographic changes around the world, resulting in vastly increased rates of hip fracture in Asia and Latin America [1]. This shift will largely be accounted for by population increases and increasing life expectancy in these regions. It is projected that half of the world's hip fractures in 50 years' time will occur in Asia, so that, by the year 2050, more than 3 million hip fractures will occur in Asia.

Interestingly, the incidence of hip fracture varies markedly even within a region. In Asia, the incidence of hip fracture among women in the urban areas of Hong Kong and Singapore is almost as high as that reported in Caucasian women, and is approximately 400 per 100 000 population per year [2]. This is almost ten times that reported in Korea [3]. Similarly, the incidence of hip fracture in Beijing, northern China, is among the lowest in the world [4]. Hip fracture is almost always associated with falls and trauma. Thus, apart from ethnic differences, co-existing factors predisposing to falls, such as poor muscle co-ordination and balance, visual impairment, and frailty, affect the incidence of hip fracture.

Offprint requests to: A. Kung
(e-mail: awckung@hkucc.hku.hk)
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Epidemiology of spine fracture

Among the various kinds of osteoporotic fractures, vertebral fractures are the most common worldwide. Unlike hip fracture, many vertebral fractures are asymptomatic and go undetected, and less is known about their epidemiology. Up to 75% of vertebral fractures are silent, as less than 1% of back pain is due to vertebral fractures. In Caucasian women, about 20%–25% of women aged above 50 years have vertebral fractures [5]. The incidence rate for clinically diagnosed vertebral fractures in Caucasian women increases from approximately 30 per 100 000 patient–years at age 50 years to approximately 1000 per 100 000 patient–years at age 85 years [6].

It has been difficult to compare the prevalence of vertebral fractures in various regions of the world because studies have differed in their approaches in selecting samples of the population and they have also differed in the methods used for diagnosing vertebral fractures and in the definition of the fractures. Early epidemiological studies of vertebral fracture used subjective radiological assessment of concave, wedge, and compression deformities, but these were poorly reproducible. These methods gave way to morphometric measurement of vertebral height, with fractures defined according to fixed cutoff values. The vertebrae from T4 to L4 can be graded visually after measurement of the anterior (Ha), middle (Hm), and posterior (Hp) vertebral heights. Each vertebral body in the spineal column has unique dimensions. The mean and SD of the vertebral height ratios were defined for each vertebral body, i.e., the anterior-to-posterior ratio (Ha/Hp), middle-to-posterior ratio (Hm/Hp), and posterior-to-posterior ratio above and below (Hp/Hp-1 and Hp/Hp+1) were calculated. Although a number of algorithms have been derived [7–11], the most commonly adopted criterion for defining a fracture is 3 SDs below the mean of the vertebral height ratios. Using this criterion, the preva-

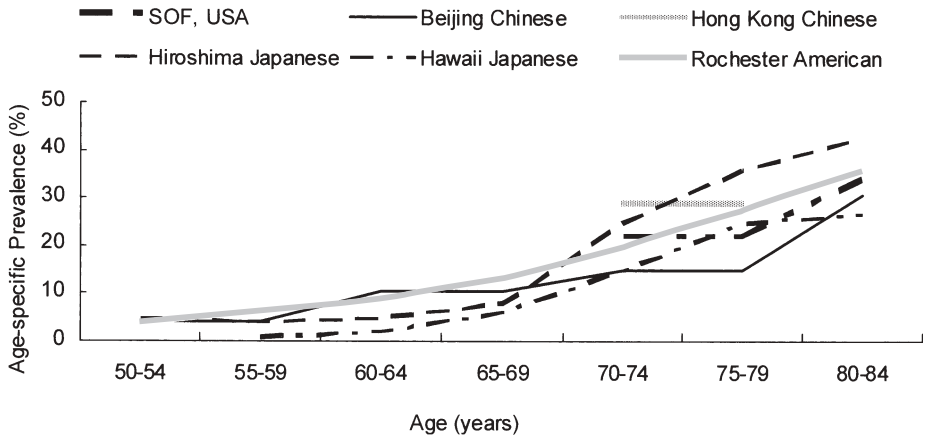

Fig. 1. Age-specific prevalence of vertebral fractures in Asian women compared to Caucasian women. Vertebral fracture is defined as more than 3 SDs below the mean of the vertebral height ratios. Data from: The Study of Osteoporotic Fractures Research Group (SOF), USA [9], Beijing Chinese [12], Hong Kong Chinese [13], Hiroshima Japanese [14], Hawaii Japanese [14], and Rochester American [15] populations

lence of vertebral fracture in different populations in Asia was compared to that in Western populations. Figure 1 shows the age-specific prevalence of vertebral fractures among Caucasians and Asians. While the hip fracture incidence among the Asian populations was generally much lower than that in the Caucasians, the prevalence of vertebral deformity in postmenopausal women aged above 50 years was actually very similar across different ethnic groups, being about 20%–25%.

The prevalence of vertebral fractures in women in Beijing, northern China, increased steeply with age, from 3.9% at age 50–59 years to 31.2% for women aged 80 years and older [12]. Similarly, in Hong Kong, southern China, the prevalence of vertebral fracture is 29% for women aged 70–79 years [13]. Similar figures were reported in Japanese residing either in Japan or Hawaii [14]. These figures were not much lower than those observed in Caucasian Americans, which were 22% for women aged 70–79, and 34% for women aged 80 and above [15]. Using a slightly different algorithm to define the cutoffs, the prevalence of vertebral fractures in Chinese women was about 5% lower among women in Beijing, China, than in Rochester, USA [12]. Thus, in contrast with the much lower incidence of hip fracture, vertebral fractures in Asians are as prevalent as they are in Caucasians. The most frequent vertebral levels involved are T12 and L1. These levels correspond with the most biomechanically compromised regions of the thoracolumbar spine.

BMD and vertebral fracture risk

The ethnic variations in the rates of hip and vertebral fractures might be explained by their divergent etiology. Unlike hip fractures, most vertebral fractures are not associated with trauma. Among all risk factors, the major independent risk factor for vertebral fracture is a low bone mineral density (BMD) [16]. Comparison of unadjusted BMD values showed that African-American women had the highest bone mass at the spine, while Caucasian women had intermediate values, and Asian women the lowest. Vertebral heights also differed across different populations [13,17]. However, in the recently published Study of Women's Health Across the Nation (SWAN) comparing different ethnic populations residing in USA, the results demonstrated that the BMD of Asian women differred little from that of Caucasian women after adjustment for body size [18]. Unadjusted lumbar spine and femoral neck BMDs were 7%–12% and 14%–24% higher, respectively, in African-American women than in Caucasian, Japanese, or Chinese women. However, among women of comparable weights (<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. Femoral neck BMD is highest in African-Americans and is similar in Chinese, Japanese, and Caucasians. The pattern and magnitude of age-related bone loss in the lumbar spine is similar between female populations in the East and the West. Whether BMD adjusted for body size is similar between Asian and Caucasian men [19,20] is less well studied.

In comparison to healthy controls, subjects with spine fracture had a reduction of 20%–30% in bone mass at the spine and hip [21]. Similar to findings in Caucasian women, there was a strong relationship between BMD and vertebral fracture risk among Asian women. Data from southern Chinese women revealed that, after adjusting for age and body size, each SD reduction in bone density increased the risk of vertebral fracture by about two fold for both spine and femoral neck measurements [21]. A similar relation was observed in northern Chinese women in Beijing, with each SD reduction in BMD at the spine or the hip being associated with a 2.5-fold increased risk of vertebral fractures [12]. Using machines for peripheral measurements, such as quantitative bone ultrasound, a similar relation was ob-

served, with each SD reduction in the quantitative ultrasound index (QUI) being associated with a two fold increased risk of vertebral fracture [21]. The relation between BMD and vertebral fracture in Asian men is unclear.

Non-BMD risk factors

As observed in other populations, the risk of vertebral fracture appeared to increase with age in Asian women, independent of the decrease in spine BMD [12]. Apart from the reduction in bone mass, lifestyle factors are important determinants of vertebral fracture in Asian women. Women who had jobs involving heavy physical labor had a lower prevalence of vertebral fractures than women who had had more sedentary jobs [12]. This suggests that strenuous physical activity during young adulthood is protective against vertebral fracture. Other important lifestyle factors include weight, reproductive history, cigarette smoking, and calcium intake. However, the associations of these risk factors with spine fracture in Asian women are less well studied.

Clinical sequelae of spine fracture

Vertebral fractures are important because of their clinical consequences and the costs associated with their treatment. Severe fractures with displacement may result in neurological complications (including paraplegia) and also bowel and bladder dysfunction. Other sequelae include reduction of pulmonary function, hiatus hernia, and lengthy hospital stay, as well as back pain, limited activity, physical impairment, and decreased quality of life [22].

It is important to diagnose vertebral fractures because they are associated with an increased risk of further vertebral fractures, as well as an increased risk of non-vertebral fractures, and this increased risk remains after correction for BMD [23,24]. Analysis of more than 4000 women who had been randomly assigned to a placebo group in four large 3-year clinical trials conducted predominantly in Caucasian women showed that women with either prevalent fractures, low femoral neck BMD, or risk factors for hip fracture had a cumulative incidence of new vertebral fracture of 6.6% in the first year. The presence of one or more vertebral fractures at baseline increased the risk of sustaining a vertebral fracture by five fold during the first year of the study compared to subjects without prevalent vertebral fractures at baseline. Among those who developed an incident vertebral fracture, the risk of a new vertebral fracture in the subsequent year was increased by more than nine fold [24]. The risk of subsequent fractures involving all sites, i.e., including non-vertebral fracture, was increased by twofold with prior vertebral fractures [24]. Thus, it is important to diagnose vertebral fracture in asymptomatic subjects, as there are now effective agents that can reduce fracture risk by about 50% [25–30].

Diagnosis of vertebral fracture

Typically, there is no history of trauma before a vertebral fracture. Clinically, vertebral fractures present with back pain at the level of the fracture. Height loss of 2 cm or more since the age of 25 can help to identify women with vertebral fractures. Kyphosis is an important indicator of vertebral compression, and the loss of more than 4 cm in height is associated with kyphosis of 15°. Occiput-to-wall distance (normally 0 cm) as well as a decrease in the gap between the costal margin and iliac crest (normally three fingerbreadths) are both clinical measures of kyphosis [31].

In all patients with vertebral fracture, secondary causes, e.g., osteoporosis and metabolic bone disease, need to be considered. Investigations to exclude conditions such as osteomalacia, renal failure, tumor metastasis, multiple myeloma, hyperparathyroidism, and hyperthyroidism are necessary. Radiological investigations of patients with vertebral fractures include spinal radiograph, CT scan, MRI, bone scan, morphometric X-ray absorptiometry, and BMD assessment.

Radiographic diagnosis

Radiographs should always be obtained in all patients with clinical vertebral fracture to exclude pathological fracture. The conventional thoracolumbar spinal radiograph remains the gold standard for the evaluation of vertebral fracture. The assessment of vertebral fracture on conventional radiographs has been refined by using either quantitative or semiquantitative criteria. Quantitative approaches [7–10] are helpful in standardizing fracture assessment, but are time-consuming and require trained personnel. Using the semiquantitative approach described by Genant et al. [11], a vertebral body was considered to be fractured if it showed distinct morphological features suggesting a fracture, and the anterior, middle, and/or posterior height was reduced by approximately 20% upon visual inspection. A 20%–25% reduction in vertebral height and a reduction in area of 10%–20% is classified as mild deformity, more than 25%–40% reduction in any height and a reduction in area of 20%–40% is considered moderate deformity, and more than 40% reduc-

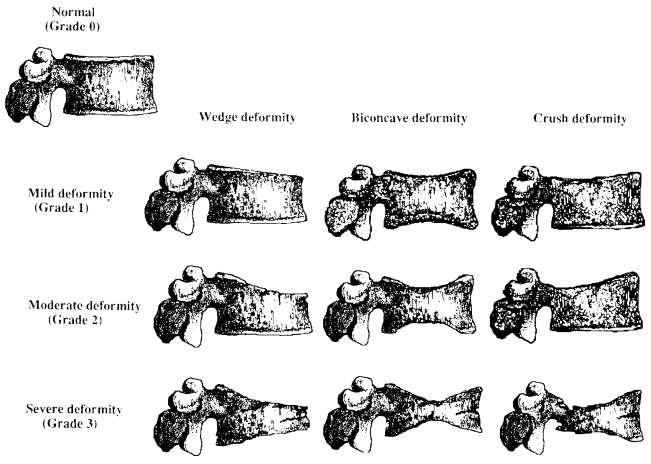

Fig. 2. Classification of vertebral fractures by the Genant semiquantitative method. Adapted from [11] with permission of the American Society for Bone and Mineral Research

tion in any height and area is considered severe deformity (Fig. 2).

However, variable radiographic quality and parallax distortion of the vertebral borders may complicate both semiquantitative and quantitative approaches. Occasionally, an initial radiograph may not demonstrate a fracture, but a bone scan may be positive in the first few months after a fracture. Furthermore, unless X-rays are performed in the entire population periodically on a routine basis, these fractures will be missed. If this were to be the practice, the cost to the health care system and the effect of radiation exposure would have to be seriously considered.

Morphometric absorptiometry

Contrary to conventional radiography, which uses cone-beam imaging geometry, fan-beam images of the spine, such as those obtained by morphometric absorptiometry (MXA), have no geometric distortion along the longitudinal axis of the spine and may increase the accuracy of vertebral dimension measurements [32]. High-resolution fan-beam images with extended-length lateral spine scan allow the visualization of both the thoracic and the lumbar spine from T4 to L4. This can be coupled with BMD evaluation in one setting. Clinical studies indicate that visual evaluation of fractures based on lateral spine images obtained from fan-beam dual-energy X-ray absorptiometry (DXA) agree strongly with radiographic assessment even with mild fractures [33]. Because of the difficulty in identifying vertebral fractures clinically, and the practical difficulties preventing routine radiographic assessment, visual assessment of vertebral status at the point of care may aid in clinical evaluation and improve risk assessment and evaluation.

Central DXA measurement

Measurement of bone mass with a DXA machine is the gold standard of diagnosing a patient with osteoporosis prior to fracture. The World Health Organisation task force group suggested a T score of 2.5 below the peak young mean as the diagnostic cutoff for osteoporosis [16]. In Japan, the cutoff BMD value is 70% below the young adult mean [34]. BMD measurement at the lumbar spine in the elderly may be falsely elevated due to the presence of osteophytes or aortic calcification, and assessment of the hip is the preferred site. The National Osteoporosis Foundation recommends BMD measurement for all women aged 65 years or above, regardless of additional risk factors [35]. Whether this practice is cost-effective among Asian populations is uncertain.

Peripheral densitometry

Machines for peripheral measurements, including quantitative bone ultrasound (QUS), peripheral quantitative computed tomography (pQCT), and radiographic absorptiometry (RA) are utilized extensively in Asian countries due to their lower cost and greater accessibility. Although there is now good evidence that peripheral measurements at the forearm, finger, or heel can predict fracture risk [36], there are still no WHO criteria for these peripheral diagnostic tools [37]. There are only limited data to define the cutoff criteria for diagnosis and treatment threshold [38–40]. Peripheral measurements such as calcaneal ultrasound and digital X-ray radiogrammetry correlate only moderately with BMD measured by DXA [37,41]. It is not certain whether patients identified using peripheral measurements will benefit from treatment to the same degree as those identified using central DXA. Furthermore, the role of peripheral measurements in monitoring treatment response is limited with the present technology.

Summary

In conclusion, vertebral fractures among Asian populations are as prevalent as they are in Caucasian populations. Most vertebral fractures are not recognized clinically. The presence of vertebral fractures increases the risk of future vertebral and non-vertebral fractures, and those with low bone density and prevalent vertebral fractures are at highest risk. To prevent the growing problem of osteoporosis in Asia, every effort should be made to evaluate vertebral fracture status and BMD, particularly in older postmenopausal women, in whom vertebral fractures are common.

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