Weak correlation between osteoporotic-like vertebral fracture severity and densitometric T-scores in older Chinese men

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Submitted Feb 08, 2023. Accepted for publication Jun 02, 2023. Published online Jun 21, 2023.
doi: 10.21037/atm-23-639
View this article at: https://dx.doi.org/10.21037/atm-23-639

Recently, we performed studies to define what portion of older community population with what severity of non-acute radiographic osteoporotic-like vertebral fracture (OLVF) corresponds to what low T-score status, i.e., we explored how we can convert severity of OLVFs to the equivalent T-score values. Using spine radiograph, for each vertebra in a subject, a score of 0, –0.5, –1, –1.5, –2, –2.5, and –3 was respectively assigned for no OLVF or OLVF of <1/5 (minimal grade), ≥1/5–1/4 (mild grade), ≥1/4–1/3 (moderate grade), ≥1/3–2/5 (moderately-severe grade), ≥2/5–2/3 (severe grade), and ≥2/3 (collapsed grade) vertebral height loss (1-4) (*Figure 1*). An OLVF sum score (OLVFss) was calculated by summing up the scores of vertebrae T1 to L5 (T1, 2, 3 not counted if not well shown on radiograph). However, two adjacent minimal OLVFs were assigned as –0.5. Three adjacent minimal OLVFs are generally rare and were assumed to –1 (1). For women's data, we used Hong Kong Chinese as an example for East Asians, and Rome Italians as an example for Caucasians, and demonstrated that two nonadjacent minimal-grade OLVFs, or a single mild OLVF (i.e., when OLVF score ≤–1), suggest osteoporosis, while three nonadjacent minimal-grade OLVF, or one minimal-grade OLVF and one mild OLVF, or one OLVF with ≥ moderate grade (i.e., when OLVF score ≤–1.5), meets the diagnosis of osteoporosis. The results were consistent between Chinese and Italian subjects (1). These results appear reasonable as even a minimal-grade OLVF may be an osteoporotic phenomenon, statistically associated with lower bone mineral density (BMD) and increased further radiographic vertebral fracture risk in older women (4,5). For men's data, we analysed Hong Kong Chinese and obtained very different results as compared with women's results. We showed that, statistically OLVFss ≤–2.5 suggests osteoporosis and OLVFss ≤–3 meets the criterion for osteoporosis diagnosis (2). While both women's results and men's results are consistent with further radiograph results based on younger subjects assumed to be have normal bone strength (6), there are two questions remain to be better addressed for men's results. The first question is whether a male patient with a single OLVF of 40% height loss (OLVFss =–2.5) is highly likely to be densitometrically osteoporotic. The second question is, since minimal-grade OLVF is very common among men of normal bone strength (6), whether it is reasonable for minimal-grade OLVFs to be used to calculate the final OLVFss, or whether it would be better to discard all minimal-grade OLVFs. To address these questions, hereby we did some additional analyses.

The data were from the osteoporotic fractures in men (MrOS) (Hong Kong) study. At baseline, 2,000 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

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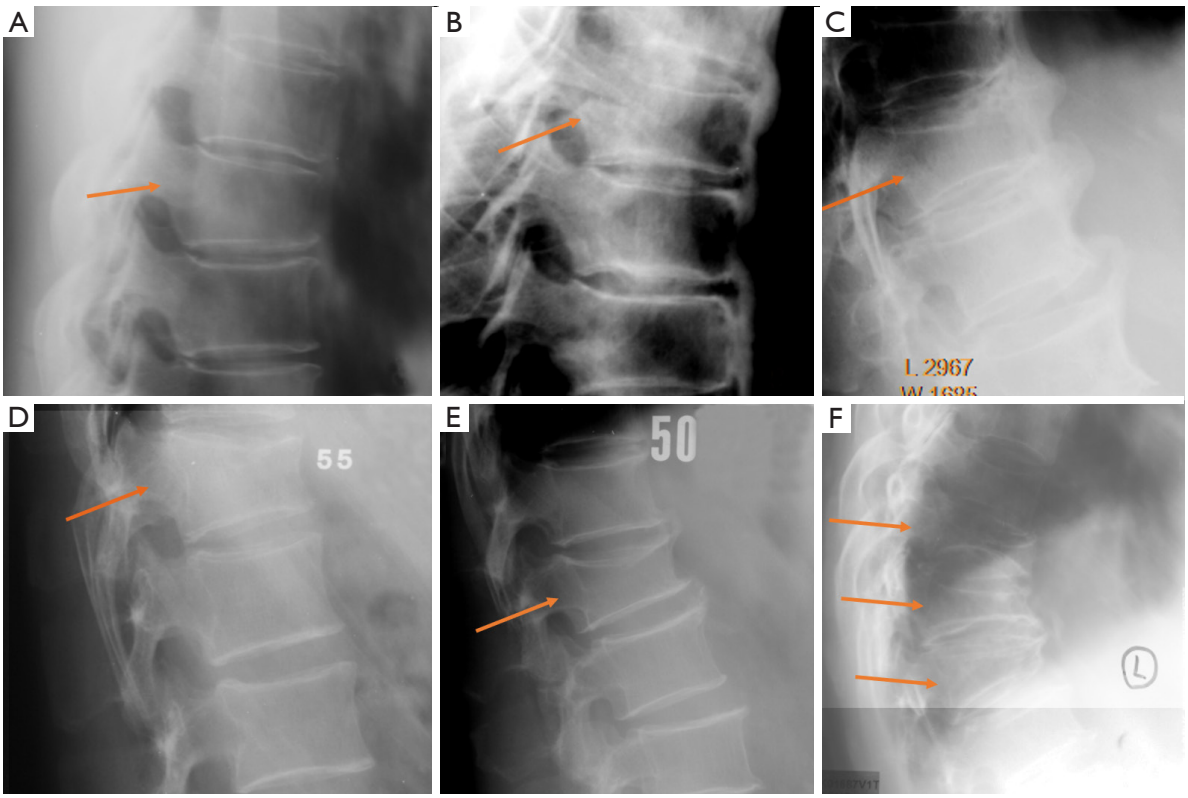

Figure 1 Radiograph examples of OLVF (arrows) in older men. (A) Minimal grade (OLVF score =–0.5). (B) Mild grade (OLVF score =–1). (C) Moderate grade (OLVF score =–1.5). (D) Moderately severe grade (OLVF score =–2). (E) Severe grade (OLVF score =–2.5). (F) Collapsed grade (OLVF score =–3/each, total for three collapsed vertebrae =–9). Reproduced with permission from reference (2) under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License (CC BY-NC-ND 4.0). OLVF, osteoporotic-like vertebral fracture.

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. 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. No participants had a known malignancy or previous lumbar spine surgery. During 2014–2017, a 14-year follow-up was carried out with a whole spine magnetic resonance imaging (MRI) performed on a random sample of 271 subjects. From our baseline database of 2,000 subjects, we randomly selected 496 cases (subgroup-A, age: 73.0±5.3 years) following the principle of 1 out of every 4 cases and also excluding the cases used in the 14-year follow-up study and those of poor radiograph quality. From the MrOS (Hong Kong) 14-year follow-up, there were 259 subjects (subgroup B, 82.8±3.7 years) with complete data. Putting these two subgroups together, in total there were 755 subjects, aged 76.4±6.7 years (range, 65–98 years). Areal BMD (unit in g/cm^2) of the anterior-posterior lumbar spine and proximal femur was measured by a Hologic QDR-4,500 W densitometers (Hologic, Inc., Bedford, MA, USA). Hong Kong local BMD reference data were used for the T-score calculation.

For the current analyses, the results are presented group-wise focusing on median values, while statistical P value was not calculated as this is dependent on the sample size.

Firstly, for the 755 men (76.4±6.7 years) in our recent study (2), we classified them according to the most severe grade of their OLVFs in each subject, and then looked at their T-scores [those without OLVF and those with only minimal OLVFs were grouped together]. The results are shown in *Figure 2*. It is observed that: (I) even the subjects with mild OLVFs had slightly lower T-scores; (II) the subjects with moderate, moderately-severe, or

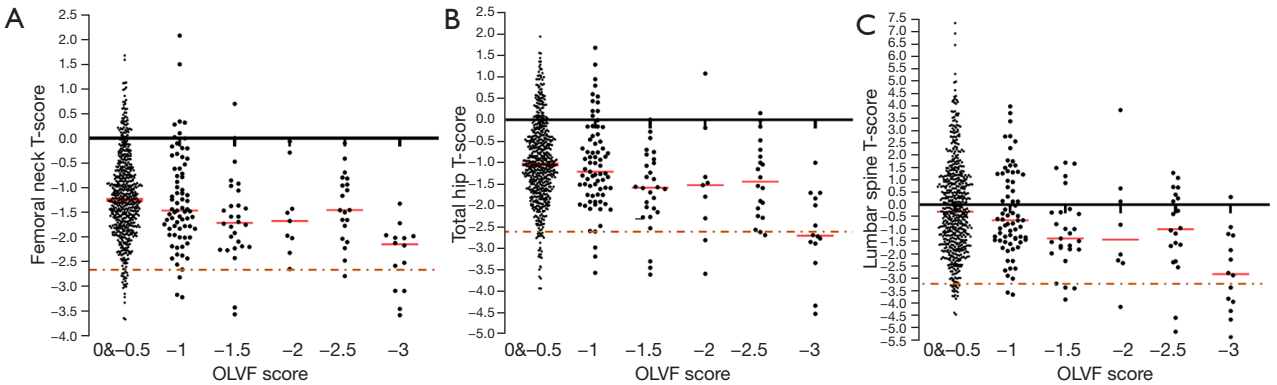

Figure 2 T-scores (Y-axis) for male subjects (n=755, mean age: 76.4 years) of no OLVF and only minimal OLVFs (group 0 & –0.5, X-axis), and the most severe grade of their OLVFs being mild grade (group –1), being moderate grade (group –1.5), being moderately-severe grade (group –2), being moderately-severe grade (group –2.5), being collapsed grade (group –3). Red solid line: median value. Orange dotted line: suggested cut-point T-score for classifying densitometric osteoporosis [–2.7 for femoral neck, –2.6 for total hip, and –3.2 for lumbar spine; reference (2)]. OLVF, osteoporotic-like vertebral fracture.

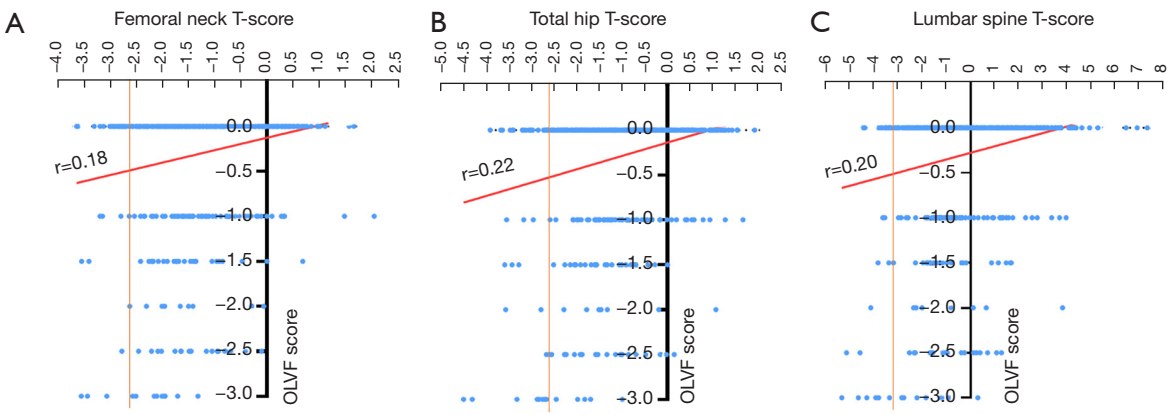

Figure 3 Correlation between T-scores (X-axis) and OLVF score (Y-axis) for male subjects (n=755, mean age: 76.4 years). OLVF score is the highest grade of OLVF in a subject. In this graph, subjects with minimal OLVF (score: 0.5) were grouped with no-OLVF subjects as OLVF score =0. Red: linear correlation (*r*: Pearson correlation). Orange vertical line: suggested cut-point T-score for classifying densitometric osteoporosis [–2.7 for femoral neck, –2.6 for total hip, and –3.2 for lumbar spine; reference (2)]. OLVF, osteoporotic-like vertebral fracture.

severe OLVF had similar T-scores among them; (III) the subjects with collapsed-grade OLVF had distinctly lower T-score than subjects with other-grade OLVF, however, many subjects with collapsed-grade OLVF were still not densitometrically osteoporotic. The correlations between T-scores and OLVF score (Y-axis), which were weak, are shown in *Figure 3*. These results suggest that it is reasonable to considerate mild OLVFs as a contributor to OLVFss in older men, and also a single severe-grade OLVF may be insufficient to establish the subject as being osteoporotic. In our recent publication of MrOS (Hong Kong) 4-year follow-up for elderly Chinese men (baseline mean age 71.7 years; range, 65–91 years), when only the highest-grade OLVF was counted at baseline, of subjects with Genant's grade-0, 2.1% developed OLVF progression or/and new OLVF, while of subjects with Genant's grade-1 (≥1/5–<1/4 vertebral height loss), grade-2 (≥1/4–<2/5 vertebral height loss), and grade-3 (≥2/5 vertebral height loss) OLVF, only 2.0% (3/149), 3.1% (3/96), and 2.8% (1/36) of the cases developed OLVF progression/new OLVF, respectively (7,8). We have reported that OLVF with ≥1/3 height loss always demonstrate radiographic endplate and/or cortex fracture

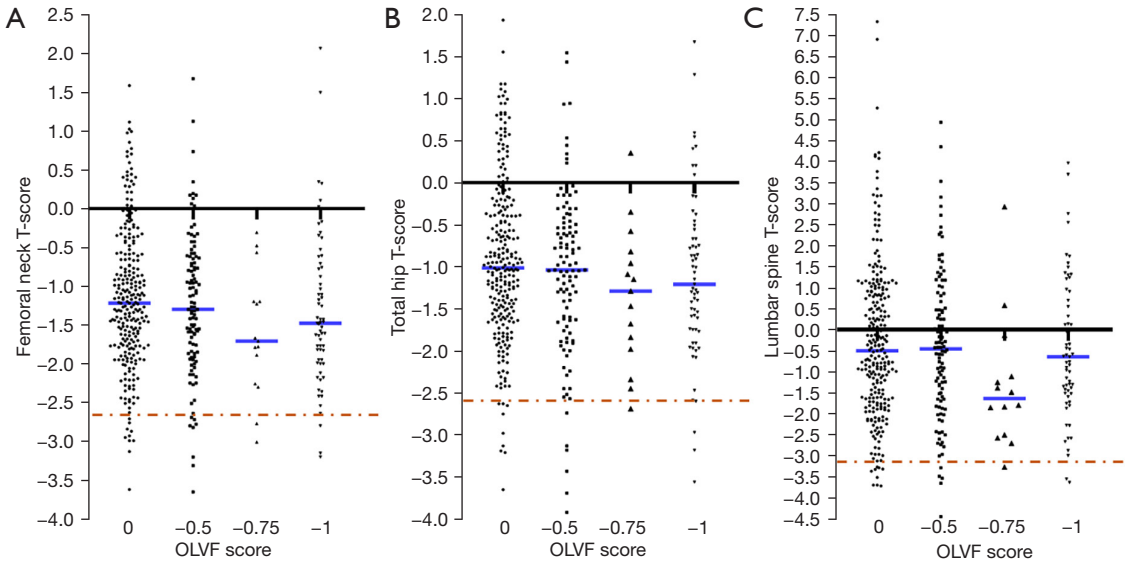

Figure 4 T-scores for male subjects (n=496, mean age: 73.0 years) of no OLVF (group 0), of only minimal OLVFs (group –0.5), of at least two non-adjacent minimal OLVF (group –0.75), and of the most severe grade of their OLVFs being mild grade (group –1). Blue solid line: median value. Orange dotted line: suggested cut-point T-score for classifying densitometric osteoporosis [–2.7 for femoral neck, –2.6 for total hip, and –3.2 for lumbar spine, reference (2)]. OLVF, osteoporotic-like vertebral fracture.

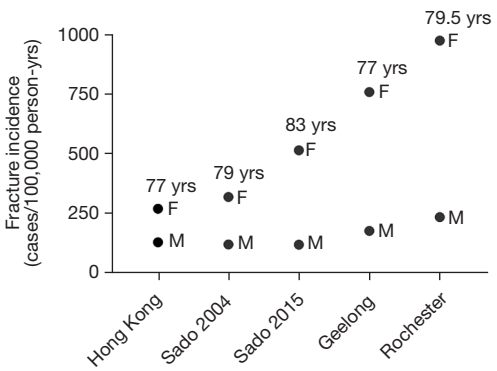

Figure 5 Incidences of clinical osteoporotic vertebral fracture in older men are mostly less than half of the incidences of clinical osteoporotic vertebral fracture in older women. Data are from MrOs (Hong Kong) and MsOS (Hong Kong) studies (10); Sakuma *et al.* (11), Imai *et al.* (12), Sanders *et al.* (13), and Cooper *et al.* (14). The mean ages (yrs) during the follow-up period for each study are noted. M, men's data; F, women' data; yrs, years; MrOs, osteoporotic fractures in male; MsOS, osteoporotic fractures in women.

(ECF) sign (7,9). We also noted that ECF is not uncommon among vertebrae of subjects assumed to have normal bone strength (6). Therefore, ECF sign positivity is insufficient to diagnose a vertebral fracture as osteoporotic vertebral fracture.

Secondly, for the 496 men assessed with spine radiograph (subgroup-A n=496, age: 73.0±5.3 years) in our recent study (2) (259 subgroup-B subjects had MRI and may not be suitable for evaluating minimal-grade OLVF thus excluded herein) we listed them according to no OLVF, OLVFss =–0.5, at least two non-adjacent minimal OLVF (minimal grade was the most severe grade of their OLVFs, marked as the –0.75 group in *Figure 4*), and the most severe grade of their OLVFs being mild grade (OLVFss =–1). The results for T-scores and the groupings are shown in *Figure 4*. It is observed that: (I) the subjects without OLVF and subjects with OLVFss =–0.5 had similar T-scores; (II) the –0.75 group had T-scores not only lower than those without OLVF, their T-scores were even lower than those with mild-grade OLVF (OLVF score =–1). These results confirm our practice that an 'additional' non-adjacent minimal OLVF should be counted rather than ignored.

In conclusion, the analysis in this letter further emphasizes the difficulty of diagnosing true osteoporotic fracture of the spine among Chinese men. Note, studies have shown prevalence of clinical osteoporotic vertebral fracture in older men is mostly less than half of prevalence of clinical osteoporotic vertebral fracture in older women (*Figure 5*). We conclude that a severe-grade OLVF (≥2/5–2/3

vertebral height loss) may not be sufficient to diagnose the patient as being osteoporotic.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was a standard submission to the journal. The article has undergone external peer review.

Peer Review File: Available at https://atm.amegroups.com/article/view/10.21037/atm-23-639/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-23-639/coif). YXJW is the founder of Yingran Medicals Ltd., which develops medical image-based diagnostics software. The other authors have no conflicts of interest to declare.

Ethics Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Cite this article as: Wáng YXJ, Leung JCS, Lam PMS, Kwok TCY. Weak correlation between osteoporotic-like vertebral fracture severity and densitometric T-scores in older Chinese men. Ann Transl Med 2023;11(10):374. doi: 10.21037/atm-23-639