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ORIGINAL ARTICLE

Elderly males with or without existing osteoporotic vertebral fracture have much lower future vertebral fracture risk than elderly females: the MrOS (Hong Kong) year-4 follow-up spine radiograph study

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Abstract

Summary MrOS (Hong Kong)'s year-4 follow-up shows, for subjects at baseline without vertebral deformity (VD) and endplate or/and cortex fracture (ECF), the VD progression/new VD rate during follow-up in males was half of our paired MsOS (Hong Kong) study's results. For those with VD or ECF, the VD progression/new VD was less than one sixth of females' rate.

Introduction This study documents MrOS (Hong Kong)'s year-4 follow-up, and the results are compared with the MsOS (Hong Kong) study. Of elderly females with Genant's grade-0, -1, -2, and -3 VD, at year-4 follow-up, 4.6%, 8%, 10.6%, and 28.9% had at least one VD progression or incident VD, respectively.

Methods Spine radiographs of 1500 Chinese males with baseline (mean age 71.7 years, range 65–91 years) and year-4 follow-up were evaluated according to Genant's VD criteria and ECF (non-existent, ECF0; or existent, ECF1). Grade-2 VDs were divided into mild (VD2m, 25–34% height loss) and severe (VD2s, 34–40% height loss) subgroups. Study subjects were graded into eight categories: VD0/ECF0, VD1/ECF0, VD2m/ECF0, VD0/ECF1, VD1/ECF1, VD2m/ECF1, VD2s/ECF1, and VD3/ECF1. With an existing VD, a further height loss of ≥ 15% was a VD progression. A new VD incident was a change from grade-0 to grade-2/3, or to grade-1 with ≥ 10% height loss.

Results Of subjects with Genant's grade-0, 2.05% (25/1219) developed at least one VD progression or/and new VD, while of subjects with Genant's grade-1, -2, and -3 VD, only 2% (3/149), 3.1% (3/96), and 2.8% (1/36) developed at least one VD progression/new VD, respectively. Among the three ECF0 groups, there was a significant difference in new ECF incidence, with VD0/ECF0 being the lowest and VD2m/ECF0 being the highest.

Conclusion VD progression/new VD is much less common in elderly men than in elderly women. Vertebrae with VD had a higher risk of developing ECF.

Keywords Endplate · Incidence · Osteoporosis · Progression · Radiograph · Spine · Vertebral fracture

Osteoporosis is characterized by low bone mass and micro-architectural deterioration, which leads to bone fragility and consequent increase in fracture risk. Vertebral fractures (VFs) are the most common osteoporotic fracture. VFs are associated with poor life quality, impaired bending and rising, difficulties in the activities of daily living, frailty, higher risk of hospitalization, and higher mortality [1–7]. Prevalent VFs increase the risk of future osteoporotic fracture independent of bone mineral density (BMD).

Spine radiograph is the recommended technique to assess osteoporotic VF. However, despite years' research, the radiographic criteria for osteoporotic VF and its grading remain debated [8]. On spine radiograph, the semi-quantitative (SQ) criteria proposed by Genant et al. is commonly used for identifying osteoporotic vertebral deformity (VD) for vertebrae T4

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to L4 [9]. According to Genant et al., a vertebra is graded 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 of area 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). Genant et al. described the importance of loss of end-plate integrity as a characteristic of fractures but did not make diagnosis contingent on this observation [9, 10].

Recent publications emphasize the importance of identifying osteoporotic vertebral endplate or/and cortex fracture (ECF) [10–21]. The algorithm-based qualitative (ABQ) approach described by Jiang et al. assumes that the endplate is always deformed in VFs and is 100% sensitive in case of VF, whereas vertebral height reduction is not an indispensable finding of VF [11–13]. It has been shown that mild vertebral fractures identified by ABQ, but not by SQ, were associated with low BMD [12, 17]. Lentle et al. [14] showed ECF positive grade-1 VF was associated with higher risk of VFs as well as non-vertebral major osteoporotic fracture, while grade-1 SQ-VD deformity was not associated with higher non-vertebral fracture. Our recent work in elderly females showed, compared with vertebrae without SQ-VD, ECF(−) mild and moderate VDs may not have a higher short-term (4 years) future risk for new incident VD; however, these vertebrae with deformity have a higher risk of short-term future turning to ECF(+). Within the same mild/moderate VD grades, compared with the subjects without ECF, the subjects with ECF are associated with a higher short-term future risk of VD progression and new incident VD [21].

The VF epidemiology in men is not well understood as the majority of prevalence and incidence studies have been undertaken in women and only few studies in men have been population based [22, 23]. Elderly men not only have lower prevalence of osteoporotic VF, they also have different VF characteristics. In our Mr. and Ms. OS (Hong Kong) baseline studies [17], we demonstrated that while the overall Genant VD prevalence is only slightly lower in men than women (i.e., 13.2% vs. 16.1%), ECF prevalence 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 [17]. VDs in males with 25–34% height loss rarely simultaneously demonstrate ECF, while it is common for VD in females with 25–34% height loss to be associated with ECF [18]. In proportion, lower endplate in elderly males is much less likely to have ECF than in elderly females [24]. A recent Swedish study reported that, where a threshold for VD of 10% estimated vertebral height loss was used, the clinical relevance of prevalent VD in elderly men was low [25].

Osteoporotic fractures in men (MrOS) Hong Kong represents the first large-scale prospective cohort study ever conducted on bone health in Asian men. The baseline characteristics of year-0 study have been published [17, 26]. Hereby, we present the year-4 follow-up (FU) results, with a particular focus on comparison with the results of our female subjects.

Materials and methods

The study cohort

Two thousand Hong Kong Chinese men aged 65 years or older were recruited from the local community for a prospective cohort study from August 2001 to March 2003, to determine the relationship between anthropometric, lifestyle, medical, and other factors with BMD at the hip and spine. The recruitment plan was designed so that the participants would represent the general elderly population in age and gender proportion. The project was designed primarily to examine the BMD of older Chinese adults prospectively for 4 years. All subjects were community dwelling, able to walk without assistance, without bilateral hip replacement, and had the potential to survive the duration of the primary study as judged by their pre-existing medical status. A total of 1519 men (76.0%) attended the year-4 FU study and attended spine radiograph examination [27]. The remaining participants were unwilling or unable to attend for follow-up or were not contactable. The baseline characteristics of those who attended and did not attend the year-4 FU is shown in supplementary table 1. Overall, those attended the year-4 FU were slightly younger than those who did not attend FU (mean 71.8 years vs. 74.7 years), and had highly higher hip BMD (mean 0.87 g/cm^2 vs. 0.84 g/cm^2), while lumbar spine BMD was similar (mean 0.95 g/cm^2 vs. 0.94 g/cm^2). The participants were interviewed using a structured standardized questionnaire, which included demographic information, socioeconomic status, medical history related to osteoporosis, history of fracture, current medications (verified by direct inspection or medical record), and alcohol and tobacco consumption [26]. Dietary intake, physical activity, height and weight, grip strength, body mass index (BMI), and lumbar and hip BMD were obtained [26]. The study protocol was approved by the Chinese University of Hong Kong Ethics Committee. Written informed consent was obtained from all subjects.

Radiographic analysis of vertebral deformity and endplate/cortex fracture

Left lateral thoracic and lumbar spine radiographs were obtained by adjusting the exposure parameters according to participants' body weight and height. In total, 1500 males (mean age at baseline and follow-up 71.7 years (range 65–91 years) and 75.5 years (range 68–95 years), respectively) who attended both BL and FU examinations and also had

radiographs with sufficient quality for analysis were included in this study. None of these subjects' spines were diagnosed as having pathological fractures or diseases other than degenerative or osteoporotic change. Both hardcopy radiograph film and digitalized formats were available for analysis.

Vertebrae T4–L4 were evaluated with both Genant SQ criteria and the grading criteria proposed by Szulc et al. [28], as well as ECF criteria. For Genant's SQ VD assessment, grade-1 refers to an involved vertebra with 20–25% height loss, grade-2 refers to an involved vertebra with 25–40% height loss, and grade-3 refers to an involved vertebra with > 40% height loss [9]. Szulc et al. [28] suggested that since T6–T9 vertebrae are more likely to be wedge shaped especially for males, and they recommended a cutoff of 25% for VD from T6 to T9 (25–30% as grade-1, 30–40% as grade-2, > 40% as grade-3), while the criteria for other vertebral levels remain unchanged. To meet the criterion for SQ VD, in addition to vertebral height loss, a qualitative (a radiological) deformity based on radiological evaluation, as detailed by Genant et al [9, 10, 29], was required. Non-fractural changes of the vertebrae shape were evaluated to exclude deformities including developmental changes and degenerative remodeling [19, 30]. The ECF analysis methodology, which was modified from the descriptions of Yoshida et al. [31] and Jiang et al [10], and very similar to Lentle et al.'s report [14], has been described earlier [17, 19, 21, 30]. In addition to the endplate, our ECF analysis also paid close attention to any vertebral cortex fracture (particularly anterior cortex fracture), and percentage height loss was measured. As Genant's criteria do not require a conventional "fracture" sign, in this study, the term "VD" is used for all cases, though the VDs with ECF sign can be formally called "fractured" (in order to be consistent with most of the existing publications, in introduction and discussion of this paper, of the term "VF" is loosely used when necessary and thus can refer to both a true fracture of a vertebra or a VD defined by Genant's criteria).

The reading procedure was the same as our female data [21]. For both BL and FU radiographs, ECF reading and SQ-VD reading were based on consensus of at least two experienced readers. Our reading results have been consistent with the published results when similar diagnosis approach were adopted [26, 32]. At the BL study, the VF/VD reading results were not immediately communicated to the patients, as the current VF/VD evaluation criteria are designed for epidemiological study rather than for individual care [8, 20, 33].

Eight categories classification of vertebral deformity/fracture

The same as our female subjects' analysis approach [21], in this study grade-2 VDs were further divided into mild (vd2m) and severe (vd2s) subgroups using a threshold of ≤ 34% height loss or > 34% height loss [18]. At BL, all vd2s were ECF(+) [18]. Based on the BL subjects' ECF and VD/ECF status, we divided our study subjects into eight sub-categories with the following order: (1) vd0/ecf0, (2) vd1/ecf0, (3) vd2m/ecf0, (4) vd0/ecf1, (5) vd1/ecf1, (6) vd2m/ecf1, (7) vd2s/ecf1, and (8) vd3/ecf1. Vd0/ecf0 means a vertebra without VD and without ECF; vd1/ecf1 means a vertebra with grade-1 VD and with ECF (1 = positive, 0 = negative). The first three groups were all ECF(−), while the last five groups were all ECF(+).

Criteria for incident vertebral deformity and vertebral deformity progression

At FU, the same as our female study [21, 29], to define the progression of a baseline VD, a further height decrease of at least 15% vertebral height was considered as a VD progression. A new incident VD was defined as a qualitative VD occurred in a vertebra that was not deformed at baseline (i.e., SQ grade-0), which could be either a change from grade-0 at baseline to grade-2 or grade-3 VD at FU, or a change from grade-0 at baseline to grade-1 VD with at least 10% height loss during the FU period. This requirement is necessary, as if a normal vertebra (grade-0) progressed to grade-1 is considered a new VD without such height loss requirement, then there is a theoretical possibility that a qualitative VD with 19% height loss (may be graded as grade-0.5) progressed to SQ grade-1 VD with only 2% further height loss during FU. This will lead to an "overcall" of new VD incidents.

In addition, as our initial testing showed few VD progression or new VD occurred during FU using these criteria, we also tested a lower threshold for VD progression/new VD. For this, to define the progression of a baseline VD, a further height decrease at FU of 8% vertebral height was a VD progression; also, a new incident VD was either a change from grade-0 at baseline to grade-2/3 VD at FU, or a change from grade-0 at baseline to grade-1 VD with 8% height loss during FU.

For the three ECF(−) groups of vd0/ecf0, vd1/ecf0, and vd2m/ecf0, a newly occurred ECF at follow-up was also considered an additional criteria for VF progression. These VD progressions and new incident VD/ECF were counted both "by subject" and "by vertebra," i.e., how many subjects had these incidents and how many vertebrae had these incidents.

Statistical analysis

All statistical analyses were performed using the statistical package SAS, version 9.4 (SAS Institute, Inc., Cary, NC). Among different categories of vertebral deformity grading, continuous variables including age and BMD were tested by analysis of variance (ANOVA). Categorical variables were analyzed by χ^2 test or Fisher exact test. All statistical tests were two-sided. A p value of less than 0.05 was considered statistically significant.

Results

According to Genant's SQ criteria, at baseline 1219, 149, 96, and 36 subjects were classified as grade-0 VD, grade-1 VD, grade-2 VD, and grade-3 VD, respectively. At year-4 follow-up, 2.05% (25/1219), 2% (3/149), 3.1% (3/96), and 2.8% (1/36) of the subjects in these four groups had at least one VD progress or new incident VD, respectively (Table 1). The results using Szulc's SQ criteria shows at baseline 1234, 141, 89, and 36 subjects were classified as grade-0 VD, grade-1 VD, grade-2 VD, and grade-3 VD, respectively (Table 2). Table 2 shows the VD progression/new VD rate at year-4 for groups 2–4 combined (all VD groups, 4.5%) was significantly higher than that of group 1 (those without VD/without ECF, 2.4%).

According to the eight categories grading and Genant's SQ criteria, the VD progression by subject, the VD progression by vertebra, new incident VD, and new ECF are shown in Table 3. The vd0/ecf0 group had new VD incidence of 2.05% (95% CI 1.26%, 2.85%), while there were few new VD progression/new VD incidents virtually in all other subgroups. Statistical analysis were thus not feasible. For the three BL ECF(−) groups, subjects of vd0/ecf0, vd1/ecf0, and vd2m/ecf0 had a ECF new incident (by subject) of 2.3%, 1.4%, and 10.2% according to Genant criteria and 2.2%, 3.08%, and 10.91% by Szulc criteria (with vd2m/ecf0 group being significantly higher; Tables 3 and 4). Figure 1 shows for the vd0 vertebrae in vd0/ecf0 group the overall probability of turning to ECF(+) during 4 years' follow-up was 0.19%. For the vd1 vertebrae in vd1/ecf0 group and vd2m group, and vd2m vertebrae in vd2m/ecf0 group, the overall probability of turning to ECF(+) during 4 years' follow-up was 1.4% (3/208) and 10.4%, respectively. Thus, higher extent of VD at BL was associated with higher probability of developing ECF at FU.

The results of BL grading using Szulc's SQ criteria and the lowered threshold for VD progression and new VD definition are shown in Table 4. The results broadly mirrored Table 3, i.e., even lower thresholds for VD progression and new VD definition was applied, the cases had VD progression and new VD for elderly males during the 4 years' FU were still few. Statistical analysis shows there was no significant difference in incidence of VD progression/new VD for group 1 (without VD/without ECF, 2.4%) and groups of with VD but without ECF (groups 2–3 combined, 3.2%). Groups with ECF (groups 4–8 combined, 8.0%) had a higher incidence of VD progression/new VD than group 1 ($p < 0.005$), and this rate was marginally higher than the rate of groups 2–3 combined ($p = 0.088$).

The same as reported previously [33], the reading of follow-up radiographs showed all VDs with > 34% height loss (i.e., vd2s and vd3 vertebrae) were ECF(+).

Discussion

There have not been many well-characterized longitudinal cohort studies in community-based elderly men to determine prevalence of VD/VF and their progression. Similar to women, bone loss in men is related to aging, but at a lower rate and magnitude. Differences in skeletal size, mechanical loading, and muscle mass may also play a role in the patterns of bone

Table 1 Vertebral deformity progression of subjects with baseline SQ grade-0 vertebrae and three categories of Genant vertebral deformity grading

Genant SQ grading	Group 1 SQ grade-0	Group 2 SQ grade-1	Group 3 SQ grade-2	Group 4 SQ grade-3	Groups 2–4 SQ grade-1, -2, -3
Number of subjects at baseline	1219	149	96	36	281
Subject age at baseline (years, mean ± SD)	71.46 ± 4.41	72.36 ± 4.94	73.02 ± 5.54[1]	73.81 ± 5.32[1]	72.77 ± 5.21[1]
Subject height at baseline (cm, mean ± SD)	163.37 ± 5.58	163.37 ± 6.30	162.54 ± 5.27	162.13 ± 7.51	162.93 ± 6.14
Subject total hip BMD at baseline (g/cm^2)	0.88 ± 0.12	0.87 ± 0.12	0.84 ± 0.13[1]	0.74 ± 0.14[1,2,3]	0.84 ± 0.13[1]
Subject lumbar BMD at baseline (g/cm^2)	0.96 ± 0.18	0.95 ± 0.17	0.94 ± 0.18	0.81 ± 0.18[1,2,3]	0.93 ± 0.18[1]
N progression of existing VD—by subject	n/a	1	0	0	1
% progression of existing VD—by subject	n/a	0.7%	0%	0%	0.4%
N VD new incident—by subject	25	2	3	1	6
% VD new incident—by subject	2.05%	1.3%	3.1%	2.8%	2.1%
Progression or new incident—by subject[#]	25	3	3	1	7
% progression or new incident—by subject[§]	2.05% (25/1219)[A]	2% (3/149)	3.1% (3/96)	2.8% (1/36)	2.49% (7/281)[B]
% progression or new incident—female ref*	4.56% (58/1271)	8% (6/75)	10.58% (11/104)	28.92% (24/83)	15.65% (41/262)

*Results of female MsOS (Hong Kong) study [21]. "By subject" = how many subjects had these incidents. % new incident = number of incidents divided by number of subjects at baseline potentially would have these incidents at follow-up (e.g., [§] 25/1219 = 2.05%); this is the same for % progression of existing VD. Note, a new incident VD in each group does not necessarily mean a new VD of the same severity. [#] A combination of VD progression and new VD, note VD progression and new VD may have occurred in the same subject. *P* value < 0.05, [1] for groups 2–4 comparing with group 1, [2] for groups 3–4 comparing with group 2, [3] for group 4 comparing with group 3 with Bonferroni adjustment. The difference between [A] vs. [B] was not significant with $p = 0.65$

Table 2 Vertebral deformity progression of subjects with baseline grade-0 vertebrae and three categories of vertebral deformity using Szulc et al.'s criteria*

	Group 1	Group 2	Group 3	Group 4	Groups 2–4
Number of subjects at baseline	1234	141	89	36	266
Subject age at baseline (years, mean ± SD)	71.47 ± 4.43	72.40 ± 4.73	73.03 ± 5.72[1]	73.81 ± 5.32[1]	72.80 ± 5.16[1]
Subject height at baseline (cm, mean ± SD)	163.36 ± 5.57	163.33 ± 6.42	162.65 ± 5.29	162.13 ± 7.51	162.94 ± 6.22
Subject total hip BMD at baseline (g/cm^2)	0.88 ± 0.12	0.86 ± 0.12	0.84 ± 0.13[1]	0.74 ± 0.14[1,2,3]	0.84 ± 0.13[1]
Subject lumbar BMD at baseline (g/cm^2)	0.96 ± 0.18	0.94 ± 0.17	0.95 ± 0.18	0.81 ± 0.18[1,2,3]	0.93 ± 0.18[1]
Progression of existing VD—by subject	n/a	4	2	2	8
% progression of existing VD—by subject	n/a	2.8%	2.2%	5.6%	3.0%
VD new incident—by subject	29	1	3	1	5
% VD new incident—by subject	2.4%	0.7%	3.4%	2.8%	1.9%
Progression or new incident—by subject[#]	29	4	5	3	12
% progression or new incident—by subject[§]	2.4% (29/1234)[A]	2.8% (4/141)	5.6% (5/89)	8.3% (3/36)	4.5% (12/266)[B]

*According to Szulc et al. [28], for vertebrae T6–T9, VDs with 25–30% height loss are grade-1, with 30–40% height loss are grade-2, and > 40% height loss are grade-3, the criteria for other vertebral level remain unchanged. "By subject" = how many subjects had these incidents. % new incident = number of incidents divided by number of subjects at baseline potentially would have these incidents at follow-up (e.g., [§] 29/1234 = 2.4%); this is the same for % progression of existing VD. Note, a new incident VD in each group does not necessarily mean a new VD of the same severity. [#] A combination of VD progression and new VD, note VD progression and new VD may have occurred in the same subject. *P* value < 0.05, [1] for groups 2–4 comparing with group 1, [2] for groups 3–4 comparing with group 2, [3] for group 4 comparing with group 3 with Bonferroni adjustment. The difference between [A] vs. [B] was significant with $p = 0.049$

loss in men and women. Karlsson et al. [34] reported that prevalent osteoporotic VD in elderly men has low clinical relevance. They noted that in men with one or several fractures, 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. Waterloo et al. [35] reported that presence of osteoporotic VD 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. However, one concern is that while Genant's VD criteria are commonly used for osteoporotic VD grading in elderly females, how this criteria can be applied for elderly males remains unknown, though using the same VD criteria would allow easier comparison between females' results and males' results. Based on BMD characteristics, Szulc et al. [28] 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 grade-1 deformities are often either false positive or deformities related to non-osteoporotic disease of the spine.

For our 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 males' results versus females' results. Our men's results from this study were in sharp difference to our female data from MsOS (Hong Kong) study. For subjects without VD at BL, the VD progression/new VD rate in males during the FU was half of those of the females, while for those with VD at BL, the progression/new VD rate in males (2.49%, Table 1) was less than one sixth of those of females (according to SQ criteria, 15.6%, estimated from table 1 of reference [21]). Even for the 36 cases with grade-3 VD, only one of them had VD new incident during the FU. Our results further attest that the osteoporotic VD/VF criteria for women are not suitable for men [20, 36]. Our results may contradict some older reports [37, 38]. The EPOS group [37] reported that the presence of a baseline vertebral deformity was a stronger predictor of incident vertebral fracture than gender.

Following our females' results, we would like to answer the same questions for male subjects: (1) do subjects with grade-1 VD but without ECF (i.e., ECF(−)) have a higher VF risk than those without VD? (2) In the same Genant's SQ grades, do the ECF(+) subjects have a higher future VF risk than those ECF(−)? Tables 3 and 4 show, despite we tried a much lower threshold for VD progression definition, these questions cannot be satisfactorily answered due to the very low VD progression/new VD incidences that occurred during the FU period, thus the statistical power was weak. However, Table 4 does show the same trends we have observed for the females. There was no significant difference in incidence of VD progression/new VD for group 1 without VD/without ECF (2.4%) and groups of with VD but without ECF (3.2%). Groups with ECF not only had a higher incidence of VD progression/new VD than group 1 (8.0% vs. 2.4%, $p < 0.005$) but also this rate was higher than the rate of groups with VD but without ECF (3.2%, $p = 0.088$). For this study for males, a trend of higher VD grade associated with a higher VD

Table 3 Vertebral deformity progression of subjects with eight sub-categories based on Genant's semi-quantitative criteria and endplate/cortex fracture

	Group 1 vd0/ecf0	Group 2 vd1/ecf0	Group 3 vd2m/ecf0	Group 4 vd0/ecf1	Group 5 vd1/ecf1	Group 6 vd2m/ecf1	Group 7 vd2s/ecf1	Group 8 vd3/ecf1	Groups 2–3 vd/ecf0	Groups 4–8 ecf1
Number of subjects at BL	1214	139	59	5	10	16	21	36	198	88
Subject age (years, mean ± SD) at BL	71.46 ± 4.41	72.38 ± 4.96	73.24 ± 6.17	71.20 ± 4.55	72.10 ± 4.91	73.31 ± 3.75	72.19 ± 4.90	73.81 ± 5.32	72.64 ± 5.35[1]	72.99 ± 4.85[1]
Subject height at BL (cm, mean ± SD)	163.35 ± 5.58	163.30 ± 6.48	162.25 ± 5.79	167.20 ± 6.06	164.31 ± 3.03	163.05 ± 5.26	162.97 ± 3.62	162.13 ± 7.51	162.99 ± 6.29	163.03 ± 5.88
Subject total hip BMD (g/cm^2) at BL	0.88 ± 0.12	0.88 ± 0.12	0.85 ± 0.13	0.84 ± 0.09	0.76 ± 0.12	0.75 ± 0.12[1,2]	0.87 ± 0.1	0.74 ± 0.14[1,2,3,7]	0.87 ± 0.12	0.78 ± 0.13[1]
Subject lumbar BMD (g/cm^2) at BL	0.96 ± 0.18	0.96 ± 0.17	0.96 ± 0.18	0.9 ± 0.19	0.8 ± 0.15	0.86 ± 0.17	0.95 ± 0.2	0.81 ± 0.18[1,2,3]	0.96 ± 0.17	0.86 ± 0.19[1]
Mean number of VDs per subject at BL		1.32	1.71		1.30	1.44	1.52	1.72	1.44	1.48
Mean number of ecf1 vertebrae per subject BL				1.0	1.00	1.13	1.1	1.64		1.31
Progression of existing VD—by subject		1	0	0	0	0	0	0	1	0
Progression of existing VD—by vertebra		1	0	0	1	0	0	0	1	1
VD new incident—by subject	25	2	1	0	0	0	2	1	3	3
VD new incident—by vertebra	26	2	1	0	0[a]	0[a]	2[b]	1[c]	3	3
% VD progression or new VD—by subject[#]	2.05% (25/1214)[A]	1.4% (2/139)	1.7% (1/59)	0% (0/5)	0% (0/10)	0% (0/16)	9.5% (2/21)	2.8% (1/36)	1.5% (3/198)[B]	3.4% (3/88)[C]
% VD progression or new VD—by subject – Ref female data	4.56% (58/1271)	8% (4/50)	9.5% (2/21)	0% (0/1)	20% (5/25)	27.3% (12/44)	17.9% (7/39)	55.4% (46/83)	8.5% (6/71)	36.5%[1] (70/192)
ECF new incident—by subject	28	2	6						8	
ECF new incident—by vertebra	31	2	9						11	
% ECF new incident—by subject	2.30%	1.44%	10.17%[1]						4.04%	
% ECF new incident by subject – Ref female data	4.01% (51/1271)	24% (12/50)	71.43% (15/21)						38.03% (27/71)	

ecf1: with endplate/cortex fracture (ECF); ecf0: without ECF; vd2m: grade-2 vertebral deformity with ≤ 34% height loss; vd2s: grade-2 vertebral deformity with > 34% height loss [18]. All vd2s and vd3 vertebrae are ECF(+). "By subject" and "by vertebra" = how many subjects and how many vertebrae had these incidents. % new incident = number of incidents divided by number of vertebrae or subjects at baseline potentially would have these incidents at follow-up. Note, a new incident VD in each group does not necessarily mean a new VD of the same severity. [#] A combination of VD progression and new VD, note VD progression and new VD may have occurred in the same subject. [a] One vertebra had new ECF; [b] two vertebrae had new ECF; [c] three vertebrae had new ECF. *P* value < 0.05; [1] for groups 2–8 comparing with group 1; [2] for groups 3–8 comparing with group 2; [3] for groups 4–8 comparing with group 3; [4] for group 8 comparing with group 7 with Bonferroni adjustment. The differences between [A] vs. [B], [B] vs. [C], and [A] vs. [C] are all not significant with $p = 0.6$, 0.3, and 0.4, respectively

Table 4 Lowered threshold vertebral deformity progression of subjects with eight sub-categories based on Szulc et al.'s semi-quantitative criteria and endplate/cortex fracture*

	Group 1 vd0/ecf0	Group 2 vd1/ecf0	Group 3 vd2m/ecf0	Group 4 vd0/ecf1	Group 5 vd1/ecf1	Group 6 vd2m/ecf1	Group 7 vd2s/ecf1	Group 8 vd3/ecf1	Groups 2–3 vd/ecf0	Groups 4–8 ecf1
Number of subjects at BL	1227	130	55	7	11	13	21	36	185	88
Subject age (years, mean ± SD) at BL	71.47 ± 4.43	72.35 ± 4.78	73.27 ± 6.36	70.4 ± 4.43	73 ± 4.22	73.38 ± 4.0	72.19 ± 4.9	73.81 ± 5.32	72.62 ± 5.30[1]	72.99 ± 4.85[1]
Subject height at BL (cm, mean ± SD)	163.35 ± 5.57	163.27 ± 6.58	162.32 ± 5.90	165.39 ± 6.10	164.03 ± 4.10	163.52 ± 5.03	162.97 ± 3.62	162.13 ± 7.51	162.99 ± 6.39	163.03 ± 5.88
Subject total hip BMD (g/cm^2) at BL	0.88 ± 0.12	0.87 ± 0.12	0.85 ± 0.14	0.81 ± 0.1	0.76 ± 0.11[1]	0.76 ± 0.14[1,2]	0.87 ± 0.1	0.74 ± 0.14[1,2,3,4]	0.86 ± 0.13	0.78 ± 0.13[1]
Subject lumbar BMD (g/cm^2) at BL	0.96 ± 0.18	0.95 ± 0.17	0.97 ± 0.18	0.86 ± 0.17	0.8 ± 0.17	0.87 ± 0.16	0.95 ± 0.2	0.81 ± 0.18[1,2,3]	0.96 ± 0.17	0.86 ± 0.19[1]
Mean number of VDs per subject at BL		1.29	1.73		1.18	1.46	1.52	1.69	1.42	1.42
Mean number of ecf1 vertebrae per subject BL				1.0	1.09	1.08	1.1	1.64		1.31
Progression of existing VD—by subject		3	1	0	1	0	1	2	4	4
Progression of existing VD—by vertebra		3	2	0	1	0	1	3	5	5
VD new incident—by subject	29	1	1	0	0	0	2	1	2	3
VD new incident—by vertebra	30	1	1	0	0[a]	0[a]	2[b]	1[c]	2	3
% VD progression or new VD—by subject[#]	2.4% (29/1227)[A]	3.1% (4/130)	3.6% (2/55)	0% (0/7)	9.1% (1/11)	0% (0/13)	14.3%[1] (3/21)	8.3% (3/36)	3.2% (6/185)[B]	8.0%[1] (7/88)[C]
ECF new incident—by subject	27	4	6						10	
ECF new incident—by vertebra	30	4	9						13	
% ECF new incident—by subject	2.20%	3.08%	10.91%[1]						5.41%[1]	

*According to Szulc et al. [28], for vertebrae T6–T9, VDs with 25–30% height loss are grade-1, with 30–40% height loss are grade-2, and > 40% height loss are grade-3; the criteria for other vertebral levels remain unchanged. For the lowered threshold for VD progression, a further height decrease at FU of ≥ 8% vertebral height of a BL existing VD is a VD progression. A new incident VD is either a change from grade-0 at baseline to grade-2/3 VD at follow-up, or a change from grade-0 at baseline to grade-1 VD with at least 8% height loss during FU. ecf1: with endplate/cortex fracture (ECF); ecf0: without ECF; vd2m: grade-2 vertebral deformity with ≤ 34% height loss; vd2s: grade-2 vertebral deformity with > 34% height loss [18]. All vd2s and vd3 vertebrae are ECF(+). "By subject" and "by vertebra" = how many subjects and how many vertebrae had these incidents. % new incident = number of incidents divided by number of vertebrae or subjects at baseline potentially would have these incidents at follow-up. Note, a new incident VD in each group does not necessarily mean a new VD of the same severity. [#] A combination of VD progression and new VD, note VD progression and new VD may have occurred in the same subject. [a] One vertebra had new ECF; [b] two vertebrae had new ECF; [c] three vertebrae had new ECF. *P* value < 0.05; [1] for groups 2–8 comparing with group 1; [2] for groups 3–8 comparing with group 2; [3] for groups 4–8 comparing with group 3; [4] for group 8 comparing with group 7 with Bonferroni adjustment. The difference between [A] vs. [B] is not significant with p=0.47; the difference between [B] vs. [C] is marginally significant with p=0.088; the difference between [A] vs. [C] is significant with $p < 0.005$

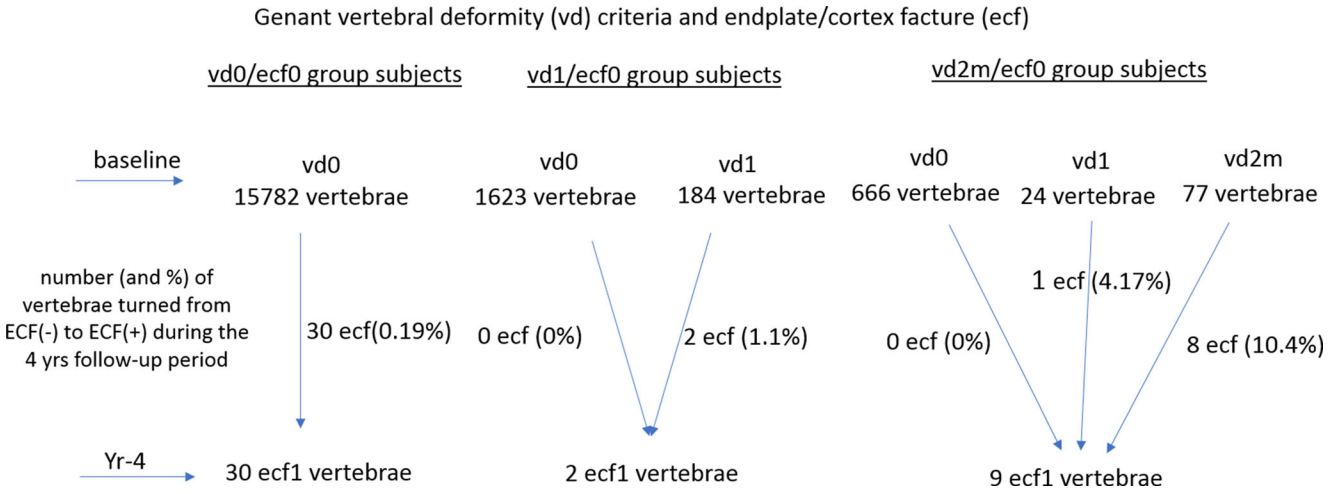

Fig 1. New incident ECF in three baseline ECF(−) groups (vd0/ecf0, vd1/ecf0, and vd2m/ecf0). It is shown that greater vertebral height loss at baseline is associated with a higher risk for a mild/moderate deformed ECF(−) vertebra turning to ECF(+) at follow-up

progression/new VD incidence was better shown in Table 2 using Szulc criteria than Table 1 using Genant's criteria, thus our data tentatively support Szulc criteria for assessing elderly males' osteoporotic VD.

The same as our female subjects' data [21], cases of VD without ECF showed a higher risk of near future incident ECFs. The endplate and vertebral cortex support the physiological morphology of vertebrae. With weakened protection, a vertebra with deformity, such as in cases of vd1/ecf0 or a vd2m/ecf0, is more likely to turn into ECF(+) under compressive pressure compared with a vd0/ecf0 vertebra. Furthermore, higher extent of VD at BL is associated with higher probability of developing ECF at FU. However, the probability of a VD turning into ECF(+) was still lower compared with females' data. Also, Fig. 1 shows for the vd0 vertebrae in vd0/ecf0 group the overall probability of turning to ECF(+) during 4 years' follow-up was 0.19% per vertebra in males, as opposed to 0.34% per vertebra for females [21].

Direct comparison with other studies of fracture rate in men is difficult because of the differences in study methodologies, which include the differences in baseline age, length of FU period, as well as the VD/VF definitions. We estimate that our new VD/VF incident during the 4 years' FU is broadly similar to, but slightly lower than, other reports of Caucasian subjects. In van der Klift et al.'s Rotterdam study (mean age at BL, 65.4 ± 6.6 years; FU period, 6.3 years) [39], for those with baseline normal spine, the VD/VF incident rate was 2.8% for males (5.2% for females), as compared to 2.05% (25/1219) in our study for males. In the EPOS study (mean age at BL, 63.3 ± 7.9 years; mean FU period, 3.8 years) [37], the VD/VF incidence was 5.7/1000 person-years in men (10.7/1000 person-years in women), as compared to 5.33/1000 person-years in men in our study (estimated from Table 1, inclusive of all study participants). Moreover, for subjects at BL without VD/VF, the FU new VD/VF incidence rate of females to males was all approximately 2:1 for our study and the aforementioned reports [37, 39]. In MrOS (USA) study [16, 40], 5994 men were followed for an average of 4.7 years; they used the criteria that incident radiographic VF defined as those with a change in SQ reading of ≥ 1 from BL to FU, and for incident VF with grade 1 severity, endplate fracture was also required. And they reported VD/VF incidence of 4.5% for all participants, thus broadly comparable to our results if we include VD progression/new VD as well as new ecf only (2.13% (Table 1) + 2.5% (Table 3) = 4.63%).

This study has a number of limitations. Firstly, despite 1500 elderly subjects were followed up for 4 years, in each subgroup with BL VD/VF, there were very limited number of subjects who had VD progression or new VD incidents. Therefore, much longer FU is necessary to confirm the trends observed in this study. Compared with female's vertebrae, male's vertebrae are harder and more resistant to compressive force. The risk for osteoporotic fracture increases greatly in elderly men after age of 80 years [40, 41], thus to study osteoporotic VF in men (as opposed to in women), a much older age group would be preferred. As noted above, relatively healthier subjects were more likely to attend the FU (supplementary table 1), thus there was a slight sampling bias. However, three fourths of the subjects attended the FU, which was not a low rate, and such a sampling bias would be unavoidable for FU of elderly subjects. Moreover, this sampling bias may not affect male–female results comparison, as females' results would also suffer from this issue. Radiographic ECF analysis is subjective, and some microfractures might have been missed with radiograph. Our experience is that CT is much better in showing small ECFs, but CT is associated with higher radiation as well as higher cost. This study only involved elderly Chinese subjects. However, we estimate our observations in this study can be to a large extent generalized to other ethnic groups; though compared

with Caucasians, both elderly Chinese males and females may have slightly lower VD/VF prevalence and also slightly slower VD/VF progression rate [21, 26, 37, 42–46, also see discussion above]. It has also been noted that, compared with Caucasians and African Americans, Asian men have a slightly slower BMD decline rate [47].

In conclusion, compared with age-matched elderly Chinese females, elderly Chinese males at their early seventies have lower risk of short-term (4-year period) VD progression/new incident VD. Even for those with existing VD at BL, elderly males are associated with much less further risk of VD progression/new VD as compared with elderly females. Our results call for caution when interpreting the clinical significance of osteoporotic VDs in males encountered in clinical practice.

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Compliance with ethical standards

Conflicts of interest Yì Xiáng J. Wáng, Nazmi Che-Nordin, Min Deng, Jason C. S. Leung, Anthony W. L. Kwok, James F. Griffith, Ping Chung Leung, and Timothy C.Y. Kwok declare that they have no conflict of interest.

References

1. Klotzbuecher CM, Ross PD, Landsman PB, Abbott TA 3rd, Berger M (2000) Patients with prior fractures have an increased risk of future fractures: a summary of the literature and statistical synthesis. J Bone Miner Res 15:721–739
2. Ross PD (1997) Clinical consequences of vertebral fractures. Am J Med 103:30S–42S
3. Kado DM, Browner WS, Palermo L, Nevitt MC, Genant HK, Cummings SR (1999) Vertebral fractures and mortality in older women: a prospective study. Study of osteoporotic fractures research group. Arch Intern Med 159:1215–1220
4. Cooper C, Atkinson EJ, Jacobsen SJ, O'Fallon WM, Melton LJ 3rd (1993) Population-based study of survival after osteoporotic fractures. Am J Epidemiol 137:1001–1005
5. Nevitt MC, Ettinger B, Black DM, Stone K, Jamal SA, Ensrud K, Segal M, Genant HK, Cummings SR (1998) The association of radiographically detected vertebral fractures with back pain and function: a prospective study. Ann Intern Med 128:793–800
6. Bliuc D, Nguyen ND, Milch VE, Nguyen TV, Eisman JA, Center JR (2009) Mortality risk associated with low-trauma osteoporotic fracture and subsequent fracture in men and women. JAMA 30: 513–521
7. Wáng YX (2018) Senile osteoporosis is associated with disc degeneration. Quant Imaging Med Surg 8:551–556
8. Lentle BC, Hg Oei E, Goltzman D, Rivadeneira F, Hammond I, Oei L, Kovacs CS, Hanley DA, Prior JC, Leslie WD, Kaiser SM, Adachi JD, Probyn L, Brown J, Cheung AM, Towheed T (2018) Vertebral fractures and morphometric deformities. J Bone Miner Res 33:1544–1545
9. Genant HK, Wu CY, van Kuijk C, Nevitt MC (1993) Vertebral fracture assessment using a semiquantitative technique. J Bone Miner Res 8:1137–1148
10. Genant HK, Jergas M (2003) Assessment of prevalent and incident vertebral fractures in osteoporosis research. Osteoporos Int 14(Suppl 3):S43–S55
11. Jiang G, Eastell R, Barrington NA, Ferrar L (2004) Comparison of methods for the visual identification of prevalent vertebral fracture in osteoporosis. Osteoporos Int 15:887–896
12. Ferrar L, Jiang G, Adams J, Eastell R (2005) Identification of vertebral fractures: an update. Osteoporos Int 16:717–728
13. Ferrar L, Jiang G, Clowes JA, Peel NF, Eastell R (2008) Comparison of densitometric and radiographic vertebral fracture assessment using the algorithm-based qualitative (ABQ) method in postmenopausal women at low and high risk of fracture. J Bone Miner Res 23:103–111
14. Lentle BC, Berger C, Probyn L, Brown JP, Langsetmo L, Fine B, Lian K, Shergill AK, Trollip J, Jackson S, Leslie WD, Prior JC, Kaiser SM, Hanley DA, Adachi JD, Towheed T, Davison KS, Cheung AM, Goltzman D, CaMos Research Group (2018) Comparative analysis of the radiology of osteoporotic vertebral fractures in women and men: cross-sectional and longitudinal observations from the Canadian Multicentre Osteoporosis Study (CaMos). J Bone Miner Res 33:569–579
15. Oei L, Koromani F, Breda SJ, Schousboe JT, Clark EM, van Meurs JB, Ikram MA, Waarsing JH, van Rooij FJ, Zillikens MC, Krestin GP, Oei EH, Rivadeneira F (2018) Osteoporotic vertebral fracture prevalence varies widely between qualitative and quantitative radiological assessment methods: the Rotterdam study. J Bone Miner Res 33:560–568
16. Fink HA, Litwack-Harrison S, Ensrud KE, Shen J, Schousboe JT, Cawthon PM, Cauley JA, Lane NE, Taylor BC, Barrett-Connor E, Kado DM, Cummings SR, Marshall LM, Osteoporotic Fractures in Men (MrOS) Study Group (2017) Association of incident, clinically undiagnosed radiographic vertebral fractures with follow-up back pain symptoms in older men: the Osteoporotic Fractures in Men (MrOS) Study. J Bone Miner Res 32:2263–2268
17. Deng M, Zeng XJ, He LC, Leung JCS, Kwok AWL, Griffith JF, Kwok T, Leung PC, Wáng YX (2017) Osteoporotic vertebral fracture prevalence in elderly Chinese men and women: a comparison of endplate/cortex fracture-based and morphometrical deformity-based methods. J Clin Densitom 22:409–419. https://doi.org/10.1016/j.jocd.2017.11.004
18. Deng M, Kwok TCY, Leung JCS, Leung PC, Wáng YX (2018) All osteoporotically deformed vertebrae with >34% height loss have radiographically identifiable endplate/cortex fracture. J Orthop Translat 14:63–66
19. Wáng YX, Santiago RF, Deng M, Nogueira-Barbosa MH (2017) Identifying osteoporotic vertebral endplate and cortex fractures. Quant Imaging Med Surg 7:555–591
20. Wáng YX, Che-Nordin N (2018) Informed communication with study subjects of radiographically detected osteoporotic vertebral deformity. Quant Imaging Med Surg 8:876–880
21. Wang YX, Che-Nordin N, Deng M, Leung JC, Kwok AWL, He LC, Griffith JF, Kwok TCY, Leung PC (2019) Osteoporotic vertebral deformity with endplate/cortex fracture is associated with higher further vertebral fracture risk: the Ms. OS (Hong Kong) study results. Osteoporos Int. https://doi.org/10.1007/s00198-019-04856-4
22. Adler RA (2018) Update on osteoporosis in men. Best Pract Res Clin Endocrinol Metab 32:759–772
23. Seeman E, Bianchi G, Khosla S, Kanis J, Orwoll E (2006) Bone fragility in men—where are we? Osteoporos Int 17:1577–1583
24. Che-Nordin N, Deng M, Griffith JF, Leung JCS, Kwok AWL, Zhu YQ, So RHY, Kwok TCY, Leung PC, Wáng YX (2018) Prevalent osteoporotic vertebral fractures more likely involve the upper

endplate than the lower endplate and even more so in males. Ann Transl Med 6:442
25. Kherad M, Rosengren BE, Hasserius R, Nilsson JA, Redlund-Johnell I, Ohlsson C, Lorentzon M, Mellstrom D, Karlsson MK (2015) Low clinical relevance of a prevalent vertebral fracture in elderly men—the MrOs Sweden study. Spine J 15:281–289
26. Kwok AW, Gong JS, Wang YX, Leung JC, Kwok T, Griffith JF, Leung PC (2013) Prevalence and risk factors of radiographic vertebral fractures in elderly Chinese men and women: results of Mr. OS (Hong Kong) and Ms. OS (Hong Kong) studies. Osteoporos Int 24:877–885
27. Wáng YX, Deng M, Griffith JF, Kwok AW, Leung JC, Ahuja AT, Kwok T, Leung PC (2016) Lumbar spondylolisthesis progression and de novo spondylolisthesis in elderly Chinese men and women: a year-4 follow-up study. Spine (Phila Pa 1976) 41:1096–1103
28. Szulc P, Munoz F, Marchand F, Delmas PD (2001) Semiquantitative evaluation of prevalent vertebral deformities in men and their relationship with osteoporosis: the MINOS study. Osteoporos Int 12:302–310
29. Schwartz EN, Steinberg D (2005) Detection of vertebral fractures. Curr Osteoporos Rep 3:126–135
30. Wáng YX, Deng M, He LC, Che-Nordin MN, Santiago RF (2018) Osteoporotic vertebral endplate and cortex fractures: a pictorial review. J Orthop Translat 15:35–49
31. Yoshida T, Nanba H, Mimatsu K, Kasai T (2000) Treatment of osteoporotic spinal compression fractures. Conservative therapy and its limitation. Clin Calcium 10:53–58
32. Lentle B, Koromani F, Brown J, Oei L, Ward L, Goltzman D, Rivadeneira F, Leslie WD, Probyn L, Prior J, Hammond I, Cheung A, Oei E (2019) The radiology of osteoporotic vertebral fractures revisited. J Bone Miner Res 34. https://doi.org/10.1002/jbmr.3669
33. Kendler DL, Bauer DC, Davison KS, Dian L, Hanley DA, Harris ST, McClung MR, Miller PD, Schousboe JT, Yuen CK, Lewiecki EM (2016) Vertebral fractures: clinical importance and management. Am J Med 129:221.e1–221.10
34. Karlsson MK, Kherad M, Hasserius R, Nilsson JÅ, Redlund-Johnell I, Ohlsson C, Lorentzon M, Mellström D, Rosengren BE (2016) Characteristics of prevalent vertebral fractures predict new fractures in elderly men. J Bone Joint Surg Am 98:379–385
35. Waterloo S, Søgaard AJ, Ahmed LA, Damsgård E, Morseth B, Emaus N (2013) Vertebral fractures and self-perceived health in elderly women and men in a population-based cross-sectional study: the Tromsø study 2007–08. BMC Geriatr 13:102
36. Wáng YX (2019) A modified semi-quantitative (mSQ) grading scheme for osteoporotic vertebral fracture in elderly women. Quant Imaging Med Surg 9:146–150
37. European Prospective Osteoporosis Study Group, Felsenberg D, Silman A, Lunt M, Armbrecht G, Ismail A et al (2002) Incidence of vertebral fracture in Europe: results from the European prospective osteoporosis study (EPOS). J Bone Miner Res 17:716–724
38. Ross PD, Lombardi A, Freedholm D (1999) The assessment of bone mass in men. In: Orwoll ES (ed) Osteoporosis in men: the effect of gender on skeletal health. Academic Press, San Diego, pp 505–525
39. Van der Klift M, De Laet CE, McCloskey EV, Hofman A, Pols HA (2002) The incidence of vertebral fractures in men and women: the Rotterdam study. J Bone Miner Res 17:1051–1056
40. Freitas SS, Barrett-Connor E, Ensrud KE, Fink HA, Bauer DC, Cawthon PM, Lambert LC, Orwoll ES, Osteoporotic Fractures in Men (MrOS) Research Group (2008) Rate and circumstances of clinical vertebral fractures in older men. Osteoporos Int 19:615–623
41. Hopkins RB, Pullenayegum E, Goeree R, Adachi JD, Papaioannou A, Leslie WD, Tarride JE, Thabane L (2012) Estimation of the lifetime risk of hip fracture for women and men in Canada. Osteoporos Int 23:921–927
42. Delmas PD, Genant HK, Crans GG, Stock JL, Wong M, Siris E, Adachi JD (2003) Severity of prevalent vertebral fractures and the risk of subsequent vertebral and nonvertebral fractures: results from the MORE trial. Bone. 33:522–532
43. Fink HA, Milavetz DL, Palermo L, Nevitt MC, Cauley JA, Genant HK, Black DM, Ensrud KE, Fracture Intervention Trial Research Group (2005) What proportion of incident radiographic vertebral deformities is clinically diagnosed and vice versa? J Bone Miner Res 20:1216–1222
44. Nevitt MC, Cummings SR, Stone KL, Palermo L, Black DM, Bauer DC, Genant HK, Hochberg MC, Ensrud KE, Hillier TA, Cauley JA (2005) Risk factors for a first-incident radiographic vertebral fracture in women > or = 65 years of age: the study of osteoporotic fractures. J Bone Miner Res 20:131–140
45. European Prospective Osteoporosis Study (EPOS), Roy DK, O'Neill TW, Finn JD, Lunt M et al (2003) Determinants of incident vertebral fracture in men and women: results from the European Prospective Osteoporosis Study (EPOS). Osteoporos Int 14:19–26
46. Shin MH, Zmuda JM, Barrett-Connor E, Sheu Y, Patrick AL, Leung PC, Kwok A, Kweon SS, Nam HS, Cauley JA, Osteoporotic Fractures in Men (MrOS) Research Group (2014) Race/ethnic differences in associations between bone mineral density and fracture history in older men. Osteoporos Int 25:837–845
47. Sheu Y, Cauley JA, Wheeler VW, Patrick AL, Bunker CH, Ensrud KE, Orwoll ES, Zmuda JM, Osteoporotic Fracture in Men (MrOS) Research Group (2011) Age-related decline in bone density among ethnically diverse older men. Osteoporos Int 22:599–605