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ORIGINAL ARTICLE

Osteoporotic vertebral deformity with endplate/cortex fracture is associated with higher further vertebral fracture risk: the Ms. OS (Hong Kong) study results

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Abstract

Summary Compared with vertebrae without deformity, vertebrae with mild/moderate deformity have a higher risk of endplate or/and cortex fracture (ecf). Compared with subjects without ecf, subjects with ecf are at a higher risk of short-term (4-year period) deformity progression and new incident deformity.

Introduction The progression and incidence of osteoporotic vertebral deformity/fracture (VD/VF) in elderly Chinese females remain not well documented.

Methods Spine radiographs of 1533 Chinese females with baseline and year-4 follow-up (mean age 75.7 years) were evaluated according to Genant's VD criteria and endplate/cortex fracture (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. According to their VD/VF, subjects were graded into seven categories: vd0/ecf0, vd1/ecf0, vd2m/ecf0, 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 incident VD was a change from grade-0 to grade-2/3 or to grade-1 with ≥ 10% height loss.

Results Of subjects with Genant's grades 0, − 1, − 2, and − 3 VD, at follow-up, 4.6%, 8%, 10.6%, and 28.9% had at least one VD progression or new incident VD respectively. Among the three ecf0 groups, there was no difference in VD progression or new VD; while there was a significant difference in new ecf incidence, with vd0/ecf0 being lowest and vd2m/ecf0 being highest. Vd1/ecf0 and vd2m/ecf0 vertebrae had a higher risk of turning to ecf1 than vd0/ecf0 vertebrae. If vd1/ecf0 and vd2m/ecf0 subjects were combined together (range 20–34% height loss) to compare with vd1/ecf1 and vd2m/ecf1 subjects, the latter had significantly higher VD progression and new VD rates.

Conclusion Vertebrae with grade-1/2 VDs had a higher risk of developing ECF. Subjects with pre-existing ECFs had a higher risk of worsening or new vertebral deformities.

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

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Osteoporosis is characterized by low bone mass and microarchitectural 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. Appropriate management of osteoporosis can reduce future fracture risk: it is important to identify and report VFs clearly and precisely, so that appropriate investigation and treatment can be initiated [1, 2].

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 [2]. Despite years' research, the radiographic criteria for osteoporotic VF and its grading remain highly debated [1–5]. On spine radiograph, the semi-quantitative (SQ) criteria proposed by Genant et al. is commonly used for identifying vertebral deformity (VD) for vertebrae T4 to L4 [6]. 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 [2, 7].

Recent works emphasized the importance of identifying osteoporotic at vertebral endplate or/and cortex fracture (ECF) [1, 3, 5, 8–20]. Yoshida et al. classified vertebral fracture into four morphological types, namely anterior cortex protruding type, anterior cortex–indented type, endplate-slipped type, and endplate compression type [8, 9]. 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 [10–13]. Ferrar et al. [13] showed mild vertebral fractures identified by ABQ, but not by SQ, were associated with low BMD; interobserver agreement for radiographic diagnosis of prevalent VF was better for the ABQ compared with the SQ method. Lentle et al. [14] showed ABQ positive grade-1 VF was associated with higher risk of VFs as well as nonvertebral major osteoporotic fracture, while grade-1 SQ-VD deformity was not associated with higher non-vertebral fracture.

Osteoporotic Fractures in Women (MsOS) Hong Kong represents the first large-scale prospective cohort study ever conducted on bone health in Asian women [21]. Interestingly, the results demonstrated that the age-specific osteoporotic VF prevalence of elderly Chinese women is very similar to Japanese and Korean women as well as Latin American women, while slightly lower than elderly Caucasian females, suggesting the VF epidemiology difference among different ethnic groups might be smaller than initially thought [21]. The ECF analysis of MsOS (Hong Kong) baseline study has been reported [17]. We showed subjects with grade-1 SQ-vertebral deformity had a similar BMD compared with subjects without fracture, while subjects with grade-1 ECF VF had lower BMD [17]. Hereby, we present the year-4 follow-up results. The current study primarily aims to answer two important questions: (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(−)? Though it has been repetitively reported that even mild VD is associated with future fracture risk, these results were based on epidemiological data and statistical analysis. Previous reports of mild/moderate groups included a mixture of both ECF(−) and ECF(+) [22, 23]. The answers to the two questions may contribute to the assessment of future fracture risk at individual patients' level [1, 24], and ultimately toward the goal of personalized clinical care.

Materials and methods

The study cohort

Two thousand Hong Kong Chinese women 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. One thousand five hundred forty-six women (77.3%) attended the year-4 follow-up study [25]. The remaining participants were unwilling or unable to attend for follow-up or were not contactable. 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 [21]. Dietary intake, physical activity, height and weight, grip strength, body mass index (BMI), and lumbar and hip BMD were obtained [21]. 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, 1533 females (mean age at baseline and follow-up 71.9 years (range 65–98 years) and 75.7 years (range 68–102 year) respectively) who attended both baseline and follow-up 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 hard copy radiograph film and digitalized formats were available for analysis. Vertebrae T4–L4 at baseline and follow-up were evaluated both with ECF criteria and Genant SQ criteria. The ECF analysis methodology, which was modified from the descriptions of Yoshida et al. and Jiang et al. [8, 10], has been described earlier [17], Supplementary Fig. 1]. There is no minimum threshold for reduction in vertebral height for a prevalent ECF [10]. Our ECF analysis was very similar to the modified ABQ (mABQ) approach described by Lentle et al. [3]. In contrast to Jiang et al.'s initial description, our ECF analysis also pays close attention to any vertebral cortex fracture (particularly anterior cortex fracture), and percentage height loss was measured. In addition, conceptually, we consider that an osteoporotic VF can occur without radiographically identifiable endplate fracture [1, 4, 19]. For Genant's SQ VD assessment, as described previously, 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 [6]. The same as the recent trend in using Genant's criteria [2], the percentage area loss criteria, as initially described by Genant et al. [6], was dropped. In this study, to ensure consistency, quantitative measurement of potential vertebral height loss was used to confirm the presence of prevalent and incident VD. The measurement was based on comparisons with adjacent normal appearing vertebral bodies' height. To meet the criterion for SQ VD, in addition to vertebral height loss, a qualitative deformity based on radiological evaluation, as detailed by Genant et al. [2, 6, 7], was required. These qualitative deformities included, among others, endplate deformities, the lack of parallelism of end plates, buckling of cortices, and the loss of vertical continuity of vertebral morphology [6]. The common developmental wedge deformities of the mid-thoracic and thoracolumbar regions, the reverse wedging of lower lumbar vertebrae, and the common mild endplate bowing of the lower lumbar vertebrae were recognized. Nonfractural changes of the vertebrae shape were evaluated to exclude deformities including developmental short vertebral height, Cupid's bow deformity, Scheuermann's disease, Schmorl's nodes, and degenerative remodeling [4, 6]. 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).

For baseline radiographs, two readers (reader-1 and reader-2), both experienced radiologists, assessed the radiographs simultaneously, and consensus was reached [17]. At the baseline study, the VF/VD reading results were not communicated to the patients, as the current VF/VD evaluation criteria are designed for epidemiological study, rather than to provide a basis for the care of individual patients [3, 20, 24]. For follow-up, reader-1 completed the initial reading, with reader-2 available for consultation for ambiguous cases, and then the results were all checked by a trained radiographer (reader-3) and final consensus were all reached. During the process, both ECF reading and SQ-VD reading were based on consensus of at least two experienced readers. The inter-reader agreement among our readers has been reported to be satisfactory [17, 21].

Seven category classification of vertebral deformity/fracture

It has been reported that while grade-1 VDs and grade-2 VDs with ≤ 34% height loss may, or may not, be associated with ECF, those grade-2 VDs with > 34% height loss and grade-3 VDs are always associated with ECF [18]. Therefore, using a threshold of ≤ 34% height loss or > 34% height loss, in this study, grade-2 VDs were further divided into mild (vd2m) and severe (vd2s) subgroups. To test our hypothesis outlined in the introduction, based on the baseline ECF and VD assessment, we divided our study subjects into seven possible categories with the following order: (1) vd0/ecf0, (2) vd1/ecf0, (3) vd2m/ecf0, (4) vd1/ecf1, (5) vd2m/ecf1, (6) vd2s/ecf1, and (7) 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 four groups were all ECF(+). Subjects graded as qualitative SQ grade-0.5 [6] (i.e., qualitatively suspected VD without meeting height loss ≥ 20% criteria) were grouped with grade-0 for analysis, and subjects graded as vd0/ecf1 at baseline were not included, as the subject number was too small to constitute an independent group for meaningful statistical comparison with other groups [17].

Criteria for incident vertebral deformity and vertebral deformity progression

For follow-up in this study, new incident VD, VD progression, and new ECF were recognized according to the

following criteria: a new incident VD was defined as a qualitative VD occurred in a vertebra that was not deformed at baseline (i.e., SD grade-0), which could be either a change from grade-0 at baseline to grade-2 or grade-3 VD at follow-up, or a change from grade-0 at baseline to grade-1 VD with at least 10% height loss during the follow-up period. For an existing VD at baseline, a further height decrease at follow-up of at least 15% vertebral height is considered as a VD progression [2]. Additionally, for the three ECF(−) groups of vd0/ecf0, vd1/ecf0, and vd2m/ecf0, a newly occurred ECF at follow-up is also considered an additional criteria for VF progression. These VD progression 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 including incident VD, progression of existing VD, and progression of new VD were analyzed by chi-square 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, 1271, 75, 104, and 83 subjects were classified as grade-0 VD, grade-1 VD, grade-2 VD, and grade-3 VD, respectively. At year-4 follow-up, 4.56%, 8%, 10.58%, and 28.92% of the subjects in these four groups had at least one VD progress or new incident VD respectively (Table 1).

According to the seven category grading, the VD progression by subject, the VD progression by vertebra, new incident VD, and new ECF are shown in Table 2. Overall, at baseline, the vd0/ecf0 group had slightly younger age and the vd3/ecf1 group had slightly older age. At baseline, the vd3/ecf1 group had lower BMD, more mean number of VDs and more number of ECF per subject. At follow-up, the vd3/ecf1 group had the greatest number of VD progressions and greatest number of new incident VDs.

Comparing the three ECF(−) groups (i.e., vd0/ecf0, vd1/ecf0, and vs vd2m/ecf0), there was no difference in VD progression (vd1/ecf0 vs. vd2m/ecf0) and no difference in new incident VD. However, there was a significant difference in new ECF incidence, with the vd0/ecf0 group being the lowest, and the vd2m/ecf0 group being the highest (Table 2, p value details in Supplementary Table 1). Figure 1 shows that for the vd0 vertebrae in vd0/ecf0 group, the overall probability of turning to ECF(+) during 4-year follow-up was 0.34%. For the vd1 vertebrae in vd1/ecf0 group and vd2m vertebrae in vd2m/ecf0

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
7 category classifications	vd0/ecf0	vd1/ecf0 and vd1/ecf1	vd2m/ecf0 and vd2m/ecf1 and vd2s/ecf1	vd3/ecf1
Subject no. at baseline	1271	75	104	83
Subject age at baseline (years, mean ± SD)	71.53 ± 4.85	73.03 ± 5.19	73.39 ± 4.89 [1]	74.76 ± 5.66 [1]
Subject total hip BMD at baseline (g/cm^2)	0.73 ± 0.11	0.70 ± 0.10	0.67 ± 0.12 [1]	0.64 ± 0.11 [1, 2]
Subject lumbar BMD at baseline (g/cm^2)	0.76 ± 0.14	0.74 ± 0.14	0.74 ± 0.16	0.67 ± 0.14 [1, 2, 3]
Progression of existing VD—by subject	n/a	6 [c]	11	24
% Progression of existing VD—by subject	n/a	8%	10.58%	28.92% [2,3]
VD new incident—by subject	58	3 [d]	10	22
% VD new incident—by subject	4.56% [b]	4% [#]	9.6% [#]	26.51% [1, 2, 3]
Progression or new incident—by subject [a]	58	6 [e]	11	24
% Progression or new incident—by subject	4.56%	8%	10.58% [1]	28.92% [1, 2, 3]

New incident ECF analysis is not included in this table. All vd2s and vd3 vertebrae had ECF. "By subject"' = how many subjects had these incidents. % New incident = no. of incidents divided by no. of subjects at baseline that potentially would have these incidents at follow-up (for example, [b] 58/1271 = 4.56%); 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, i.e., a new incident VD in group-3 does not necessarily mean a new SQ grade-3 VD, for example, it could be a change from grade-0 at baseline to grade-1 VD with at least 10% height loss during the follow-up period. [a] A combination of VD progression and new VD: note that VD progression and new VD can occur in the same subject (for example, e = c + d, and e remains to be 6)

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 (reference [18]

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; [#] $p = 0.15$

Table 2 Vertebral deformity progression of subjects with baseline SQ Grade-0 vertebrae and six categories of vertebral deformity grading considering endplate/cortex fracture

	Group 1 vd0/ecf0	Group 2 vd1/ecf0	Group 3 vd2m/ecf0	Group 4 vd1/ecf1	Group 5 vd2m/ecf1	Group 6 vd2s/ecf1	Group 7 vd3/ecf1
Subject no. at baseline	1271	50	21	25	44	39	83
Subject age at baseline (years, mean ± SD)	71.53 ± 4.85	73.42 ± 5.38 [1]	73.24 ± 4.17	72.24 ± 4.79	73.59 ± 5.37	73.26 ± 4.78	74.76 ± 5.66 [1]
Subject total hip BMD at baseline (g/cm^2)	0.73 ± 0.11	0.69 ± 0.09	0.67 ± 0.08	0.71 ± 0.10	0.65 ± 0.11 [1]	0.69 ± 0.14	0.64 ± 0.11[1]
Subject lumbar BMD at baseline (g/cm^2)	0.76 ± 0.14	0.74 ± 0.15	0.76 ± 0.13	0.74 ± 0.12	0.73 ± 0.18	0.74 ± 0.16	0.67 ± 0.14 [1]
Mean no. of VD per subject at baseline		1.26	1.52 [2]	1.16 [3]	1.39	1.41	1.92 [2, 3, 4, 5, 6]
Mean no. of ECF (+) vertebrae per subject at baseline				1.08	1.25	1.18	1.84 [4, 5, 6]
Progression of existing VD—by subject		3	1	3	6	4	24
% Progression of existing VD—by subject		6.0%	4.76%	12.0%	13.64%	10.26%	28.92% [2]
Progression of existing VD—by vertebra		3	1	3	12	8	35
(No. of VD possible for progression)		63	32	27	61	54	149
% Progression of existing VD—by vertebra		4.76%	3.13%	11.11%	19.67%	14.81%	23.49% [2]
VD new incident—by subject	58	1	1	2	6	3	22
VD new incident—by vertebra	64	1	1	2 [a]	11 [b]	6 [c]	31 [d]
% New incident VD—by subject	4.56%	2%	4.76%	8%	13.64%	7.69%	26.51% [1, 2]
ECF new incident—by subject	51	12	15				
ECF new incident—by vertebra	56 [e]	14 [e]	25 [e]				
% ECF new incident—by subject	4.01%	24% [1]	71.43% [1, 2]				

All vd2s and vd3 vertebrae are ECF(+). "By subject" and "by vertebra"' = how many subjects and how many vertebrae had these incidents. % New incident = No. of incidents divided by No. of vertebrae or subjects at baseline that potentially would have these incidents at follow-up. [b, d] All these new incident VDs had ECF. [a, c] Each had one new incident VD which were ECF(−) while the others were ECF(+). Note, a new incident VD in each group does not necessarily mean a new VD of the same severity, i.e., a new incident VD in group 6 does not necessarily mean a new VD of vd2s/ecf1, for example, it could be a change from grade-0 at baseline to grade-1 VD with at least 10% height loss during the follow-up period

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 (reference 18)

p value < 0.05; [1] for groups 2–7 comparing with group 1; [2] for groups 3–7 comparing with group 2; [3] for groups 4–7 comparing with group 3; [4] for groups 5–7 comparing with group 4; [5] for groups 6–7 comparing with group 5; [6] for group 7 comparing with group 6, with Bonferroni adjustment

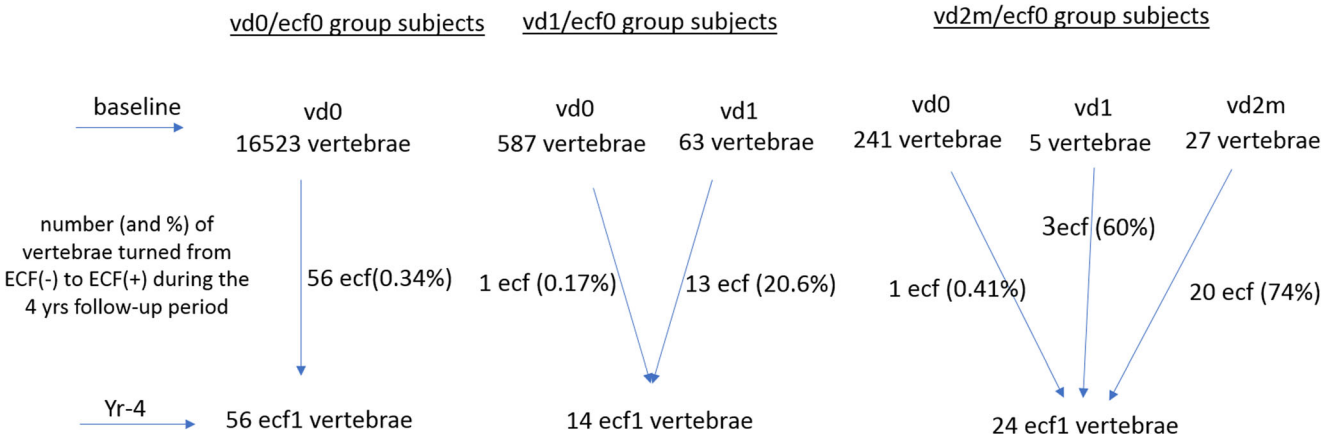

Fig. 1 New incident ECF in three baseline ECF(−) groups (vd0/ecf0, vd1/ecf0, and vd2m/ecf0). It is shown that greater height loss at baseline is associated with a higher risk for a mild/moderate deformed ECF(−) vertebra turning to ECF(+) at follow-up

group, the overall probability of turning to ECF(+) during 4-year follow-up was 20.6% and 74%, respectively. Therefore, higher extent of vertebral deformity at baseline is associated with higher probability of developing ECF at follow-up.

Comparing vd1/ecf0 group and vd1/ecf1 group, the vd1/ecf1 group had a trend of higher VD progression rate at per subject level, higher VD progression rate at per vertebra level, and higher incident new VD rate at per subject level (Table 2). However, statistical significance was not achieved (all $p > 0.05$), likely due to the overall low incident rates. Comparing vd2m/ecf0 group and vd2m/ecf1 group, the vd2m/ecf1 group had a trend of higher VD progression rate at per subject level ($p > 0.05$) and had higher VD progression rate at per vertebra level ($p = 0.029$), and higher incident new VD rate at per subject level ($p = 0.032$) (Table 2, p value details in Supplementary Table 1).

If vd1/ecf0 and vd2m/ecf0 subjects were grouped together to compare the combination of vd1/ecf1 and vd2m/ecf1 subjects (i.e., a comparison of ECF(−) VDs with 20–34% height loss vs. with ECF(+) VDs with 20–34% height loss), the latter ECF(+) group had statistically higher VD progression rate at per vertebra level ($p = 0.0045$) and higher incident new VD rate at per subject level ($p = 0.044$), and also had higher VD progression rate at per subject level (13.04% vs 5.63%, $p = 0.13$ with marginal statistical significance, Table 3).

The same as reported previously [18], the reading of follow-up radiographs that showed all VDs with > 34% height loss (i.e., vd2s and vd3 vertebrae) were ECF(+).

Discussion

Till now, Genant's SQ method is the most commonly used method for osteoporotic VD grading, though the justification for the proposed VD lower cutoff threshold of 20% height reduction remains not fully validated. It has been recognized that purely morphometrical assessment is not only time-consuming, it can also lead to "overcall" as some of the congenital short vertebrae or degenerative vertebral compressive changes are wrongly classified osteoporotic VD. The current evidences favor the approaches incorporating ECF identification for VF assessment [1, 3, 5, 8–20]. There is no minimum threshold for reduction in vertebral height for a prevalent ECF. In this study, we used a combination of both Genant's SQ method and ECF analysis which can also be considered a modification of the ABQ approach.

The criteria for defining incident vertebral deformities usually include two aspects: (1): change in vertebral height of the same vertebral body with existing VD and defines a VD progression as a further decrease in vertebral height of 15% or 20% or 4 mm or (2) increase in the number or presence of prevalent vertebral deformities [2, 26, 27]. In this study, for VD progression, we chose the criterium of further height loss at follow-up of ≥ 15%, which is more liberal than the 20% further height decrease used in a number of other studies [2]. This was to increase the sensitivity for comparison between the seven subgroups in this study (Table 2). On the other hand, to qualify for a new VD, if it was a change from grade-0 to grade-1 VD, then in addition to the qualitative changes as required by the Genant SQ criteria, we required at least 10% height loss during the follow-up period. 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 18% height loss (may be graded as grade-0.5) progressed to SQ grade-1 VD with only 2% further height loss during the 4-year follow-up. This may lead to "overcall" of incident new VDs. On the other hand, changes from grade-0 at baseline to grade-2 or grade-3 VD at follow-up were both considered to be new incident VD [2].

It has been well known that the severity and number of VD at baseline are independent risk factors for future vertebral VF [28–30]. Moreover, the current evidences favor the approaches incorporating ECF identification for VF assessment [1, 3, 5, 8–20]. In addition to Jiang et al.'s description of

osteoporotic endplate fracture, anterior cortex fracture is also commonly seen (Supplementary Fig. 1); therefore, we use the term endplate/cortex fracture (ECF) in our study. ECF may be a distinct sign of VF and should be recognized, though without radiographically identifiable ECF does not necessarily exclude the existence of an osteoporotic VF [1, 19, 31, 32]. It can be postulated that, within the same VD grades, those with ECF are at greater risk of future fracture than those without ECF; however, this point has not been well explored. The results of our analysis confirm that, for vertebrae in the same grades of deformity, those with ECF had a higher risk of near future (a 4-year span) of VD progression or new incident VD than those without ECF, such as the cases of vd1/ecf0 vs. vd1/ecf1 and vd2/ecf0 vs. vd2/ecf1. Notably, a trend is noted that vd1/ecf1 cases had a higher risk of near future of incident VF than cases of vd2m/ecf0 (Table 2).

It has been reported that even mild VD is associated with greater future risks of VF [22, 26]. However, in the past studies, mild VDs, such as vd1, were composed of a mixture of ECF(−) and ECF(+) vertebrae, while as shown in this study, vd1/ecf1 is associated with future risk; the significance of vd1/ecf0 for predicting further risk remains unknown till now. The current study showed that cases with ECF(−) VDs, i.e., vd1/ecf0 or vd2m/ecf0, did not show higher risk of near future of VD progression or new incident VD compared with SQ normal cases (vd0/ecf0). However, cases of VD without ECF showed a higher risk of near future incident ECFs. The endplate and vertebral cortex are harder than trabecula bone, and they support the physiological morphology of vertebrae. With weakened protection, vertebrae with fractured endplate and cortex, i.e., ECF(+), will be more likely to develop new deformity or deformity progression under compressive pressure. On the other hand, a vertebra with deformity, such in cases of vd1ecf0 or a vd2m/ecf0, is more likely to turn into ECF(+) under compressive pressure compared with a vd0/ecf0 vertebra. Of the 63 vd1/ecf0 vertebrae, 13 of them (20.6%) turned to EFC(+) during the 4-year follow-up; of the 27 vd2m/ecf0 vertebrae, 20 of them (74%) turned to EFC(+) during the 4-year follow-up; therefore, greater height loss is associated with higher risk for a mild/moderate ECF(−) VD turning to ECF(+). Thus, our previous results [17, 18] and results from this study suggest that ECF and VD are closely related. While less commonly ECF can occur in a vertebra without meeting the Genant's SD grade-1 VD criteria (less than 20% height loss), the majority of ECF is associated with a deformed vertebra [17]. The progression of VD severity is associated with an increasing probability of ECF(+), so that nearly all VDs with > 34% height loss (i.e., vd2s and vd3) are ECF(+) in females).

This study has a number of limitations. Firstly, despite 1533 elderly subjects were followed-up for 4 years, in each seven subgroups, there were limited number of subjects who had VD progression or incident new VD. This has led to difficulty in statistical analysis for comparing vd1/ecf0 vertebrae vs. vd1/ecf1 vertebrae and vd2m/ecf0 vertebrae vs.

Table 3 Vertebral deformity progression of vertebral deformity (20–34% height loss) with or without endplate/cortex fracture

	Group 1 vd1/ecf0 and vd2m/ecf0	Group 2 vd1/ecf1 and vd2m/ecf1
Subject no. at baseline	71	69
Subject age at baseline (years, mean ± SD)	73.37 ± 5.03	73.10 ± 5.17
Subject total hip BMD at baseline (g/cm^2)	0.68 ± 0.09	0.67 ± 0.11
Subject lumbar BMD at baseline (g/cm^2)	0.75 ± 0.14	0.73 ± 0.16
Mean no. of VD per subject at baseline	1.34 ± 0.63	1.30 ± 0.58
Mean no. of ECF(+) vertebrae per subject at baseline		1.19
Progression of existing VD—by subject	4	9
% Progression of existing VD—by subject	5.63% #	13.04% #
Progression of existing VD—by vertebra	4	15
(No. of VD possible for progression)	95	88
% Progression of existing VD—by vertebra	4.21%*	17.05%*
VD new incident—by subject	2	8
VD new incident—by vertebra	2	13
% New incident VD—by subject	2.82% §	11.59% §

ecf1 with endplate/cortex fracture (ECF), *ecf0* without ECF, *vd2m* grade-2 vertebral deformity with ≤ 34% height loss. Group 1, 20–34% height loss with ECF(−) and group 2, 20–34% height loss with ECF(+). "By subject" and "by vertebra"' = how many subjects and how many vertebrae had these incidents. % New incident = no. of incidents divided by no. of vertebrae or subjects at baseline that potentially would have these incidents at follow-up

$p = 0.13$; * $p = 0.0045$; § $p = 0.044$

vd2m/ecf1 vertebrae. Further studies with longer follow-up are necessary to confirm the trends observed in this study. Secondly, radiographic ECF analysis is subjective, and some micro-fractures might have been missed with radiograph. However, this would not have substantially affected the groupwise comparison results of this study. Thirdly, this report only looked at spine radiographs, other non-vertebral fractures with longer follow-period are being further studied by us. Fourthly, in this study, the small number of Genant criteria VD grade-0.5 were grouped together with grade-0 VD. In addition, the cases of vd0/ecf1 were excluded from analysis, as their number at follow-up was too small to allow proper statistical comparison with other groups. Finally, this study only focused on elderly females. It has been noted that compared with females, osteoporotic VF in males may have different characteristics [17, 18, 33]. For example, VD in males with 25–34% height loss rarely have 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 osteoporotic fracture than in elderly females [34]. Therefore, whether the results in this study can also be applied to males require further studies.

In conclusion, this study in elderly Chinese females suggests that 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. While our results cannot be considered final and conclusive, this study does support the notion that identifying osteoporotic vertebral ECF should be incorporated into clinical practice of assessing osteoporotic spine fracture. Furthermore, VD without ECF may also be clinically relevant, it carries important prognostic information as VD itself is associated with future risk of the vertebra turning into ECF(+).

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Compliance with ethical standards

The study protocol was approved by the Chinese University of Hong Kong Ethics Committee. Written informed consent was obtained from all subjects.

Conflicts of interest None.

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