



# Radiographic osteoporotic vertebral fractures in elderly men: a brief review focusing on differences between the sexes

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**Abstract:** Bone loss occurs in both sexes as a result of ageing but is exacerbated in women by the hormonal changes associated with menopause. Unlike in women, secondary osteoporosis occurs in almost half of men diagnosed with osteoporosis. Moreover, vertebral fractures (VFs) seen in elderly men may more likely be the result of high energy trauma. The osteoporotic vertebral fracture (OVF) radiograph diagnosis criteria for women may not be directly applicable for men. Particular attention should be paid to the mid-thoracic level where over-diagnosis commonly occurs. For wedge-shaped vertebral deformities (VDs) or VDs with anterior height reduction only, a diagnosis of OVF requires great caution, as they are poorly correlated to bone mineral density (BMD). For age-matched subjects, it is likely that elderly men's prevalent radiographic OVFs are approximately half of the elderly women's. This male-female ratio is very similar to other clinical fractures such as those occurring at the hip. Even so, the clinical relevance of OVF in elderly men may be less than that of elderly women. On the other hand, for elderly men with hip BMD-based osteoporosis, the OVF risk is as high as that of osteoporotic women. Elderly Chinese men have a lower OVF prevalence than age-matched Caucasian men.

**Keywords:** Osteoporosis; vertebral fracture (VF); radiograph; progression; incidence; men; women

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## Introduction

Over recent decades, osteoporosis has evolved from being considered as an inevitable consequence of ageing, to being recognized as an important and treatable disease. Osteoporotic vertebral fractures (OVFs) are the most common osteoporotic fracture. Appropriate interventions can reduce the occurrence of osteoporotic fractures, reducing pain and related disabilities (1-5). It is important to identify OVF, so that appropriate investigation, prevention, and treatment can be instigated, both for women and men (6). Osteoporosis affects men differently from women in a number of respects. Bone loss occurs in both sexes as a result of ageing but is exacerbated in women by the hormonal changes associated with the menopause.

Differences in skeletal size, mechanical loading and muscle mass also play a role in the patterns of bone loss in men and women.

Unlike in women in whom it is much rarer, secondary osteoporosis occurs in almost half of men diagnosed with osteoporosis (7,8). Major causes include hypogonadism due to treatment for prostate carcinoma with androgen withdrawal therapy, primary hyperparathyroidism, alcohol abuse, as well as glucocorticoid therapy for arthritis or asthma. For the diagnosis of osteoporosis in elderly men, a complete history and physical examination is essential and may reveal remediable disorders (7-9). Moreover, a vertebral fracture (VF) seen in elderly men may more likely be associated with high energy trauma. In their studies with 10 years' follow-up (FU), Ensrud *et al.* (10) reported that

although the majority of major osteoporotic fracture (MOF) events in each sex were classified as low energy trauma with most resulting from a fall from standing height or less, these proportions were lower in men compared with women (82% of MOF in men *vs.* 93% of MOF in women). MOF events were more commonly classified as related to high energy trauma in men compared with women (14.6% of MOF in men *vs.* 6.3% of MOF in women). MOF classified as moderate trauma also occurred more frequently in men compared with women (3% of MOF in men *vs.* 1% of MOF in women).

Much is known about OVF in women but OVF in men have been less well studied. This review focuses on the radiographic diagnosis of OVF, especially where this may differ between men and women. The clinical relevance of OVF, and possible ethnic differences in OVF prevalence, are also discussed.

### Sex-differences in the epidemiology of osteoporotic fractures

Before discussing OVF for which there are as yet no uniformly agreed diagnostic criteria, it may be helpful to look at those osteoporotic fractures which are definitively diagnosed. Though osteoporosis appears later in life in men than it does in women, bone loss in both sexes takes place in trabecular and cortical compartments with increased cortical porosity with age (6-9). Skeletal fragility with aging, in combination with a greater propensity to fall, results in an increased susceptibility to fractures. The most common non-vertebral osteoporotic fractures occur in distal forearm, humerus, hip, ribs and ankle. The annual incidence of fractures is higher in women than in men because at any age, there are more women than men below any given value of bone mineral density (BMD).

Hip fractures are associated with more disability, mortality and resource use than all other osteoporotic fractures combined. The epidemiology of hip fractures is well documented. In both sexes the incidence of hip fracture rises with increasing age. This increase begins at 60 to 65 years of age in women and at ~75 years of age in men (8,11). The majority of hip fractures in men occur in individuals aged >80 years (7). In Western countries approximately three out of four hip fractures occur in women (12). This huge difference in the absolute number of fractures is partly explained by the greater life expectancy of women. The age-standardized difference between women and men is lower with a ratio of about 2:1 in most countries of the world (13).

Wrist (Colles') fractures, a common type of fragility fracture in women, are much less common in men. Of every five incident wrist fractures, four occur in women (14). In their MrOS (USA) study, Wright *et al.* reported that during an average of nearly 11 years FU, the overall age-adjusted incidence of wrist fractures in the MrOS population was 1.60 per 1,000 person-years (15).

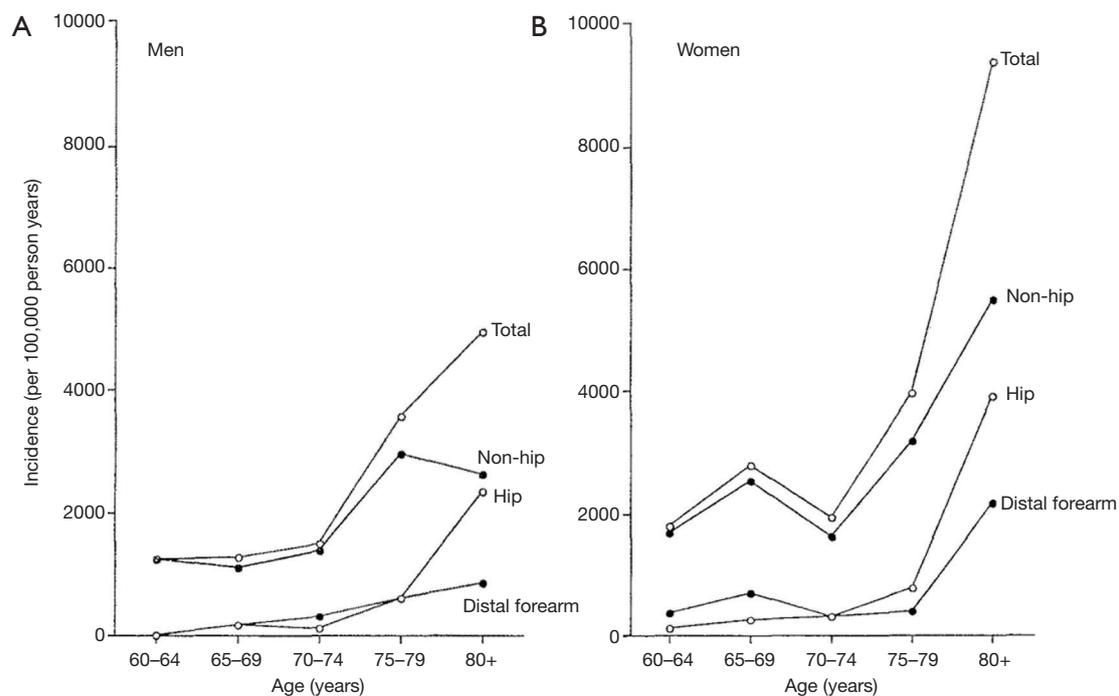
The age-specific fracture incidence for men and women from the Dubbo study in Australia is shown in *Figure 1* (16). This population-based study documents the incidence of all symptomatic fractures from 1989 to 1992 in a predominantly Caucasian population ( $\geq 60$  years). The overall fracture incidence in women was 3,250 per 100,000 person-years and in men was 1,940 per 100,000 person-years (1.67:1). It is estimated that residual lifetime fracture risk in a person aged 60 years with average life expectancy was 29% for men and 56% for women.

To summarize, women suffer twice as many incident non-vertebral fractures as men. On average, men have hip fractures about 10–15 years later in life than women (17).

### Clinical significance of radiographic OVF in men

The semi-quantitative (SQ) criteria proposed by Genant *et al.* are now commonly used for identifying osteoporotic vertebral deformity (VD) for vertebrae T4 to L4 (18,19). According to Genant *et al.*, a vertebra is graded based on visual inspection of the anterior, middle, or posterior heights as normal (grade-0), mildly deformed (grade-1, a 20–25% reduction in one of the three heights and a reduction in area of 10–20%), moderately deformed (grade-2, a 25–40% reduction in any height and a reduction in area of 20–40%), and severely deformed (grade-3, a 40% or more reduction in height and area). In addition to the vertebral height reduction estimation, emphasis is also placed on the radiological evaluation of osteoporotic deformity. Though the initial description of the SQ method request readers to estimated height loss, calculated height loss by direct measure is commonly incorporated into practice, thus it become a mixture of qualitative and quantitative approach. Genant's SQ criteria were initially developed for epidemiology and clinical trials for elderly women; the use of these criteria in elderly men has been less validated than it has in women. Moreover, radiologists may often apply only the iconic classification of VF without reference to the radiological findings as a whole.

In terms of population statistics, radiographic OVs in men have been documented to be relevant. There



**Figure 1** Age-specific fracture incidence for men (A) and women (B) in Dubbo study (Australia). There is an exponential increase in total and hip fractures for both sexes with increasing age. There is also an exponential increase in non-hip and distal forearm fractures in women but not men. [Reproduced with permission from (16)].

is a positive relationship between the severity of OVs and the deterioration of the microstructure in trans-iliac bone biopsies: the more severe the OVs, the lower the trabecular number and connectivity in women (20) and men (21,22). Fink *et al.* (23) reported that, unlike in men without incident OVF, those with incident radiographic-only OVF were also significantly more likely at FU to report back pain and limited usual activity from back pain. Karlsson *et al.* (24) reported that elderly men with a prevalent OVF had an increased risk of sustaining new fractures compared with men without an OVF. Elderly men with two or more prevalent VF, different types of fractures, fractures in both the thoracic and lumbar regions, and a degree of vertebral body compression in the three worst quartiles are at an especially high risk of sustaining new fractures (24).

On the other hand, there is evidence that radiographic OVF in elderly men diagnosed according to most of the commonly used criteria (morphometric criteria, Genant's SQ criteria) generally have less clinical relevance than radiographic OVF with morphologic abnormalities in elderly women. With a modified Genant SQ method and OVF considered when a reduction in vertebral height and/or compression of  $\geq 10\%$  of the estimated vertebral body

height, Kherad *et al.* (25) reported that in men with one or several OVs, there were no significant differences in the presence of back pain in any ages, nor there were differences in the presence of back pain regarding type or number of fractures. Based on vertebral morphometry applied to DXA derived images, Waterloo *et al.* (26) reported that presence of OVF in women was associated with an increased risk of back pain and lower quality of life score, but these associations were not present in men. In MrOS (USA) FU study (mean base-line age: 72.9 years), Ensrud *et al.* (27) reported 13.5% of incident SQ radiographic OVF in elderly men were also clinically diagnosed as incident fractures. In contrast, studies on elderly women suggest that one-quarter to one-third of incident radiographic OVF are also clinically diagnosed as fracture events (27,28). For example, in the postmenopausal women attending the Fracture Intervention Trial Research study, Fink *et al.* (28) reported that about 25% of incident radiographic OVF were also diagnosed as clinical VF.

Clinical OVF are less common in elderly men than in elderly women. Cooper *et al.* (29) reported incidence of clinically diagnosed VF in the predominantly white population of Rochester, Minnesota, USA. In the 5-year

study period of 1985–1989, the age-adjusted incidence rate in women (145 per 100,000 person-years) was almost twice that in men (73 per 100,000 person-years). Freitas *et al.* (30) reported that, despite a large number of elderly men ( $n=5,995$ ) followed-up for ~5 years, there were relatively few clinical VFs. They further noted that VFs in elderly men identified in community clinical settings are usually associated with falls and other low-energy trauma.

Recently Wáng *et al.* demonstrated that, compared with age-matched elderly Chinese women, elderly Chinese men at their early seventies have lower risk of short-term (4-year period) incident new OVF. Even for those with existing VF at baseline (BL), elderly Chinese men are associated with much lower further risk of incident new OVF as compared with elderly Chinese women (31–33).

OVF can be associated with decreases in trunk extension torque, spinal motion, functional reach, mobility skills and walking distance (34). Schlaich *et al.* (35) reported that pulmonary function is significantly diminished in patients with OVF as compared with chronic low back pain patients without evidence of manifest osteoporosis. Of concern are studies in women suggesting increased mortality rates in patients with OVF with a 23% to 34% increase in mortality over an 8-year period in one study (36). However, these mortality rates are in general not directly related to fracture; rather, OVF is a marker for medical frailty. In European Prospective Osteoporosis Study (EPOS) study, Ismail *et al.* (37) reported that for 6,480 subjects, 189 deaths (56 women and 133 men) occurred during a total of 14,380 person-years of FU (median 2.3 years). In women, after age adjustment, there was a modest excess mortality in those with, compared with those without, osteoporotic VD: rate ratio (RR) = 1.9 (95% CI: 1.0, 3.4). In men, the excess risk was smaller and non-significant with RR = 1.3 (95% CI: 0.9, 2.0). After further adjusting for smoking, alcohol consumption, previous hip fracture, general health, body mass index and steroid use, the excess risk was reduced and non-significant in both sexes: women, RR = 1.6 (95% CI: 0.9, 3.0); men, RR = 1.2 (95% CI: 0.7, 1.8). There was a residual, though non-significant excess risk of death after adjustment for adverse health factors. Ismail *et al.* (37) suggested that this may be due to failure to adequately control for adverse health factors or to residual confounding. There was no evidence of a dose-response relationship between mortality and number of deformities, suggesting that the excess mortality associated with osteoporotic VD is due to adverse health factors linked with both VD and increased mortality. However, it remains possible that, in uncommon cases,

OVF may influence mortality more directly because of their association with chronic back pain, immobility and change in posture, which may increase the risk of infection and death.

### Radiographic diagnosis of OVF in men

Despite years of research, the radiographic criteria for diagnosing OVF and its grading remain debated (38–44). VDs can be due to a number of causes such as osteoporotic fracture, traumatic fracture, and causes other than fracture such as osteoarthritis, or adolescent epiphysitis (Scheuermann disease). A substantial portion of radiographic OVF are asymptomatic, and because of this, the diagnosis of radiographic OVF is difficult. This is different from, for example, the case of diagnosis of malignant tumors, where a biopsy, a FU of a couple of months, or surgical pathology, usually establish the conclusive diagnosis. For OVF, biopsy is usually not obtained, and even years of FU may not necessarily provide the conclusive diagnosis.

For both men and women's results, VD's shapes are commonly classified into (I) biconcave (II) wedged, (III) both biconcave and wedged, (IV) crush. Whether wedged VD reflects OVF is a matter of dispute. Based on morphometrical evaluation for EPOS subjects, Lunt *et al.* (45) noted that VDs in which the mid-height loss only, or mid and anterior heights loss were both reduced, and crush deformities were associated with reduced BMD; and those VDs were significantly more prevalent in women than in men. However, VDs involving loss of anterior vertebral body height alone, which represent 21% of deformities in women and 29% of deformities in men, were poorly correlated with low BMD. With EPOS subjects, for a mean FU of 3.8 years, Lunt *et al.* (46) reported relative OVF risk during FU differ according to the shape of the prevalent VD, ranging from 5.9 (95% CI: 4.1, 8.6) if the anterior and mid heights were reduced, 3.3 (2.3, 4.8) if the mid height was reduced, and 1.9 (1.0, 3.4) if the anterior height was reduced. They also described the most common type of deformity as biconcavity (46).

Hence, for wedge-shaped VDs (or VD with anterior height reduction only), a diagnose of OVF may be questionable if rarely valid. It is possible that wedged OVF may indeed occur, particularly when these VDs are associated with some degree of external low energy trauma. Trabecular density is lower in the anterior versus posterior regions of the vertebral centrum (47). With difference which increases with degeneration of the adjacent

intervertebral disc and with aging, the vertebra integrity is less resistant to anterior flexion force than axial compression force (48,49). Disc degeneration may have an important influence on VF etiology, with disc material properties may influence vertebral strength (50). In an *ex-vivo* specimen study, Jackman *et al.* (51) noted that under the combined loading of axial compression combined with anterior flexion, deflection initiated and remained the largest at the anterior central endplate or the anterior ring apophysis, depending in part on health of the adjacent intervertebral disc. This deflection was accompanied by outward bulging of the anterior cortex. With an *ex-vivo* study, Adams *et al.* (48) noted that intervertebral disc degeneration is associated with locally reduced BMD of the anterior vertebral body and inferior trabecular architecture. Vertebrae specimens from elderly subjects shows the anterior third of the vertebral body had lower trabecular volume fraction, fewer trabeculae, and greater intertrabecular spacing compared with the posterior third (48). These predispose to anterior fracture when the spine is flexed. Flexed postures concentrates loading on the weakened anterior vertebral body, leading to compressive failure at reduced load.

Leidig-Bruckner *et al.* (52) applied an algorithm for radiological differential classification (RDC), and their RDC's reading were compared with BMD measurement as well as Eastell and McCloskey's morphometric criteria (53,54). They noted the agreement between RDC and morphometric methods was poor, and more so for elderly men than for elderly women. In men, 62–86% of cases with morphometric VD were classified by RDC as non-osteoporotic, compared with 31–68% in women, with most of these VDs had wedge deformities of the thoracic spine. On the other hand, up to 80% of OVF's in men and up to 48% in women were missed by morphometry, in particular endplate fractures at the lumbar spine. Although VDs by most definitions were significantly and inversely related to BMD in both sexes, a much stronger association existed between BMD and osteoporotic fractures defined by RDC. Leidig-Bruckner *et al.* (52) concluded that assessment of vertebral osteoporotic fracture by quantitative methods alone will result in considerable misclassification, especially in men. Leidig-Bruckner *et al.* also suggested the criteria derived from women is likely to be unsuitable for men.

The diagnosis of OVF among VDs is difficult and even more so in men than in women for a number of reasons. Duan *et al.* (55) suggested that VF risk is the same in young women and men but, during aging, subperiosteal bone formation increases vertebral cross-sectional area more in

men than in women and volumetric BMD decreased less in men than in women. Thus, VF risk does not generally increase in elderly men as much as in elderly women; though in the smaller subgroups of elderly men with osteoporosis, the VF risk may be only slightly less than the elderly women with osteoporosis (56). The vertebrae of men may be physiologically more wedge-shaped than those of women (57,58). Men are more likely to have high energy trauma than women across the whole life span. Differentiation of OVF from VD due to old traumatic cause may not be easy (59). There is a high likelihood that OVF has been over-reported in previous epidemiological studies and even more so in men, an issue discussed by Szulc *et al.* (60). Ismail *et al.* (61) described that risk factors for men with multiple VDs are consistent with those well known for osteoporotic women. However, this is not true for men with single/dual deformities where the correlation with low BMD was poorer. There was a marked increase in the prevalence of multiple VDs with increasing age, but only a modest effect of age on the prevalence of single deformities (61), suggesting a portion of the VDs might not be osteoporotic. Similar observations have been made in a report from the Canadian Multicentre Osteoporosis Study (62). To address this problem, based on BMD characteristics, Szulc *et al.* (60) recommended a cutoff of 25% for wedge deformities from T6 to T9, and they further commented that a cutoff of 30% for wedge deformities from T6 to T9 and of 25% for other deformities has a high specificity and a moderate sensitivity for identifying VDs related to low BMD in men, while SQ grade-1 deformities are often deformities related to non-osteoporotic disease of the spine. One study showed, comparing Genant's SQ criteria, Szulc *et al.*'s criteria demonstrated better association between existing osteoporotic VD at BL and further incident new OVF at year-4 FU (32).

Recent reports emphasize the importance of identifying osteoporotic endplate and/or cortex fractures (ECF) [also called algorithm-based qualitative (ABQ) fracture, osteoporotic endplate depression and anterior cortex buckling] (31,33,41,56,63-68). It has been shown that mild VDs identified by ABQ, but not by SQ, were associated with lower BMD (56,68). Lentle *et al.* (67) showed ECF positive grade-1 VF was associated with higher risk of VF's as well as non-vertebral major osteoporotic fracture, while grade-1 SQ-VD was not associated with nonvertebral fracture risk. In MrOS & MsOS (Hong Kong) BL studies (56), it was demonstrated that while the overall Genant SQ criteria based VD prevalence is only slightly lower in men

than women (i.e., 13.2% *vs.* 16.1%), ECF is substantially lower in men than women (i.e., 5.88% *vs.* 11.93%). Moreover, 63.2% of the VDs in men were grade-1, while only 30.5% of the VDs in women were grade-1 (56). VFs in men with 25–34% height loss rarely simultaneously demonstrate ECF, while it is common for VF in women with 25–34% height loss to be associated with ECF (69). Recently Wáng *et al.* (31) showed, in elderly women, within the same mild/moderate SQ grades, compared with the subjects without ECF, the subjects with ECF are associated with a higher short-term future risk of new incident OVF.

Particular care is important in diagnosing OVF at mid-thoracic level, as this is where false positive diagnoses more likely are made. There is a high possibility that OVF at mid-thoracic level (T7–T9) have been over-diagnosed in many cases (52,70). Wedging from remodeling in osteoarthritis may be confused with wedging due to osteoporotic fracture (71). Abdel-Hamid Osman *et al.* (71) noted that while osteoporotic fracture of the thoracic spine is characterized by an exaggerated reduction of the mid-height to posterior height in addition to reduction of the anterior to posterior height. In the osteoarthritic wedging, the anterior/posterior height ratio is lower than the mid/posterior height ratio. In osteoarthritis, reduction in anterior height of the vertebral body is the consequence of remodeling, likely a silent adaptation over years of hyper-lordosis.

Taken together from the above discussions, it is likely that OVF may have been over-diagnosed in many epidemiological studies of men, particularly diagnosing wedge-shaped VDs as OVF requires great caution. A more stringent criterion for definition of OVF for epidemiological studies in men is needed. Cawthon *et al.* (72) used the criteria that, unless there is evidential ECF for SQ grade-1 deformity, VF should be considered only when  $\geq$  grade-2 deformity exists. Even so, we expect there is a possibility that some ECF negative grade-2 deformities may not be true fracture. Thus, another possibility will be that only ECF positive osteoporotic VD and osteoporotic VD with  $\geq 1/3$  vertebral height loss are considered OVF (69). For men, the criteria of Szulc *et al.* (60) may also be considered. However, convertible criteria between men and women will facilitate comparative studies. As noted above, before suggesting a VF to be osteoporotic, in addition to considering the possibility of physiological wedging, degenerative wedging and other causes, secondary causes such as old trauma, metabolic diseases, and oncologic conditions, should be excluded.

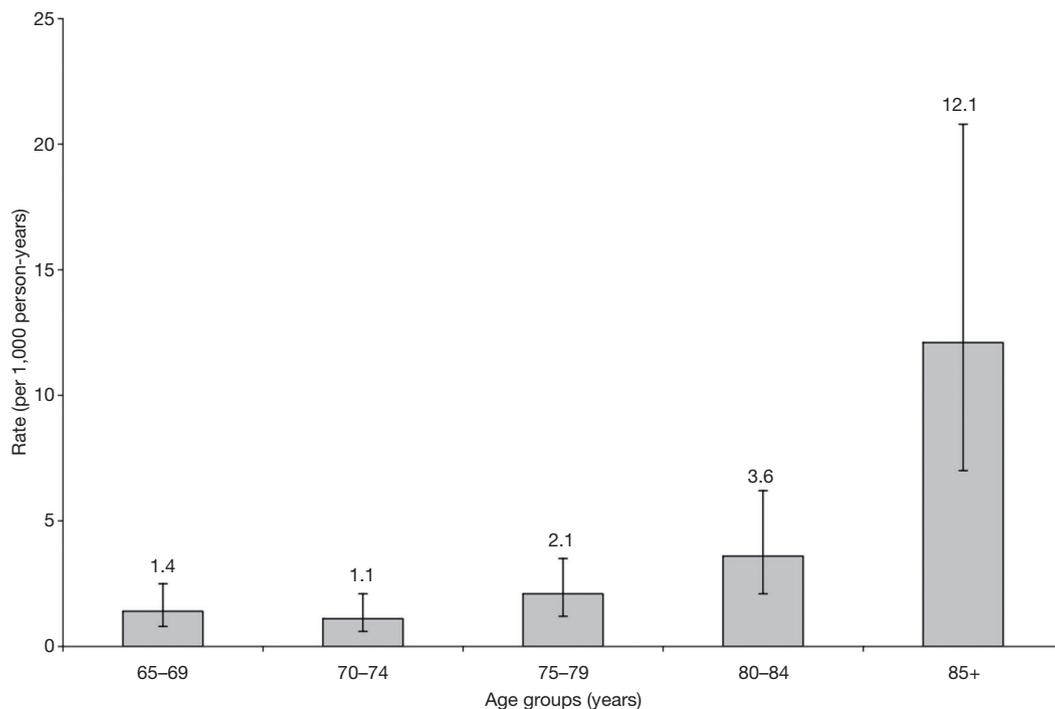
However, apart from epidemiological studies and clinical trials, for clinical patients seen with back pain we

emphasize the importance of identifying VDs with less than 20% vertebral body height loss (41,64,73–75). In cases of ambiguity and if clinical decision-making hinges on the diagnosis of a fracture, then comparison with previous images, a radionuclide scan, computed tomography (with sagittal reformation), and/or MRI may provide clearer evidence (65). To depict the bone marrow edema at acute stage VF, MRI fat suppression on T2-weighted images (commonly STIR sequence) is essential. Chronic vertebral compression fractures are characterized by morphologic changes but normal signal apropos of the bone marrow.

### Comparative prevalence of radiographic OVF in elderly men and women

Because there is no universally accepted definition of OVF, and a substantial proportion of OVF do not come to medical attention, the epidemiology of VFs is less well understood than that of hip fractures. The risk for osteoporotic fracture increases greatly in elderly men after age of 80 years (30,76) (*Figure 2*). For epidemiological studies of OVF, it may not be meaningful to study OVF in men younger than 60 years. Some previous publications on OVF for men may have included subjects of too young age.

For MsOS (Hong Kong) and MrOS (Hong Kong) studies, men and women of similar age and from the same community-based population were investigated using the same methodology, thereby enabling direct comparison of the results in men and women. MsOS (Hong Kong) and MrOS (Hong Kong)'s data iterate that there is a high proportion of SQ grade-1 VD in men which may not be true OVF (*Table 1*). If only accepting vertebrae with ECF, the VF prevalence in men is about half of that of women (49.3%). By accounting those with grade-2/3 VD and grade-1 VD co-existing with ECF, the VF prevalence in men is slightly less half of that in women (41%, *Table 1*) (56). Based on morphometrical assessment, Lunt *et al.* (46) estimated a total OVF incidence of 5.9 fractures per 1,000 person/years in men (95% CI: 4.6, 7.4) and 10.1 OVF per 1,000 person/years in women (95% CI: 8.5, 11.9). This male-female ratio is very similar to other clinical fracture of such as hip (9,12–16). *Figure 3* from MsOS (Hong Kong) and MrOS (Hong Kong) studies shows while male-female ratios are the same for the three age groups, with the prevalence of male grade-2/3 VF and ECF being approximately half of the women, the absolute difference in VF prevalence between men and women actually increase over age (*Figure 3A*). OVF's vertebral level distribution is



**Figure 2** Clinical VFs rates (per 1,000 person-years) and 95% confidence intervals by 5-year age categories in the MrOS (USA) Study. The mean FU was 4.7 years. [Reproduced with permission from (30)]. VF, vertebral fracture; FU, follow-up.

**Table 1** Comparison of Genant's VD vs. ECF in assessing spine OVF in MrOS (Hong Kong) and MsOS (Hong Kong) studies

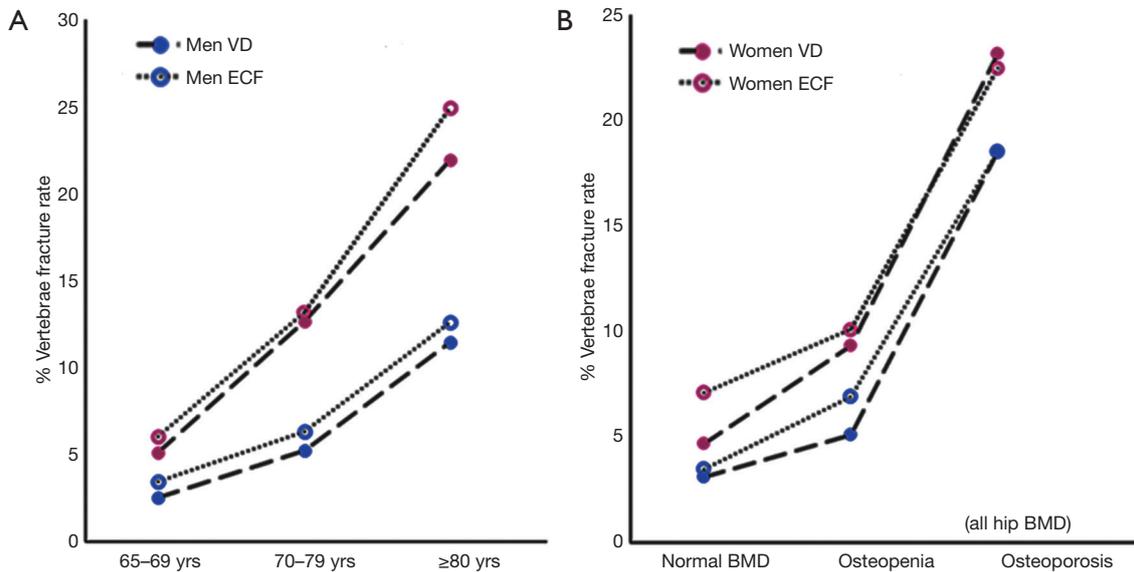
Grade	Men (n=1,954)		Women (n=1,953)		P value of chi-square	
	VD	ECF	VD	ECF	VD (M vs. F)	ECF (M vs. F)
Grade-0, %	86.80	94.12	83.92	88.07		
Grade-1, %	8.34	1.89	5.07	3.33	0.0004	0.0022
Grade-2, %	2.61	1.74	5.12	3.07	<0.0001	0.0030
Grade-3, %	2.25	2.25	5.89	5.89	<0.0001	<0.0001
Total (Grade 1-3), %	13.20	5.88	16.08	11.93	0.0111	<0.0001

Grade 1, 2, 3 indicate prevalence of deformity/fracture in each grade. VD, vertebral deformity; ECF, endplate and/or cortex fracture; OVF, osteoporotic vertebral fracture. [Reproduced with permission from (56)].

similar between men and women (56).

However, for men with osteoporosis (based on hip BMD measurement), MsOS (Hong Kong) and MrOS (Hong Kong)'s results show OVF prevalence is similar between men and women (though still slightly lower in men) (Figure 3B). Schuit *et al.* (77) also reported that men and women  $\geq 55$  years of age participating in the Rotterdam Study had similar associations between BMD and risk of hip and other nonvertebral fractures. Nguyen *et al.* (78) found similar patterns of BMD and fracture risk in men

and women. Johnell *et al.* (79) also reported in a meta-analysis that low BMD is a risk factor for fracture of substantial importance and is similar in both sexes. At the age of 65 years, hip fracture risk ratio increased by 2.94 (95% CI: 2.02, 4.27) in men and by 2.88 (95% CI: 2.31, 3.59) in women for each standard deviation (SD) decrease in BMD. At the age of 65 years, the risk of osteoporotic fractures increased in men by 1.41 per SD decrease in BMD (95% CI: 1.33, 1.51) and in women by 1.38 per SD (95% CI: 1.28, 1.48). Cummings *et al.* (80) suggested the



**Figure 3** Prevalence of OVF among three age groups of Hong Kong Chinese men and women (65–69, 70–79, and ≥80 years) (A), and among normal BMD, osteopenia and osteoporosis subjects (B). Genant's VD included deformities grade-2 and 3 only as grade-1 may not be true fracture; ECF included fracture grade-1, 2 and 3. Blue circles for men and red circles for female. [Reproduced with permission from (56)]. OVF, osteoporotic vertebral fracture; BMD, bone mineral density; VD, vertebral deformity; ECF, endplate and/or cortex fracture

relationship between hip BMD and hip fracture risk was no less strong in men than that of women, with each SD decrease in hip BMD increased the risk of hip fracture 3.2-fold. Shin *et al.* (81) reported that despite large differences in the prevalence of fracture and in the characteristics of the men, the associations between BMD and fracture status were remarkably similar across differential ethnic/race groups.

### Ethnic differences in radiographic OVF prevalence

Ethnic differences for BMD and clinical fragility fractures have been documented. It has been noted that spine and hip BMD are relatively high in men of African origin, and relatively low in East Asian men (Chinese, Korean, and Japanese) (81,82). Clinical fragility fractures tend to be more prevalent among elderly Caucasian men, while relatively less prevalent among elderly East Asian men (82-84). African descendants may have even lower prevalence of clinical fragility fractures (84). The lower BMD observed among men of Asian descent compared with Caucasian men can be largely explained by differences in body size (82). Rates of BMD loss with aging appear to be similar between Caucasian and African Americans but slower in Asian men (85). The association between BMD and fracture risk appears to

be similar across race and ethnic groups (81).

Direct comparison with prevalence and incident VFs among different studies is difficult because of the differences in study methodologies, which include the differences in BL age as well as the VD/VF definitions. Kwok *et al.* reported that the age-specific OVF prevalence of elderly Chinese women in Hong Kong (mostly southern Chinese) is very similar to that of women in Beijing (mostly northern Chinese), and to that of Japanese women and Korean women, while lower than elderly Caucasian women (estimated to be 30% lower) (86). Other aspects of spine degeneration also tend to be slightly more severe in elderly Caucasian subjects than in East Asians. It was shown that Caucasian Americans have a higher degenerative spondylolisthesis prevalence, being approximately 60–70% higher than that of elderly Chinese (87,88).

The same with the OVF prevalence ratio of Chinese women *vs.* Caucasian women (86), elderly Chinese men's OVF prevalence is likely to some extent lower than that of elderly Caucasian men. The European Vertebral Osteoporosis Study (EVOS) reported that approximately 20% of men aged 50 to 79 years had at least one OVF (Eastell method with 3 SD criteria) (89). Using morphometry applied to DXA images, Waterloo *et al.* reported at least one OVF is present in 14% of men

aged >50 years in Norway (26). With a more comparable methodology to MrOS (Hong Kong) study, the MrOs (Sweden) study (24,25) shows all-inclusive SQ OVF prevalence of 15.1% (SQ threshold of >10% vertebral height loss) as compared with all-inclusive SQ VF prevalence of 13.2% (SQ threshold of >20% vertebral height loss) in MrOS (Hong Kong) results. In Van der Klift *et al.*'s Rotterdam study (mean age at baseline BL: 65.4±6.6 years, FU period 6.3 years) (90), for those with BL normal spine, the osteoporotic VD/VF incident rate was 2.8% for men (5.2% for women), as compared to 2.05% (25/1,219) in MrOS (Hong Kong) study (mean age at BL: 71.7 years, range 65–91 years, FU period 4 years). In the EPOS study (91) (mean age at BL: 63.3±7.9 years, mean FU period of 3.8 years, an incident morphometric VF was a 20% (+4 mm) or more reduction in anterior, middle, or posterior vertebral height-plus satisfying criteria for VD using the McCloskey-Kanis method in the FU radiograph), the osteoporotic VD/VF incidence was 4.5/1,000 person-years in men (9.3/1,000 person-years in women), as compared to 5.33/1,000 person-years MrOS (Hong Kong) study (criteria: for progression of a BL VD, a further height decrease of ≥15% was a VD progression; a new incident VD was a qualitative VD which could be either a change from grade-0 at BL to grade-2/3 VD at FU, or a change from grade-0 to grade-1 VD with ≥10% height loss during the FU period) (32). In MrOS (USA) study, Fink *et al.* reported that, of 5,994 men followed-up for an average of 4.7 years, 4.65% had incident radiographic VFs (SQ methods: a distinct alteration in morphology of vertebral body resulting in a higher grade (grade 1–3) when compared to BL radiograph) (23). In MrOS (Hong Kong) study, for 38 cases who had SQ grade-3 OVF, only two cases had new OVF or OVF progression (including one new OVF at L5) at year-4 FU (32,33).

In conclusion, for epidemical studies and clinical trials we suggest that OVF criteria for women may not be directly applicable for men. Before better evidence is available, ECF sign positive Genant SQ grade-1, as well as GSQ grade-2/3 VDs can be accepted as valid for prevalent OVF. Another possibility will be that only ECF positive osteoporotic VD and osteoporotic VD with ≥1/3 vertebral height loss are considered OVF. The OVF prevalence for men is expected to be approximately half (or even slightly less than half) of prevalence for age-matched women. Even so, the clinical relevance for elderly men with OVF may be less than that of elderly women. For elderly men with hip BMD based osteoporosis, the OVF risk is as high as that

for osteoporotic women. Chinese elderly men have lower OVF prevalence than age-matched Caucasian men. For wedge-shaped VDs or VDs with anterior height reduction only, to diagnose them as OVF requires caution. Particular attention should be paid to the mid-thoracic level as this is where over-diagnosis commonly occurs. If clinical decision-making hinges on the diagnosis of a fracture, then comparison with previous images, a radionuclide scan, computed tomography (with sagittal reformation), MRI, and/or careful FU is recommended.

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## Footnote

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