Editorial

A summary of our recent evidence-based works on radiographic diagnostics of prevalent osteoporotic vertebral fracture in older men and women

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The bone composition of the spine, which is predominantly trabecular bone, is more prone to the thinning and microarchitectural changes associated with osteoporosis than regions of the hip that are richer in cortical bone. Assessment of vertebral fracture (VF) status, in addition to bone mineral density (BMD), provides relevant clinical information to aid in predicting fracture risk in postmenopausal women. Despite its high clinical relevance, there is no consensus yet on the radiographic diagnosis criteria for osteoporotic VF (OVF). We have recently discussed our understanding of radiographic diagnostics for prevalent OVF in older women (1). In the current article, we summarize our recent evidence-based research results of radiographic diagnostics concerning prevalent OVF in older men and women.

'Background noise' vertebral deformity (VD) for OVF assessment

A VF may occur in various conditions, including: (I) a high energy trauma induces 'obvious' VF in normal bone strength subjects and causes clinical symptoms; (II) a high energy trauma induces micro-VF in normal bone strength subjects and does not cause clinical symptoms; (III) a low energy trauma induces micro-VF in normal bone strength subjects and does not cause clinical symptoms/signs; (IV) a high energy trauma induces 'obvious' VF in osteoporotic subjects and causes clinical symptoms; (V) a low energy trauma induces 'obvious' VF in osteoporotic subjects and causes clinical symptoms; (VI) a low energy trauma induces micro-VF in osteoporotic subjects and does not cause clinical symptoms. Since both bone strength and trauma energy level are continuous variable, it is understandable the radiographic morphology of OVF is not always distinct. Traumatic VF and OVF have very similar segmental distribution, both with the highest prevalence at the thoracolumbar junction (2). Moreover, for OVFs truly without a trauma incident, the fracture process may be a slowly progressive process without a distinct event; these OVFs can be considered that the slowly progressive microscopic fractures have progressed so much that the shape of this vertebra becomes distinctly different from the adjacent normal appearing vertebrae (1).

According to the definition of fragility fracture, when a low energy trauma induced an acute VF, a definite OVF diagnosis can be made as long as the trauma energy is not close to the borderline to define low energy (*Figure 1*). Beyond that, a "gold" radiographic standard to separate OVFs and non-osteoporotic VFs in every case does not exist. In severer grade deformities or when a vertebra is

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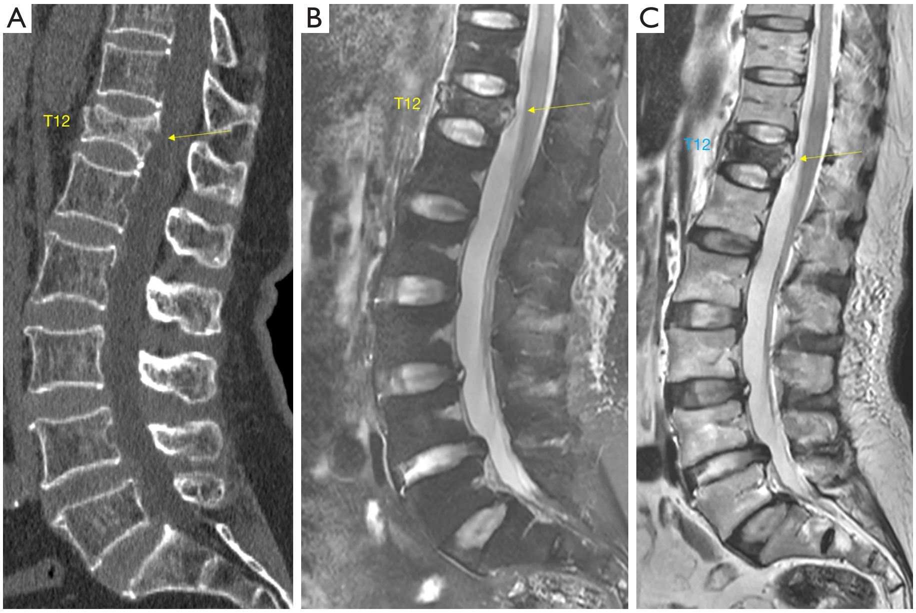

Figure 1 A 74-year-old woman with a low energy trauma induced T12 VF (arrow). Imaging (A: CT, B: T2 weighted MRI, C: T1 weighted MRI) was conducted 10 hours after the incident. Signals on MRI suggest the fracture was in acute phase. VF, vertebral fracture; CT, computed tomography; MRI, magnetic resonance imaging.

collapsed, OVF diagnosis can be made with a relatively high degree of certainty by experienced readers. In 'milder' cases, OVF is often diagnosed based on a high probability rather than an absolute diagnosis. This probability depends on many factors, including sex and age of the subjects, the morphology of the deformed vertebra with endplate depression or biconcave shape suggesting higher probability, as well as the employment history of the subjects with physical stress can cause non-osteoporotic deformities mimicking OVF (see discussions below).

We have proposed the seven grades extended semi-quantitative (eSQ) scheme for OVF grading (*Table 1*) (3-5). The rationales of this eSQ scheme have been explained previously (1,3). It is a compromise of original Genant semi-quantitative (SQ) grading and our own experience. For the morphological assessment of the severity of any pathology, simplistically three grades of mild, moderate, and severe can be assigned. Within these categories, however, a system with more categories has the potential to provide more information. Many readers like to insert the categories of "mild-to-moderate" and "moderate-to-severe" into three-grade systems (6). In addition, since precise grading is challenging both by visual estimation and even by measurement (which depends on how the points are placed on the images), one of our goals of eSQ is to 'soften' or 'smoothen' the subjectivity associated with original Genant SQ grading. It has been noted that, in many natural processes, an observer tends to distinguish seven categories; for example, the rainbow is considered to have seven colors, which is not a property of the electromagnetic radiation that comprises the visible spectrum but rather a reflection of the way the human mind organizes the visual information (6). While Genant SQ mild grade (i.e., from 1/5 to 1/4 vertebral height loss, a range of only 5%) is very difficult to precisely estimate and even difficult to measure, Genant SQ mild grade has been heavily used in literature. Thus, we kept this grade in the eSQ scheme. SQ moderate grade is subdivided into two grades because OVFs with ≥1/3 height loss always demonstrate endplate and/or cortex fracture (ECF) radiographically (7), and are more likely to be associated with multiple OVFs (*Figure 2*) (8-10). In practice, visual estimation is likely to overestimate the extent of vertebral height loss (3). It is noted that, OVFs without achieving a 1/5 height loss threshold have been commonly classified as SQ grade-1 OVF by colleagues trained in UCSF (*Figure 3*) [(1,5) and personal communications].

The limitations of Genant SQ grading, mSQ (schemes modified semi-quantitative; see *Table 1*), and eSQ grading include classifying OVF severity according to the associated vertebral height loss. This will be more applicable to OVFs

Table 1 Vertebral height loss criteria for Genant SQ grading and mSQ, eSQ (3-5)*

Grading[§]	Extent of vertebral height loss[¶]					
	<1/5	1/5–<1/4	1/4–<1/3	1/3–<2/5	2/5–<2/3	≥2/3
Genant SQ[#]	Grade-0.5	Mild	Moderate		Severe	
mSQ[#]	Mild	Moderate		Severe		Collapsed^
eSQ[#]	Minimal	Mild	Moderate	Moderately-severe	Severe	Collapsed

*, vertebrae with normal radiographical morphology is noted as grade-0; #, the grading is based on the extent of vertebral height loss, which is not suitable for fracture at acute or subacute phase. This is particularly the case for Genant SQ, as many clinically relevant vertebral fractures show <1/5 vertebral height loss at acute phase; §, for experienced readers, there is usually a very good agreement on the 'yes' or 'no' of the existence of a vertebral deformity (except for those of very minimal deformity). However, disagreement on the grading is common, which can only be resolved by measurement with an agreed method; ¶, visual estimation has a strong inclination to over-estimate the extent of vertebral height loss. It is advisable to prepare a reference image database and conduct regular re-calibrations for the readers; ^, when mSQ was proposed, we suggested three grades: mild, moderate, severe (4); now we recommend adding an additional collapsed grade (≥2/3 vertebral height loss). SQ, semi-quantitative; mSQ, modified semi-quantitative grading; eSQ, extended semi-quantitative grading.

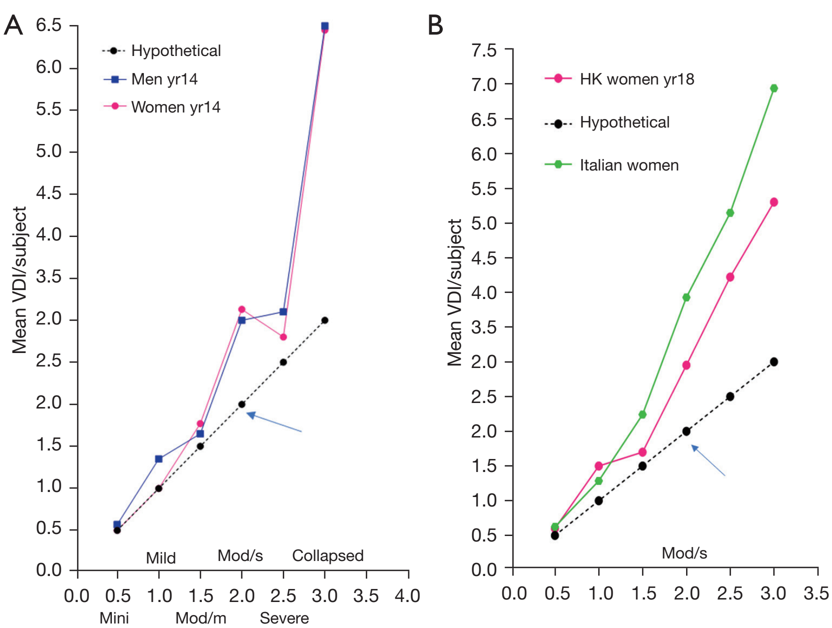

Figure 2 Relationship between the highest OLVF grading in a subject and the VDI [data from (8-10)]. One OLVF of 'minimal', 'mild', 'moderate', 'moderately severe (mod/s)', 'severe', 'collapsed' has <1/5, 1/5–<1/4, 1/4–<1/3, 1/3–<2/5, 2/5–<2/3, and ≥2/3 vertebral height loss, and is assigned a score of 0.5, 1.0, 1.5, 2.0, 2.5, 3.0 respectively. VDI is calculated by summing up the scores of vertebrae T4 to L5. X-axis: the highest OLVF grade of a subject. Y-axis: mean VDI score/subject. If each subject had one OLVF each, then the result follows the black dot and lines (hypothetical). Both (A,B) show, for subjects with one OLVF of ≥1/3 height loss (arrow), the chance of having multiple OLVFs per case increases. (A) MrOS(Hong Kong)and MsOS(Hong Kong) year-14 follow-up results for older men and older women. (B) MsOS(Hong Kong) year-18 follow-up radiograph women results and 302 Italian female cases from "Roman Osteoporosis Prevention Project". VDI, vertebral deformity index; OLVF, osteoporotic-like vertebral fracture.

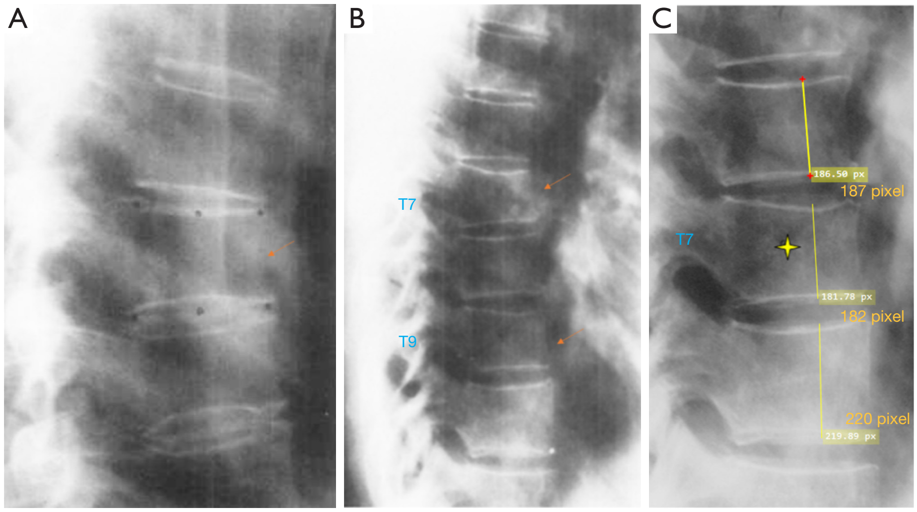

Figure 3 Examples of mild grade VD (A,B) in the article of Genant *et al.* (5) are classified by us as minimal grade deformity (arrow). (C) show a magnified image of T7 (stellate). According to our measurement approach (3), these three vertebral deformities do not reach the threshold of 1/5 vertebral height loss. For experienced readers, there is usually a very good agreement on the 'yes' or 'no' for the existence of a VD (except for those of very minimal deformities). However, disagreement on the grading is common, which can only be resolved by measurement with an agreed method. Radiographically, the VD in (A) cannot be certainly diagnosed as an OVF. In (B), two non-adjacent vertebral deformities suggest they were likely to be osteoporotic in a postmenopausal woman. Modified from *Fig. 2* and *Fig. 8* in (5). VD, vertebral deformity; OVF, osteoporotic vertebral fracture.

without trauma or caused by minimal trauma. If an OVF was caused by a substantial trauma while yet within the low energy trauma definition, then the extent of height loss is of course affected both by the energy of trauma as well as the strength of the bone. It is expected that among the general older population without being a physical laborer history, OVFs without trauma or caused by only minimal trauma may be more prevalent. Moreover, since OVF can repair (*Figure 4*) (9), the initial traumatic vertebral height loss may be regained. Among the older subjects, some OVFs might have maintained their severity unchanged due to the repairing and healing processes, i.e., their severity would have progressed if without the repairing and healing. Therefore, for screening detected OVFs, the extent of vertebral height loss and the number of OVFs in a subject may still be reasonable indicators of spine bone strength.

In order to provide 'baseline noise' VD information, recently we analyzed VDs among 408 female patients and 374 male patients who had lateral chest radiographs due to mild illness or for routine healthcheck (the Jiaxing study) (11). The indications were all other than spine disorders, trauma, malignancies, or metabolic disorders. Fracture shaped vertebral deformities (FSVDs) were graded according to eSQ scheme. The existence of a deformity is mostly distinct (*Figures 5,6*), while FSVD was considered when radiographically indistinguishable from a fracture according to the best of the readers' experience. Note the minimal grade FSVDs were not 'milder' than the mild VDs illustrated in original *Fig. 2A* and original *Fig. 8* in the article of Genant *et al.* (5). The male-female difference for FSVD prevalence was noted as early as the adolescent age (*Figure 7*). We postulate these FSVDs are mostly due to micro-fracture associated with physical stress, and FSVDs can repair and heal. Of course, it is highly likely that most of the minimal grade wedgings among young and middle-aged adults (<45 years) have little clinical significance. FSVDs among the male and female groups aged 21–44 years may represent 'baseline noises' for OVF assessment among the elderly.

The earlier works of Lauridsen *et al.* (12) and Matsumoto *et al.* (13) suggested that vertebral shape is more physiologically wedged in men than in women. Our experience suggests that while wedge shaped vertebrae (i.e., minimal/mild FSVDs) are more common among men, for the vertebrae considered to be normal shaped, no apparent difference can be observed for those of males and those of females. Our experience suggests that, in the absolute sense, while there is degenerative vertebral wedging, there

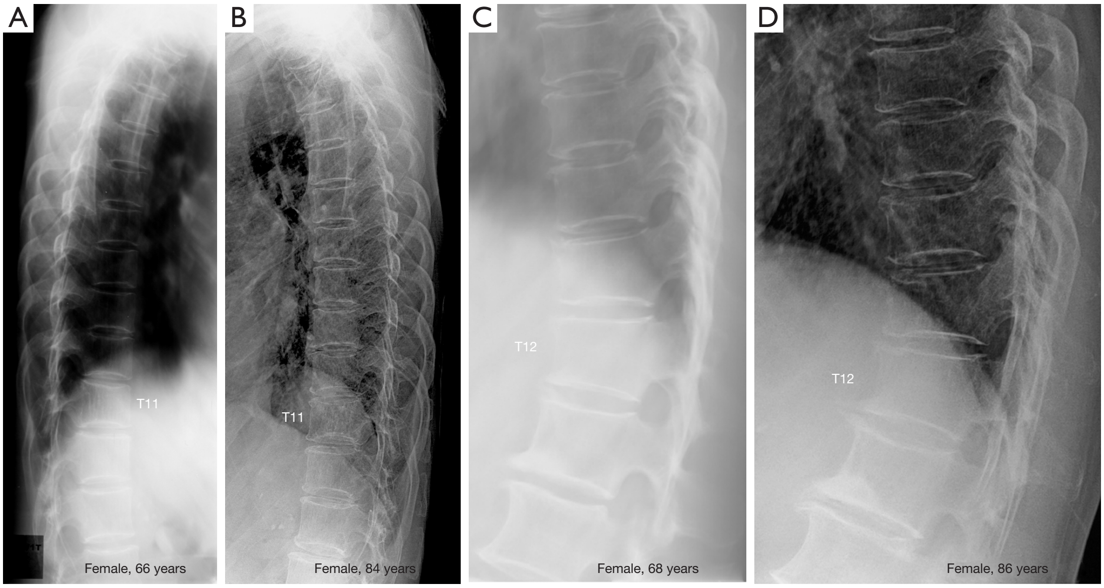

Figure 4 Radiographic recovery of OLVF of two female cases (A and C: baseline, B and D: follow-up). (A) and (B) show T11 recovered to normal shape. (C) and (D) show T12 recovered to normal shape. Images from the MsOS(Hong Kong) year-18 follow-up study. OLVF, osteoporotic-like vertebral fracture.

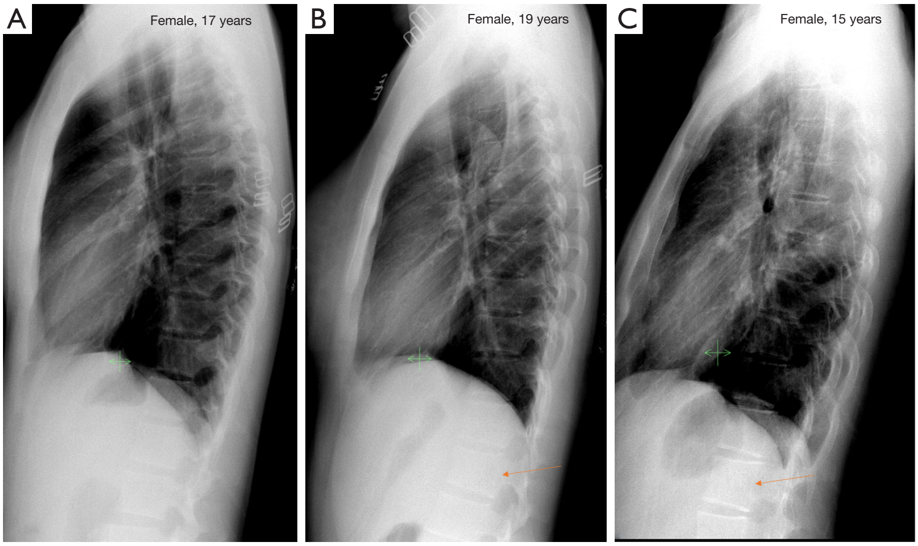

Figure 5 Examples of normal vertebrae and minimal grade VD among adolescent females. (A) Lateral chest radiograph of a 17-year-old female shows normal vertebrae. (B) Lateral chest radiograph of a 19-year-old female shows vertebra L2 minimal wedging (arrow). (C) Lateral chest radiograph of 15-year-old female shows vertebra L1 minimal wedging (arrow). Reused with permission from (11). VD, vertebral deformity.

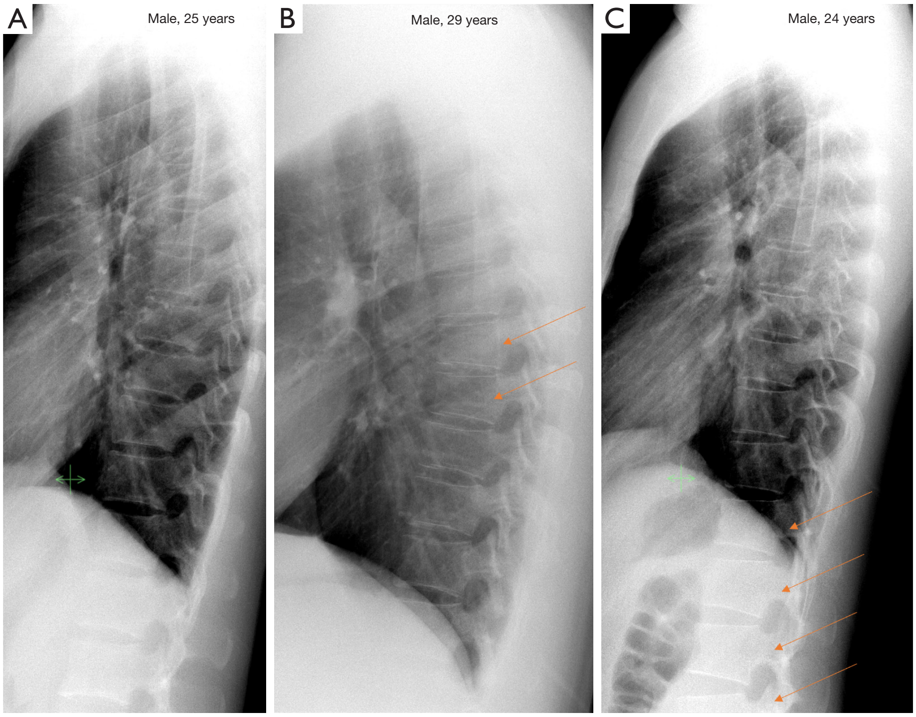

Figure 6 Examples of normal vertebrae and minimal/mild grades VD among adult males. (A) Lateral chest radiograph of a 25-year-old male shows normal vertebrae. (B) Lateral chest radiograph of a 29-year-old male shows vertebrae T7 and T8 minimal grade deformity (arrows). (C) Lateral chest radiograph of a 24-year-old male shows vertebrae T12, L1, L2 and L3 (partially seen) minimal grade deformity (arrows). Reused with permission from (11). VD, vertebral deformity.

should be no radiographical physiological wedging at mid-thoracic region and thoracolumbar region (*Figures 5,6,8*). This is supported by the fact that vertebrae of minimal wedging or mild wedging can recover to the original 'normal' shape (*Figure 4*). Thus, our experience disagrees conceptually with the reports of Lauridsen *et al.* (12), Matsumoto *et al.* (13), and Gaca *et al.* (14). Gaca *et al.* suggested there is vertebral physiological wedging among the pediatric population.

For older women, our MsOS(Hong Kong) year-14 and year-18 follow-up studies suggest that, subjects with minimal osteoporotic-like vertebral fracture (OLVF) had an incident VF risk higher than subjects without baseline OLVF (*Table 2*) (8,9). Moreover, in a study conducted among older women, we reported among 38 vertebrae in 27 cases which had anterior wedging deformity with height loss of <20% while without radiographic endplate depression, 28 vertebrae (28/38, 73.7%) demonstrated endplate depression on computed tomography (CT) (15). We suggest that, after excluding known OVF mimics, a singular vertebral wedging in older women is statistically more likely to be osteoporotic. However, our MrOS(Hong Kong) for older men year-14 and year-18 follow-up studies suggest that, male subjects with minimal OLVF did not have an incident VF risk higher than the male subjects without baseline OLVF (8,9).

Following these discussions above, we suggest that, for screening detected fracture-like deformity among older subjects, the term 'OLVF' may be used instead of OVF at least for milder cases, as only based on spine radiograph it often is not possible to certainly diagnose a 'milder' VD as OVF. On the other hand, we suggest the term 'FSVD' is used for facture-like VD among younger subjects. Radiographically, FSVD and OLVF may not be different.

OVF severity and BMD among older women

According to the WHO criteria, T-score is defined as: $(BMD_{patient} - BMD_{young\ normal\ mean})/SD_{young\ normal\ population}$. In adult women, the cutpoint value of patient BMD 2.5 standard deviation (SD) below $BMD_{young\ normal\ mean}$ satisfies that, when the femoral neck is measured, osteoporosis prevalence

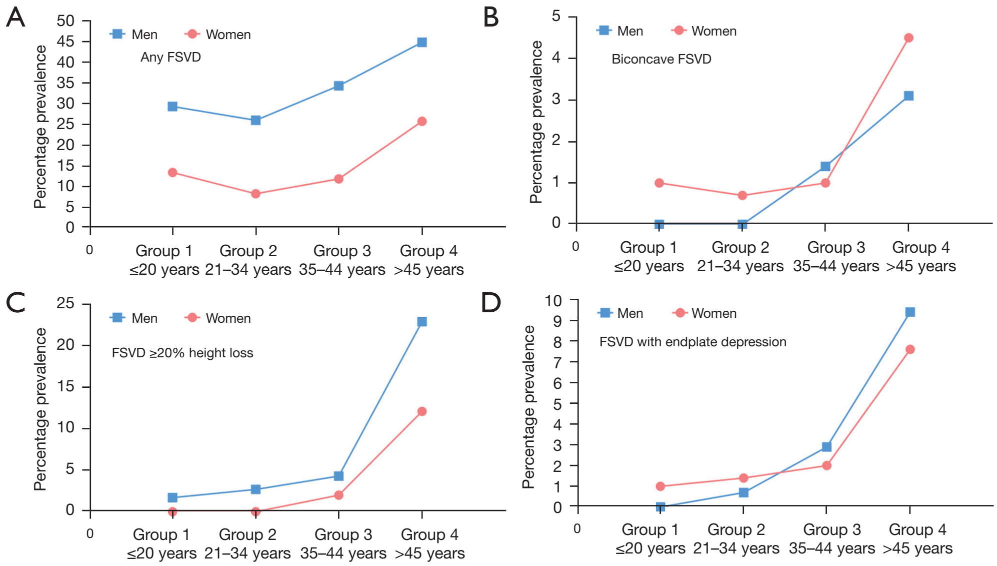

Figure 7 Prevalence of FSVDs among four age groups of female and male cases (the Jiaxing study). (A) Prevalence of all-inclusive FSVD, higher prevalences are noted among males than among females. Note a trend of lower FSVD prevalences is observed among groups 2 subjects (21–34 years) than among groups 1 subjects (≤20 years), both for females and for males. From female group-1 to group-2, there was also a reduction of multiplicity from 53.8% to 16.7% (11). (B) Prevalence of biconcave FSVDs, a weak trend of higher biconcave FSVD among females than among males is noted. (C) Prevalence of FSVDs with ≥20% vertebral height loss. (D) Prevalence of FSVDs with endplate depression. Both biconcave FSVDs and FSVDs with endplate depression are noted among subjects assumed to be with normal BMD (those <45 years). Reused with permission from (11). FSVDs, fracture shaped vertebral deformities; BMD, bone mineral density.

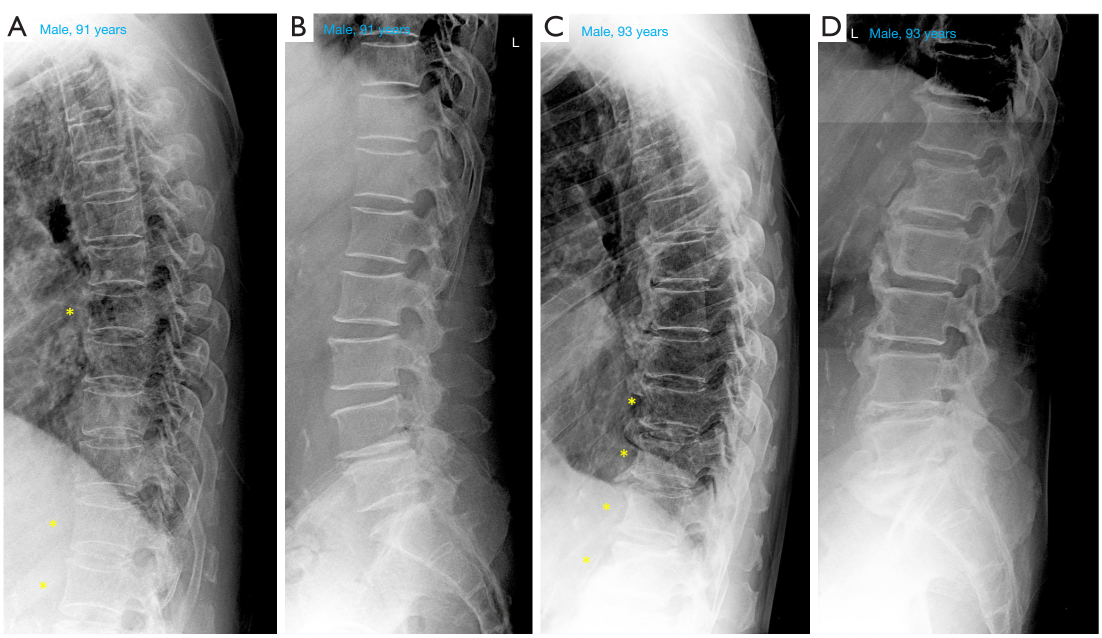

Figure 8 Thoracic and lumbar spine radiograph of two older male cases (A and B: a 91-year-old man, C and D: a 93-year-old man). Though these two cases were at an advanced age, no radiographic vertebral wedging is noted at mid-thoracic and thoracolumbar regions. *, vertebrae with endplate ring appearing as oval shape due to X-ray beam projection.

Table 2 Long-term follow-up incident VF rate among older women with baseline minimal OLVF and apparent OLVF

Baseline OLVF grading	No. of subjects and gradings#		
	No OLVF (grade 0)	Minimal OLVF	Apparent OLVF
Baseline cases for year-14 follow-up	126	5¶	19
Incident OLVF at year-14 follow-up	14.3% (18/126)A,B	60% (3/5)A,^	52.6% (10/19)B,^
Baseline cases for year-18 follow-up	114	27¶	15
Baseline hip BMD for cases with year-18 follow-up	0.773±0.105C,F	0.716±0.109C	0.683± 0.074F
% cases with incident OLVF at year-18	27.1% (31/114)D,E	59.3% (16/27)D,^	66.7% (10/15)E,^
Baseline age (years) of cases with no incident VF at year-18	68.7±3.3	69.7±2.9	68.6±3.5
Baseline age (years) of cases with incident VF at year-18	69.4±3.1	70.1±2.4	68.4±3.1

Data from (8,9). #, in total 150 cases for year-14 study, 156 cases for year-18 study; ¶, ECF sign was not documented for the year-14 study, while none of the 27 cases with minimal OLVF had ECF sign at baseline; ^, note, only the incident VF frequency was counted, while the 'amount' or 'severity' of these incident VFs was note quantified. Thus, we do not claim that minimal OLVF and apparent OLVF have the same degree of clinical relevance. A, P=0.007; B, P<0.001; C, P=0.012; D, P=0.0015; E, P=0.002; F, P=0.001. VF, vertebral fracture; OLVF, osteoporotic-like vertebral fracture; Minimal OLVF, with <1/5 vertebral height loss; Apparent OLVF, with ≥1/5 vertebral height loss; BMD, bone mineral density; ECF, endplate or cortex fracture.

is about 16.2% for those aged ≥50 years, the same as the lifetime risk of hip fragility fracture (16). If other sites are also considered, this cutpoint value identifies approximately 30% of postmenopausal women as having osteoporosis, which is approximately equivalent to the lifetime risk of fragility fracture at the spine, hip, or forearm. Following the same line of thinking as the WHO BMD definition, we performed studies to define what portion of older community women and men with what severity of radiographic OLVF correspond to what low T-score status.

For the women's study, we used materials from MsOS(Hong Kong) and "Roman Osteoporosis Prevention Project" (10). Data based on Hong Kong Chinese were used as an example for East Asians, and data based on Rome Italians were used as an example for Caucasians. An OLVF sum score (OLVFss) was calculated for each study subject. For each vertebra in a woman, a score of 0, −0.5, −1, −1.5, −2, −2.5, and −3 was assigned for no OLVF or OLVF of <1/5, 1/5–<1/4, 1/4–<1/3, 1/3–<2/5, 2/5–<2/3, and ≥2/3 vertebral height loss, respectively. Our Jiaxing study shows two adjacent FSVDs are common at the thoracolumbar region (11). On the other hand, it is likely that OLVFs at two different locations suggest more compromised bone strength than two adjacent OLVFs (17). Therefore, we applied the criteria that, two adjacent minimal OLVFs were assigned as −0.5, and three adjacent minimal OLVFs (which is overall less common, and we did not see three adjacent FSVDs among our Jiaxing study young females) were assigned to be −1. In principle, OLVFss was calculated by summing up the scores of vertebrae T4 to L5. T1–T3 are not always shown very well on radiograph, and OVF at T1–T3 levels are rare. However, in cases an OLVF is seen at T1–T3 level, it was counted for OLVFss calculation as well.

The diagnostic application of OLVFss for women is summarized in *Figures 9,10*. For both Italians and Chinese, OLVFss ≤−1 meet the $tscore_{lowest}$ (the lowest of femoral neck, total hip, and lumbar spine T-scores) ≤−2.5 criteria for suggesting osteoporosis. OLVFss ≤−1.5 meet the $tscore_{neck}$ (femoral neck T-score) criteria for diagnosing osteoporosis (10). In other words, two nonadjacent minimal grade OLVFs, or a single mild OLVF, suggest osteoporosis, while three nonadjacent minimal grade OVF, one minimal grade OVF and one mild OVF, or one OLVF with ≥1/4 height loss (≥ moderate grade), meet the diagnosis of osteoporosis. In applying these criteria, we should try to make sure the extent of vertebral height loss is measured or estimated with a reasonable degree of precision. A reader without prior training generally cannot visually estimate the degree of vertebral height loss with good reliability. The Jiaxing study results counting chest vertebral deformity index (VDI; of T4 to L1 or L2), which has the same principle as in counting OLVFss, is shown in *Figure 11*. Most of the OLVFs occur at the thoracic spine and thoracolumbar region (10). *Figure 11* confirms that, VDI score more negative than −1 is rare among young and middle-aged women, thus it appears reasonable to diagnose

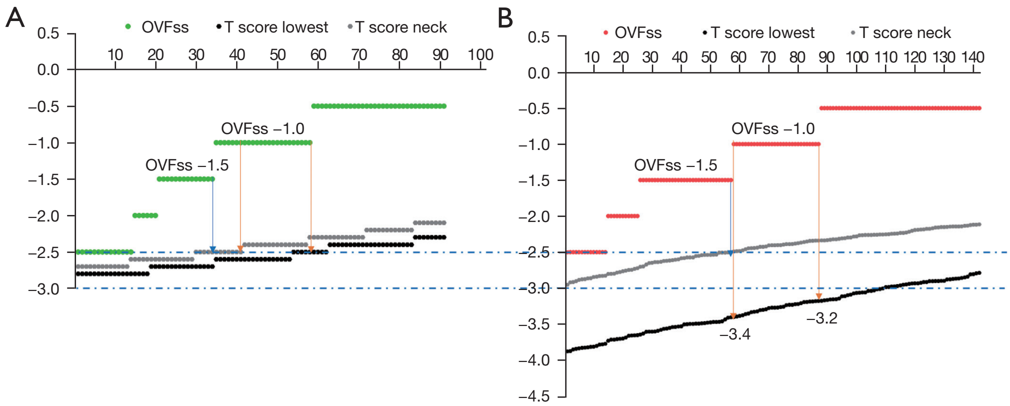

Figure 9 The relationship between OLVF sum score (denoted as OVFss in the graphs) of −1.5/−1.0 and T-scores for Italian women (A) and Chinese women (B). See reference (10) for methodology. Arrows indicate the threshold for suggesting osteoporosis. The study cohorts in these graphs had a mean age of 73.6 years for Italians and 74.0 years for Chinese. Reused with permission from (10). OVF, osteoporotic vertebral fracture; OLVF, osteoporotic-like vertebral fracture.

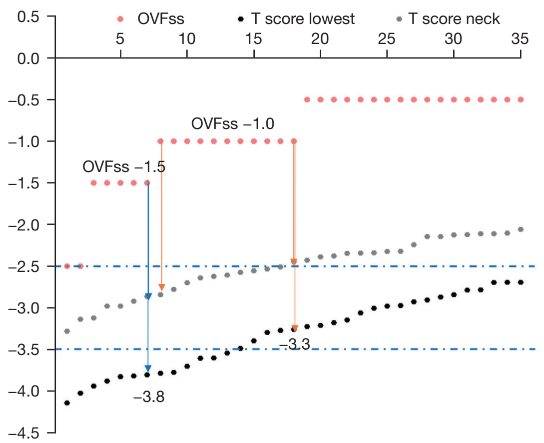

Figure 10 The relationship between OLVF sum score (denoted as OVFss in the graph) of −1.5/−1.0 and T-scores for Chinese women with a mean age of 68.9±5.5 years. See reference (10) for data and methodology. Arrows indicate the threshold for suggesting osteoporosis. OLVFss =−1.0 corresponds to highest $tscore_{lowest}$ of −3.3, and OLVFss =−1.5 corresponds highest $tscore_{lowest}$ of −3.8. Compared with the results in *Figure 9*, the results suggest that for a younger subject, in statistical terms, a lower BMD value might be required for the subject to sustain an OVF. Data from (10). OLVF, osteoporotic-like vertebral fracture; OVF, osteoporotic vertebral fracture; BMD, bone mineral density.

osteoporosis when OLVFss is ≤−1.5. When a lateral chest radiograph is taken, vertebrae T4 to L2 (or to L1) can be evaluated for possible OVF. The principle that, one minimal grade OLVF and one mild OLVF, or one OLVF ≥ moderate grade, meet the diagnosis of osteoporosis, can also be applied to lateral chest radiograph.

Recently we argued that due to the much lower fragility prevalence among older Chinese than among Caucasians, the criterion of $tscore_{lowest}$ threshold ≤−2.5 for defining osteoporosis may be too loose for Chinese (18-20). The comparative OLVFss analysis of Hong Kong Chinese women and Italian Caucasian women (*Figures 9,10,12*) further supports our suggestion that $tscore_{lumbar}$ (lumbar spine T-score) threshold for defining osteoporosis should be less than <−3.7 for Hong Kong Chinese women (18).

OVF severity and BMD among older men

How to diagnose OVF among older men has not been well established. It is likely that OVF prevalence among older males is no more than half of that of age-matched females. In our MrOS(Hong Kong) and MsOS(Hong Kong) studies, from baseline on, clinical spine fractures (mostly osteoporotic fragility fractures) were followed

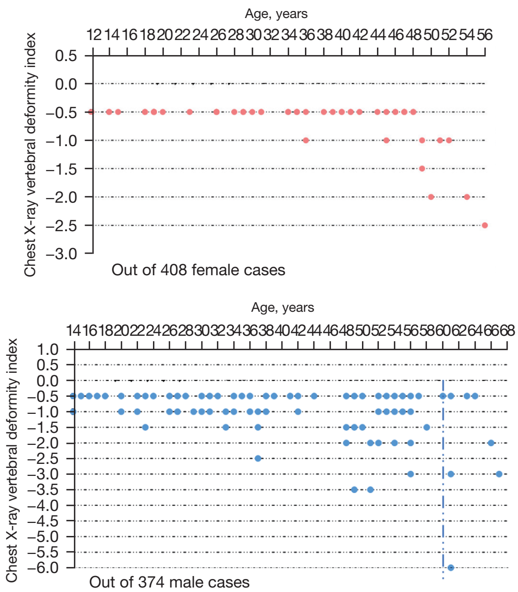

Figure 11 VDI among young and middle-aged patients unrelated to spine disorders (Jiaxing study). It can be assumed that for women younger than 44 years old and men younger than 60 years old there would be few cases, or none, had osteoporosis. One VD of 'minimal', 'mild', 'moderate', 'moderately severe (mod/s)', 'severe', 'collapsed' has <1/5, 1/5 -<1/4, 1/4 -<1/3, 1/3 -<2/5, 2/5 -<2/3, and ≥2/3 vertebral height loss, and is assigned a score of −0.5, −1.0, −1.5, −2.0, −2.5, −3 respectively. Chest VDI is calculated by summing up the scores of vertebrae T4 to L1 or L2 (depending the visibility of L2 on lateral chest radiograph). Patients with any fracture shaped VDs are presented. Vertical dotted line: separation of those <60 and ≥60 years old. Reused with permission from (11). OVF, osteoporotic vertebral fracture; VDI, vertebral deformity index; VD, vertebral deformity.

up for 10 years for the 1,954 male participants of the population-based MrOS(Hong Kong) study, and for 9 years for the 1,953 female participants of the MsOS(Hong Kong) study. Our results show clinical spine fractures ≥1 time (i.e., at least one fracture incident) were recorded 133 cases/100,000 person-years in men and 273 cases/100,000 person-years in women (21-23) (*Figure 13*). Diagnostic criteria for radiological OVF should be established so that clinically relevant OVF prevalence diagnosed by imaging among older men will also be half of

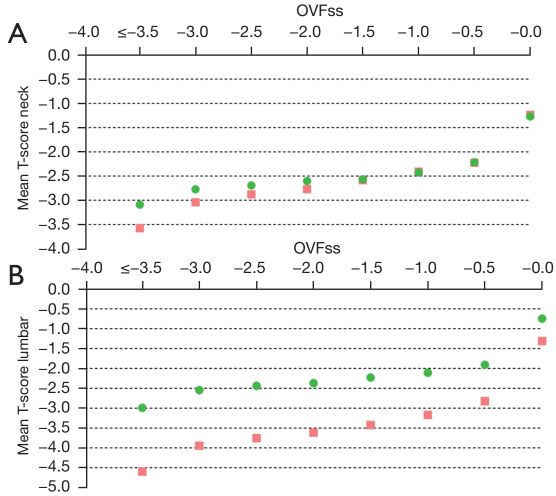

Figure 12 Relationship between OLVFss and mean femoral neck T-score (A) or mean lumbar spine T-score (B). Results for Italians (n=301, age: 73.6±6.1 years) are in green dots and results for Chinese are in pink square (n=521, 74.0±7.2 years). (A) shows, for those without OVF, the $tscore_{neck}$ values are similar between Chinese and Italians. For OVFss ≤−2.0, for each OVF grade the values for Italian were slightly less negative than those for Chinese. For example, when OVFss =−2.5, $tscore_{neck}$ is −2.60 for Italians and −2.77 for Chinese. This means, if we considered OVF severity as a surrogate clinical endpoint, then a $tscore_{neck}$ of −2.77 for Chinese is equivalent to a $tscore_{neck}$ of −2.60 for Italians. This supports our suggestion that, instead of adopting the cutpoint tscore value of ≤−2.5 for defining osteoporosis, this cutpoint tscore value for $tscore_{neck}$ can be slightly lower for Chinese, such as ≤−2.7. (B) show data for $tscore_{lumbar}$. It appears that Italians have a higher mean $tscore_{lumbar}$ value to start with even for those without OVF, once there is an OVF, then the difference between Italians and Chinese become wider. When OVFss =−2.5, $tscore_{lumbar}$ is −2.44 for Italians and −3.75 for Chinese, while when OVFss =−1.5, $tscore_{lumbar}$ is −2.23 for Italians and −3.42 for Chinese. This means, if we considered OVF severity as a surrogate clinical endpoint, then a $tscore_{lumbar}$ of −3.75 for Chinese is equivalent to a $tscore_{lumbar}$ of −2.44 for Italians. This supports our suggestion that, instead of adopting the conventional cutpoint tscore value of ≤−2.5 for defining osteoporosis, this cutpoint $tscore_{lumbar}$ value can be lowered to ≤−3.7 for Chinese women (18). Data from (10) (the same data as in *Figure 9*). $tscore_{neck}$, femoral neck T-score; $tscore_{lumbar}$, lumbar spine T-score; OVF, osteoporotic vertebral fracture; OLVF, osteoporotic-like vertebral fracture.

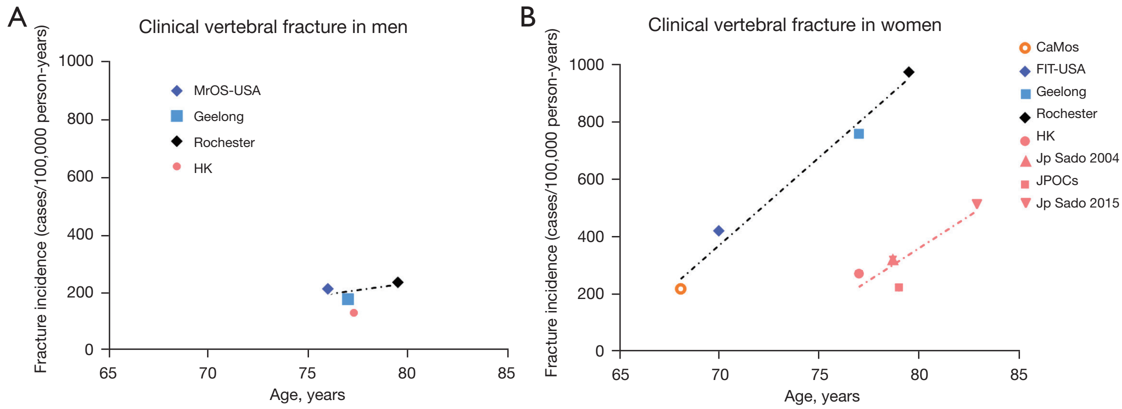

Figure 13 The clinical OVF prevalence among older men (A) and women (B). East Asians have a much lower clinical OVF prevalence than those of Caucasians. (A) Data are from MrOS(Hong Kong) study, Freitas *et al. Osteoporos Int* 2008;19:615-23 (MrOS USA study), Sanders *et al. Osteoporos Int* 1999;10:240-7 (Geelong study), and Cooper *et al. J Bone Miner Res* 1992;7:221-7 (Rochester study). (B) Data are from MsOS(Hong Kong) study; Sakuma *et al.*, *J Bone Miner Metab* 2008;26:373-8 (Japan Sado 2004), Imai *et al.*, *J Bone Miner Metab* 2019;37:484-90 (Japan Sado 2015); Kamiya *et al.*, *Maturitas* 2019;130:13-20 (JPOCS); Sanders *et al. Osteoporos Int* 1999;10:240-7 (Geelong study); Cooper *et al. J Bone Miner Res* 1992;7:221-7 (Rochester study); Fink *et al. J Bone Miner Res* 2005;20:1216-22 (FIT-USA study), and Papaioannou *et al. Osteoporos Int* 2005;16:568-78 (CaMos study). The dotted black and orange lines indicate linear fits for simplicity (ideally it should be an exponential growth fit). OVF, osteoporotic vertebral fracture.

that of age-matched older women.

Our Jiaxing study shows that even minimal FSVDs in men could be due to micro-fractures rather than physiological wedging (11). For the Chinese community male subjects with the age of ≥50 years (which will have a mean age much older than the Jiaxing study older men group's mean age: 54.1 years, considering life expectancy for Chinese men is currently 74.7 years), osteoporosis prevalence is estimated to less than 4% (18). Note that reports from the US suggest that older Asian men have a hip fragility fracture rate lower than that of Americans of African ancestry (24,25). We expect few of our male cases in the Jiaxing study older group (n=96, mean age: 54.1 years, range: 45–67 years) had osteoporosis (particularly for those younger than 60 years), while among them 6.3% had ≥ moderate grade (i.e., ≥1/4 vertebral height loss) FSVD, 9.4% had endplate depression, 3.1% had biconcave FSVD (11). Thus, VD with shapes typically considered to be associated with OVF may also be commonly seen among older men of normal bone strength.

Following our study methodology for women, using MrOS(Hong Kong) data we did a study on 755 Chinese men (age: 76.4±6.7 years, range: 65–98 years). The results show OLVFss of −2, −2.5, −3 corresponded to a mean $\text{tscore}_{\text{neck}}$ of −2.297 (range: −2.355 to −2.247), −2.494 (range: −2.637 to −2.363), and −2.773 (range: −2.898 to −2.643), a mean $\text{tscore}_{\text{lumbar}}$ of −2.495 (range: −2.656 to −2.403), −2.931 (range: −3.255 to −2.656), and −3.369 (range: −3.525 to −3.258) (26). The Pearson correlation value of OLVFss and $\text{tscore}_{\text{neck}}$ and $\text{tscore}_{\text{lumbar}}$ was r=0.21 and 0.22 (both P<0.0001) (26). Therefore, we suggest that, a single severe grade OLVF (≥2/5 height loss) or OLVFss ≤−2.5 suggest the subject is osteoporotic, and a single collapse grade (≥2/3 height loss) radiological OLVF or OLVF ≤−3 meets osteoporosis diagnosis criterion. This is consistent with our Jiaxing study results that OVFss of ≤−2.5 is relatively uncommon among men (*Figure 11*). On the other hand, since OLVFss =−2.5 may be occasionally seen among men of assumed normal bone strength, OLVFss of −2.5 still does not firmly establish the diagnosis of osteoporosis in men. With a modified Genant SQ method and OVF diagnosed when there was a reduction in vertebral height and/or compression of ≥10% of the estimated vertebral body height, Kherad *et al.* (27) reported that, in men with one or several OVFs, 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 dual-energy X-ray absorptiometry images, Waterloo *et al.* (28) reported that the 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. It is possible these earlier results of OVF in men may have been contaminated by non-osteoporotic VDs. These findings highlight the difficulty of diagnosing OVF among older men.

The above discussions do not necessarily suggest a moderate grade OLVF in men is not due to osteoporosis. A moderate grade OLVF still more likely occurs in an osteoporotic man than in a non-osteoporotic man, only that a single moderate grade OLVF in a man does not itself suggests the osteoporosis diagnosis statistically. Because the prevalence of osteoporosis among older Chinese men is low (18), thus in a group of community subjects, a moderate grade OLVF is more likely seen in a non-osteoporotic man than in an osteoporotic man. Note osteoporosis is a statistical classification, and the original osteoporosis T-score ≤−2.5 criterion for older women aims at specificity, at the cost of sensitivity (16).

In our studies (10,26), the Pearson correlation value of $tscore_{neck}$ and OLVFss for Chinese older women was r=0.33 (95% CI: 0.20–0.45; P<0.0001), while that of $tscore_{neck}$ and OLVFss for Italian older women was r=0.48 (95% CI: 0.37–0.58; P<0.0001). The Pearson correlation value of OLVFss and $tscore_{neck}$ for Chinese older men was r=0.21 (95% CI: 0.14–0.28; P<0.0001). These results suggest the correlation between T-score and OLVFss was weaker in Chinese women than in Caucasian women, and even weaker in Chinese men than in Chinese women. This may be due to that Caucasian women suffer more prevalent and more severe OVFs than Chinese women, and Chinese women suffer more prevalent and more severe OVFs than Chinese men (23). These results also suggest risk factors other than lower BMD contribute to OVF. While measurement of spine BMD is affected by spine degeneration, OLVFss can be considered a surrogate clinical endpoint (29) and may be more clinically meaningful than spine BMD measure.

It should be noted that our MrOS(Hong Kong) and MsOS(Hong Kong) study subjects are considered to be mainly city dwellers, it is possible that subjects in farming communities with routine weight-bearing labor may have an increased prevalence of non-osteoporotic vertebral deformities (9,11). It is thus possible that our results may not be readily applicable to those populations.

Endplate depression

A vertebral endplate consists of perforated cortical bone with a layer of hyaline cartilage bonded to its disc surface. The cortical bone layer contains a network of small cavities which allow bone marrow to lie adjacent to calcified hyaline cartilage for approximately 10% of the central endplate area, which is an important route for metabolite transport into the discs. The nutritional demands of the discs result in that vertebral central endplates are thin and porous, and which can be subject to fracture under stress force even bone strength is normal. In vertebral osteoporosis, the endplate becomes weakened due to the loss of support from trabecular bone, and due to thinning of the endplate itself. We consider ECF (endplate and/or cortex fracture) as an additional sign of OVF, and a positive ECF sign would increase the confidence for OVF diagnosis, but ECF is not an essential sign of OVF (1). As we noted earlier, radiograph is not a sensitive technique to detect endplate fracture (15). In our MsOS(Hong Kong) study year-18 follow-up, out of 156 female participants, 27 cases (17.3%) had minimal grade OLVF while all without ECF at baseline, and these 27 cases had a lower mean hip BMD at baseline than those without any OLVF. Among these 27 cases, 16 cases (59.3%, 16/27) had incident VF during the follow-up, with the incident VF rate significantly higher than those without any baseline OLVF (*Table 2*).

In our Jiaxing study, endplate depression (or endplate fracture) was also seen among cases assumed to be normal bone strength (*Figure 7*). Therefore, while radiographic endplate fracture or biconcave deformity is common among osteoporotic fractures, these may not be pathognomonic signs for OVF.

Schmorl's node corresponds histologically to nucleus pulposus herniation into the vertebral spongy bone with thickened trabeculae around the formed node. We propose that this pathway may exist that: osteoporosis → weakened endplate → Schmorl's node development ↔ endplate fracture of an osteoporotic vertebra. We have recently demonstrated that Schmorl's nodes may predispose an osteoporotic endplate to fracture (*Figure 14*) (30). For MrOS and MsOS studies, at year-14 follow-up, thoracic spine magnetic resonance imaging (MRI) was sampled in 270 men males (mean: 82.9±3.7 years) and 150 females (mean: 81.5±4.3 years). Schmorl's node prevalence in women (55.5%) almost doubled that in men (25.9%). Subjects with SN was more likely to have OVF, with an odds ratio for men of 4.32 (95% CI: 1.70–11.0; P=0.002) and an odds ratio for women of 3.28 (95% CI: 1.23–8.74; P=0.018). If only OVFs with >1/3 vertebral height loss were counted, the odds ratio for men increased to 5.69 (95% CI: 1.61–20.09; P<0.01). Schmorl's node prevalence was statistically significantly correlated with lower femoral neck BMD T-score, and statistically significantly correlated with

Figure 14 Examples of Schmorl node co-exist with OVF. Schmorl node can exist in the same vertebra with OVF, or in a vertebra without OVF. (A) Sagittally reconstructed spine CT image of an elderly women with acuate low energy trauma. Blue arrow denotes an acute OVF, white arrow denotes an OVF with apparent upper endplate depression and a Schmorl node. (B) L4 OVF with apparent upper endplate depression and a Schmorl node. (C) T12 OVF with apparent upper endplate depression and a Schmorl node and also with a lower endplate Schmorl node. T10 with a lower endplate Schmorl node. Yellow arrows: Schmorl node. (B) and (C) are from MsOS(Hong Kong) year-14 follow-up study. OVF, osteoporotic vertebral fracture; CT, computed tomography.

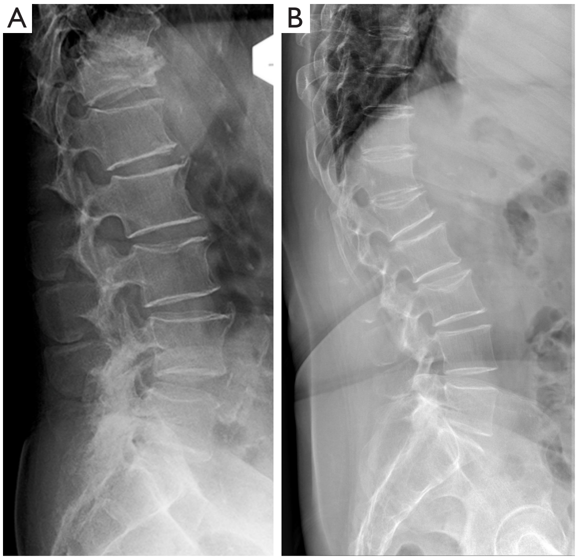

Figure 15 Endplate depression with vertebral height maintained. (A) Lumbar radiograph of a male subject aged 85 years. T12 collapsed deformity. L3 upper endplate slight depression with anterior vertebral height well maintained. (B) Lumbar radiograph of a female subject aged 74 years. L1 severe osteoporotic deformity. L3 upper endplate slight depression with anterior vertebral height well maintained.

OLVFss (30).

For thoracic and thoracolumbar regions, OVF is usually associated with some extent of anterior vertebral height loss. In fact, for thoracic and thoracolumbar regions, deformities without any anterior height loss are more likely due to X-ray projection artefacts (1). However, in the lumbar region, endplate depression can be commonly seen without anterior vertebral height loss (*Figure 15*). We emphasize the importance of checking artifact due to X-ray projection. Hereby we provide another example in *Figure 16*.

Radiographic follow-up of OVF

Once an OVF occurred, human biology starts to repair and heal the OVF (*Figure 4*), and maybe re-fracture occurs, and then further repair. Though the repair and healing may be generally weaker among very old or very osteoporotic subjects, there is no reason to suggest repair and healing do not occur in very old or very osteoporotic subjects. Moreover, vertebra re-adjustment process to stabilize the spine also occurs (*Figure 17*). We have once argued for using the term 'osteoporotic vertebral deformity (OVD)' as opposed to the term OVF. We argued that the term OVF is

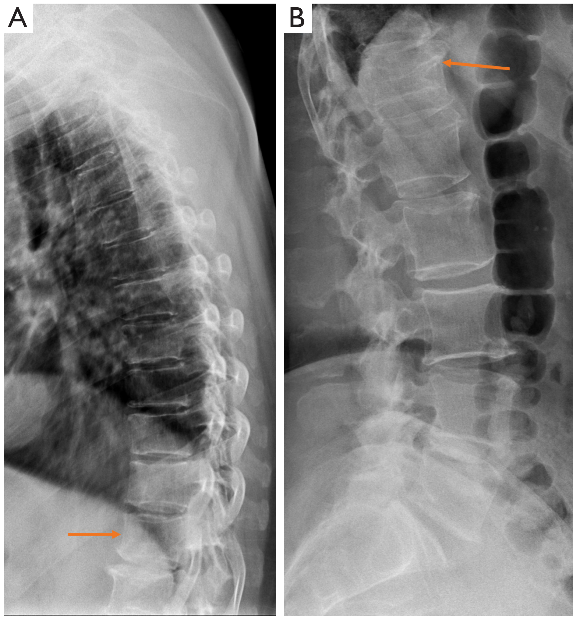

Figure 16 Spine radiograph of a 72-year-old woman. (B) show T12 (arrow) upper endplate fracture mimics, while (A) suggests the upper endplate morphology and vertebral anterior height maintained.

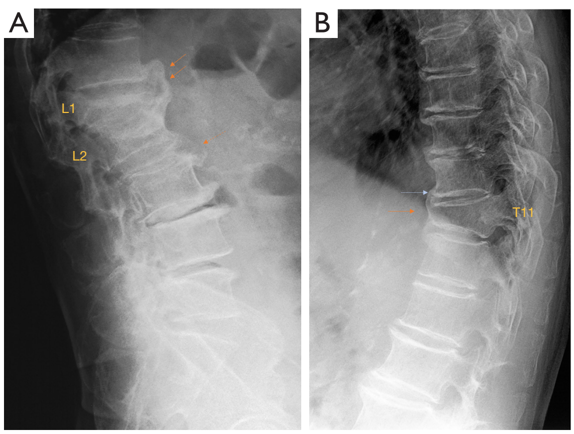

Figure 17 Formation of osteophyte bridging to stable the spine. (A) Radiograph of an 88-year-man, L1 is collapsed, while L2 is with severe OVF. From T12 to L2, there is a formation of osteophyte bridging (arrows). From L2 to L3, there is a partial formation of osteophyte bridging (arrow). (B) Radiograph of a 91-year-old man with T11 collapsed OVF and formation of osteophyte bridging from T10 to T12 (arrows). OVF, osteoporotic vertebral fracture.

better used for acute and subacute phase fracture (1). Now we like to revise this perception. Since unlike a fracture in a long bone which can completely heal, OVF is more likely under continuous compressive stress and continuous repairing and re-modeling (though maybe at a low level of activity), therefore OVF can be an appropriate term.

Though at the group level a greater OVF severity is always associated with a greater risk of further VF, at an individual patient level, apparent OVF does not mean necessarily inevitable further VF progression even among elderly subjects (*Figures 18,19*).

As shown in *Figures 18-20*, endplate fracture also does not mean necessarily inevitable further fracture progression. Though osteoporotic wedging deformity is generally considered to associate with less further fracture risk than bi-concave deformity (31), osteoporotic wedging deformity commonly occurs at the thoracolumbar junction level, which is the spine segment under the most stress. Wedging deformities at the thoracolumbar junction are likely to further progress due to the higher physical stress at this level (*Figure 21*) (32).

Acquired short vertebrae (aSV)

Congenital SV is not common. Congenital SV often have other associated changes of adjacent vertebrae (*Figure 22*), and mostly can be differentiated from aSV by an experienced reader.

We define aSV as those with decreased vertebral anterior and middle heights, while without apparent anterior wedging or apparent bi-concave changes, i.e., middle height and anterior height are reduced to a similar extent for aSV (15). In addition, other apparent OVF mimics, such as apparent osteoarthritic (OA) wedging, are excluded. In one our report, we suggested that singular aSV is often associated with CT endplate depression thus likely to be osteoporotic, while multiple adjacent aSV are without CT endplate depression and are likely due to degenerative changes (15). Therefore, when we diagnose aSV, we require at least two adjacent short vertebrae in the same subject. The differentiation of multiple adjacent aSV from multiple adjacent OVFs is that, multiple adjacent aSV appear similar in appearance, while multiple adjacent OVFs commonly

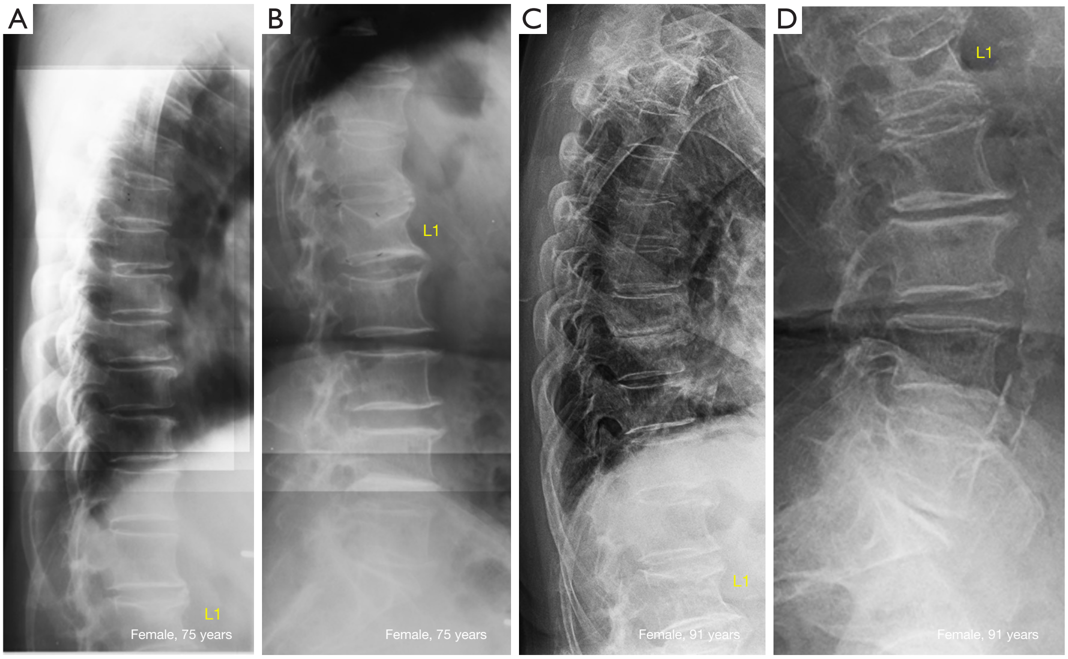

Figure 18 A female patient followed-up for 16 years (A,B: baseline thoracic and lumbar spine radiograph; C,D: follow-up thoracic and lumbar spine radiograph). L1 osteoporotic deformity and upper endplate depression are noted at baseline. After 16 years, no apparent progression was noted. Note that on (D) the L1 appears more compressed is due to the oblique X-ray projection. This patient did not take anti-osteoporosis medication during the follow-up period.

Figure 19 A female subject followed-up for 16 years (A: baseline lumbar spine radiograph; B: follow-up lumbar spine radiograph). L3 osteoporotic deformity and upper endplate depression are noted at baseline. After 16 years, no apparent progression was noted. This subject did not take anti-osteoporosis medication during the follow-up period.

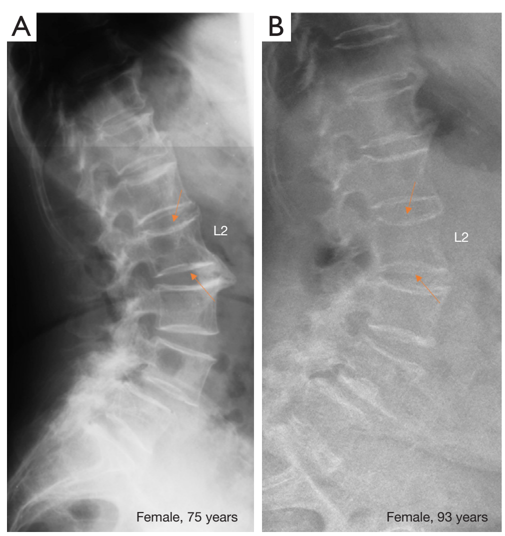

Figure 20 Baseline (A) and follow-up (B) lumbar spine radiograph of a female subject followed-up for 18 years. L2 had minimal depression of bother upper and lower endplates. After 18 years, endplate depressions only slightly progressed (arrows). The anterior vertebral height of L2 was maintained. This patient did not take anti-osteoporosis medication during the follow-up period.

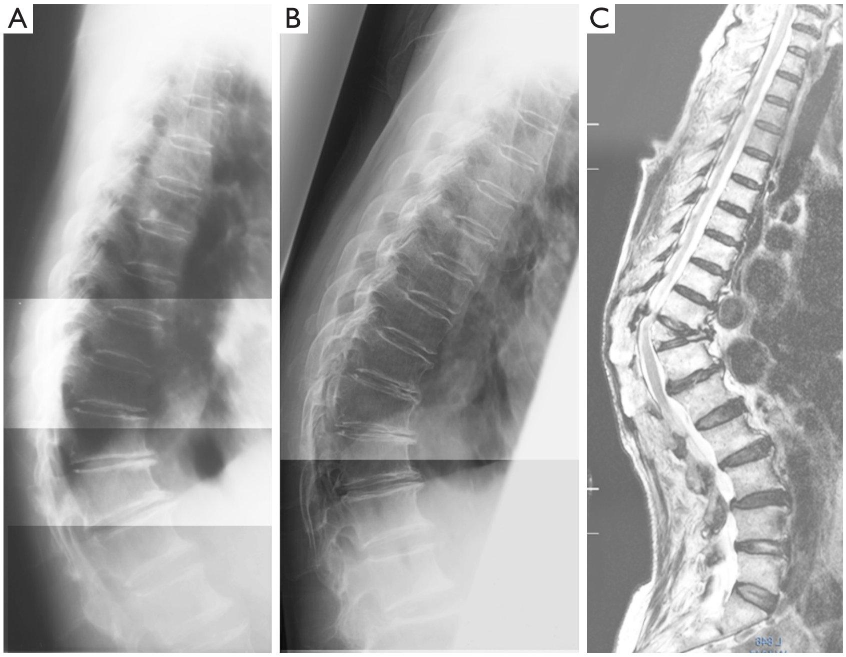

Figure 21 A female case (80 years old at baseline) had T11 mild grade deformity progressed to collapse. (A) Baseline radiograph; T10, T11, T12 appeared anterior wedging with osteoarthritic degenerative changes (with reduced intervertebral disc heights and growth of osteophytes). (B) Year-4 follow-up radiograph. (C) Year-14 follow-up magnetic resonance imaging. (C) shows T11 is collapsed. A consistent local kyphosis suggests increased stress.

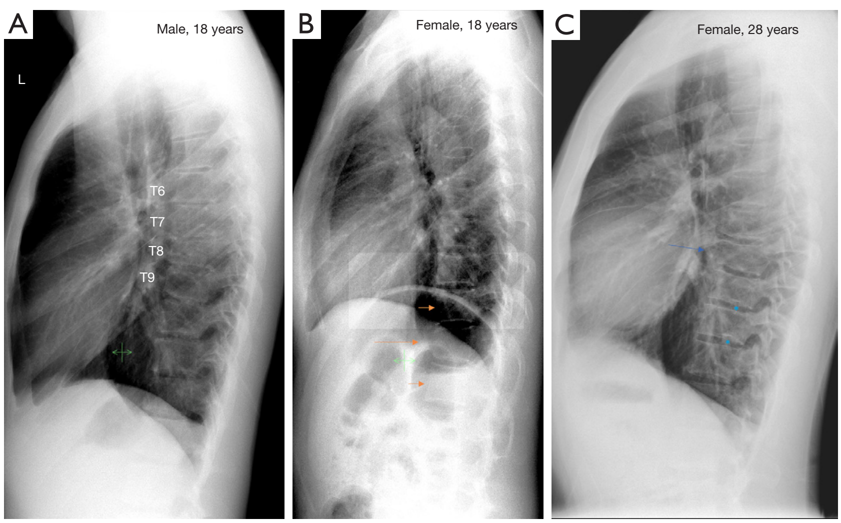

Figure 22 Three cases of congenital short vertebrae. (A) An 18-year-old man, vertebra T8 has a reduced height, and the size of T7 is larger than usual while size of T9 is smaller than usual. T10 has a longer than usual anterior length. Intervertebral disc spaces of T6/T7 and T7/T8 are narrowed. (B) An 18-year-old woman, vertebra T11 has a reduced height (long arrow). The anterior upper and lower corners are smooth. Vertebrae T10 and T12 (short arrows) have compensated overgrow. (C) A 28-year-old man vertebra (from the Jiaxing study), T8 has a reduced height (arrow), the border of T8 appears to be irregular. The lower endplates of T9 and T10 both have a notch (*), suggesting juvenile epiphysitis. (A,B) are reused with permission from (11).

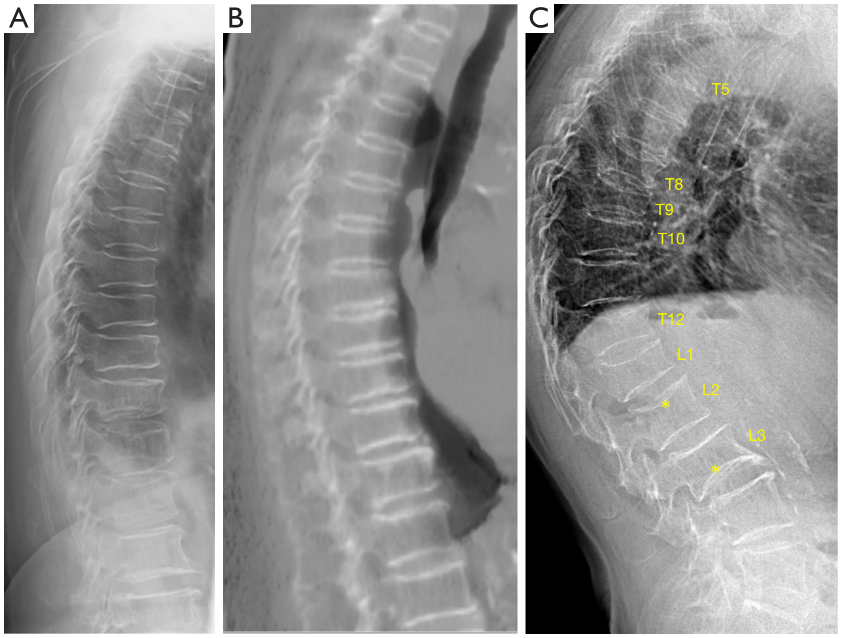

Figure 23 Differentiation of multiple aSVs and multiple OVFs. (A) A female case radiograph shows multiple aSVs. (B) Another female case sagittally reconstructed CT scan shows multiple aSVs. (C) Another female case radiograph shows multiple OVFs. In (C), OVFs vary greatly in shape and severity, and most show endplate depression. (*) on L2 shows upper endplate fracture (depression); (*) on L3 show lower expansive endplate (an anomaly). In (A,B), multiple aSVs show much less variation in shape and severity, and aSVs do not show apparent wedging or apparent endplate depression. In (B), the increased density of the involved endplates suggests regenerative inflammatory changes. While many aSV in (A) and (B) are already quite severe, it appears that they did not apparently 'fracture'. Reused with permission from (9). aSVs, acquired short vertebrae; OVF, osteoporotic vertebral fracture; CT, computed tomography.

have different shapes and different severity (*Figure 23*).

Hereby we provide a further discussion on why a singular aSV is most likely an OVF. We described that the appearance of OVF can be an anterior wedging or a 'mixed shape' (1), then the intermediate shape of anterior wedging and a 'mixed shape' will look like an aSV (*Figure 24*). Could it be that the very early stage of multiple aSV starts as a distinct singular short vertebra as shown in *Figure 24F*? In our experience, this is less likely. It appears that multiple aSV does not start from a distinct apparent singular short vertebra, and then progress to multiple aSV. Instead, multiple aSV start from multiple 'slight degree' aSV, and then these aSV progress in number and severity including an increased extent of height loss (*Figure 25*).

In the Jiaxing study, we noted that among the in total 449 male and female cases aged ≤34 years, there was no single case had aSV (note aSV commonly occur in thoracic spine rather than lumbar spine). For the group ≥45 years, of males (mean age: 54.1 years, among them 36.1% had been a farmer or physical laborer) 15.6% had aSV while only 1.5% of the females (mean age: 50.2 years) had aSV (11). Based on the demographics of the subjects, we suggest that physical labor such as weight-bearing could be associated with aSV (11). With our MsOS and MrOS(Hong Kong) year-18 study we had a few observations (9). Firstly, aSV prevalence among women was lower than that of men, which was consistent with our Jiaxing results. In addition to the subjects who were scheduled to have the year-18 follow-up radiography, their spouses were also invited to participate, and thus we were able to include additional 11 males and 41 females to have spine radiography. Counting the study participants and their spouses together, 14.2% of the males (all n=155, mean age: 87.4 years) and 8.6% of the females (all n=197, mean age: 85.2 years) had aSV. Assuming Hong Kong residents had less chance of weight-bearing labor history, and the males in our year-18 follow-up were much older than the older group subjects in our Jiaxing study (mean age: 87.4 *vs.* 54.1 years), that the aSV prevalence among Hong Kong males being not higher (14.2% *vs.* 15.6% for Jiaxing male subjects) further

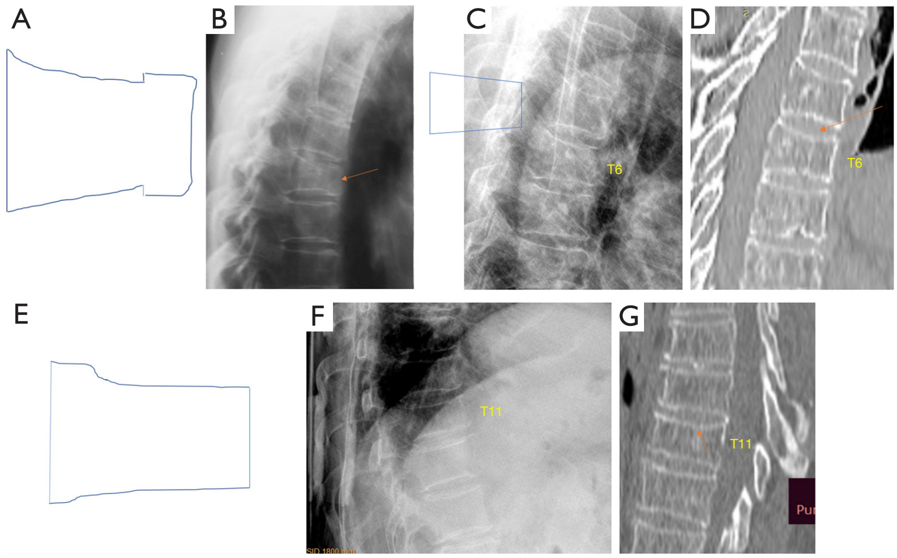

Figure 24 A singular aSV can be the 'intermediate shape' between OVF's anterior wedging and 'mixed shape' OVF, thus most likely be an OVF. (A) and (B) illustrate a 'mixed shape' OVF (arrow in B). (C) and (D) illustrate an anteriorly wedged OVF. The arrow in (D) denotes endplate depression. (E-G) illustrate an OVF with the appearance of singular aSV. Arrow in (G) suggest slight endplate depression. These images illustrate (F) can be an 'intermediate shape' between (B) and (C). (A,B) are reused with permission from (1). (E,F) are reused with permission from (15). aSV, acquired short vertebra; OVF, osteoporotic vertebral fracture.

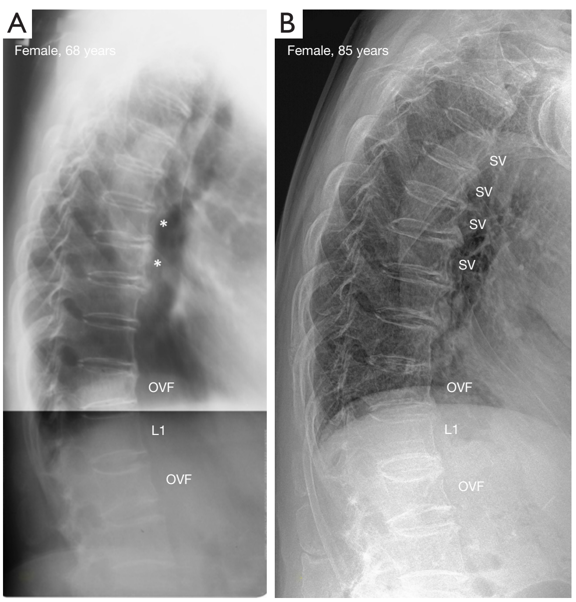

Figure 25 Multiple aSV started from multiple 'slight degree' aSV (A) and then progressed in number and severity (B). (A) T8 and T9 faint degree of aSV (*). (B) Follow-up image (17 years later) shows multiple aSV (marked as SV) at the mid- and upper thoracic spine. T12 and L2 had OVF, and no apparent progression is noted for the OVFs during the follow-up. aSV, acquired short vertebrae; OVF, osteoporotic vertebral fracture.

supports that physical labor could be associated with an increased prevalence of aSV. Both for males and females, a lower mean BMD was noted for subjects with aSV than those without aSV (9). Acquired SV were also associated with other VDs (9), probably due to that both low energy trauma and weakened bone quality may facilitate the development of aSV. *Figure 23A* also demonstrates that even when many aSV are already quite severe, they do not apparently 'fracture'. We suggest aSV itself is 'primarily' not an osteoporosis phenomenon (particularly considering its prevalence is not higher among females), and not 'strongly' associated with increased fracture risk for other vertebrae (9). On the other hand, multiple aSV more likely occur among lower BMD subjects than among normal bone strength subjects.

Another entity to be differentiated from aSV and OVF is OA wedging. Unlike aSV, OA wedging is commonly associated with osteophyte formation and intervertebral disc space narrowing (*Figure 26*). The same as aSV, OA wedging often involve multiple adjacent vertebrae. OA wedging is also without apparent endplate depression and is not associated with an increased further VF risk (33). In our experiences till now, while OA wedging is commonly associated with osteophyte and disc spacing arrowing, aSV is not commonly associated with osteophyte. However, aSV

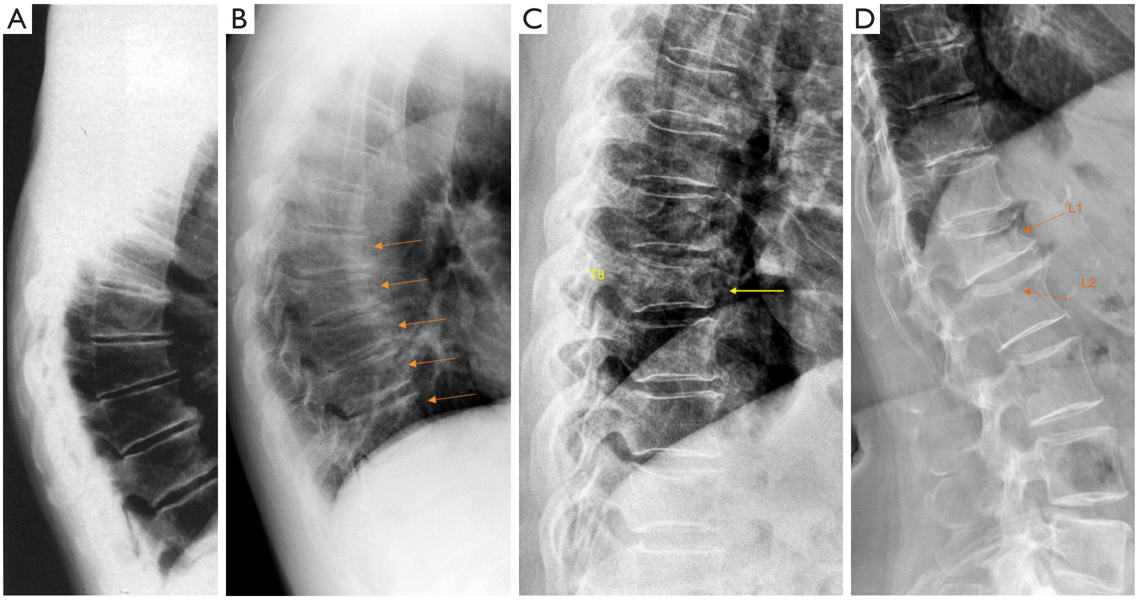

Figure 26 OA wedging and OVF. (A) Spine radiograph of an older woman with OA wedging. Mid-thoracic region shows anterior wedging of multiple vertebrae with similar appearance. Disc space narrowing and osteophytes are noted while without endplate depression. (B) Spine portion of a lateral chest radiograph of a 59-year-old man (a farmer) with OA wedging. Mid-thoracic region shows anterior wedging of multiple vertebrae with similar appearance (arrows), osteophytes are noted. It is considered that there are micro-factures among the involved vertebrae. (C) Spine portion of a lateral chest radiograph of an elderly women, T8 vertebra shows deformity consistent with OVF (arrow). (D) Spine radiograph of an elderly women. L1 vertebra shows deformity consistent with OVF (arrow), while L2 shows upper endplate depression (i.e., endplate fracture) (arrow). (A) is modified from (33); (B) is modified from (11); (C,D) are reused with permission from (1). OA, osteoarthritic; OVF, osteoporotic vertebral fracture.

and OA wedging share a number of similar features, we still do not know whether aSV and OA wedging are distinctly different two entities pathologically.

Note our definition of aSV is different from some earlier reports which used the existence of endplate depression to differentiate OVF from aSV. Of course, the vertebrae with aSV or OA wedging do have micro-VF themselves, only that aSV and OA wedging do not represent generalized weakened bone strength for the involved subject. Acquired SV is associated with physical labor and physical labor may cause endplate depression. We argue that both aSV and OA wedging have other largely distinct morphologies which are different from OVF, even faint endplate depression exists among these deformities does not suggest them to be OVF.

For the association between physical labor and VD, in the Jiaxing study 45–67 years old group men (n=96, age: 54.1±5.9 years), VDI_T4-to-L1/L2 was −0.609±1.047 (mean ± standard deviation). From the MrOS(Hong Kong) baseline study for Hong Kong older men, we randomly selected 141 cases aged between 65 to 69 years (67.3± 1.3 years) and evaluated OLVFss_T4-to-L5 to be −0.465±1.114 (Mann Whitney test, P=0.13 for comparing with the Jiaxing value). Therefore, despite the Hong Kong subjects were on average 13 years older, and L2-5 were all evaluated (Jiaxing study VDI evaluated from T4 to L1 or L2 depending on the visibility of L2 on chest radiograph), still the mean OLVFss value of Hong Kong subjects was less negative than that of Jiaxing subjects (note VDI and OLVF had the same evaluation approach except L3 to L5 was not counted for Jiaxing subjects' VDI). Assuming Hong Kong residents had less chance of weight-bearing labor history than the Jiaxing subjects (11), this result further supports that physical labor could be associated with an increased prevalence of FSVD.

In conclusion, we feel now we have a reasonably good understanding of the OLVF phenomenon. Though the semi-quantitative grading schemes based on vertebral height loss have not been well accepted outside the field of osteoporosis internal medicine (34); for screening detected OVFs, the extent of vertebral height loss and the number of OVFs in a subject may be reasonable indicators of spine bone strength. For most of the minimal and mild grade cases, OVF can only be diagnosed in the sense of statistical probability. On the other hand, severe and collapsed grade OLVFs in women can be mostly diagnosed as OVF by experienced readers. We recommend different OLVFss thresholds to diagnose osteoporosis for men and women, with a much more stringent threshold required for men. Updated training for reading OVF and ECF signs while excluding OVF mimics is highly relevant for osteoporosis clinical care. The most important differential diagnosis for OVF would be oncological deformities (metastatic bone diseases, multiple myeloma) and those due to some hematological diseases. Radiographic differential diagnosis between OVF and oncological deformities can be sometimes easy, and sometimes impossible and further imaging such as MRI is required (1,35). The common OVF mimics include scoliosis, oblique X-ray projection, and degenerative changes (aSV and OA wedging) (1,36). Both OA wedging and aSV tend to involve multiple adjacent vertebrae being similarly deformed, while milder fractural deformities tend more often to be singular with a distinct loss of expected shape (i.e., not multiple adjacent vertebrae appearing similarly deformed) (36). A singular minimal grade FSVD can occur in healthy young women with a prevalence of around 10% (11); while for women of around 70 years old, any OLVF can occur in 38% of the Chinese community women and 60% of the Caucasian community women (10,37). Therefore, while a single minimal grade OLVF in an older woman can be counted for epidemiological studies, such an OLVF (one minimal OLVF/case) may be ignored during daily radiological reporting. For men, till now the results suggest, when OLVFss is >–2.5 (less negative than –2.5), then these OLVF(s) may not be counted as OVF during daily radiological reporting for Chinese older men.

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Footnote

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