



# Around the time of a hip fracture, older East Asian female patients tend to measure lower densitometric femoral neck and total hip T-scores than older Caucasian female patients: a literature analysis

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The clinical significance of osteoporosis lies in the fractures that occur, and the most important fracture is hip fracture. According to the 1994 World Health Organization (WHO) criteria, the T-score is defined as:  $(BMD_{\text{patient}} - BMD_{\text{young normal mean}}) / SD_{\text{young normal population}}$ , where BMD is bone mineral density and SD is the standard deviation. When the femoral neck is measured in adult women, a cutpoint value of patient BMD of 2.5 SD below the  $BMD_{\text{young normal mean}}$  satisfies that the prevalence of osteoporosis for those aged  $\geq 50$  years is about 16.2%, the same as the lifetime risk of hip fragility fracture (FF) (1,2). If other sites are also considered, this cutpoint value identifies approximately 30% of postmenopausal women as having osteoporosis, which is approximately equivalent to the lifetime risk of FF at the spine, hip, or forearm. The FF prevalence of older Chinese women is slightly less than half that of Caucasians (3,4). This is the case for hip FF (5-7), radiographic vertebral FF (8), clinical vertebral FF (9-11), and many other FF sites (3,4,12,13). As compared with Caucasians, Chinese demonstrate an overall stronger skeleton property (14). For example, Walker *et al.* (15) reported that postmenopausal

Chinese women have a higher trabecular plate-to-rod ratio and greater whole bone stiffness, translating into a greater trabecular mechanical competence.

Following the 1994 WHO definition, densitometric osteoporosis prevalence among a non-Caucasian population should be in proportion to its relative osteoporotic fracture risk with Caucasian data as reference (16). To achieve this goal, various region/ethnic-specific reference BMD databases have been published (3). Furthermore, the cutpoint T-score for defining densitometric osteoporosis should be adjusted according to the osteoporotic fracture risk profile. Based on statistical modeling (3), we proposed that the femoral neck cutpoint T-score is revised from  $\leq -2.5$  to  $\leq -2.75$  for Hong Kong older women when a local BMD reference published by Lynn *et al.* (17) is applied. The same principle can also be applied to Japanese older women if a local BMD reference published by Iki *et al.* is used (3,18). In an empirical study on women with radiographic vertebral FF as a surrogate clinical endpoint, we recently demonstrated that, at the mean age of around 74, a femoral neck T-score of  $-2.60$  for Italian Caucasians is equivalent to

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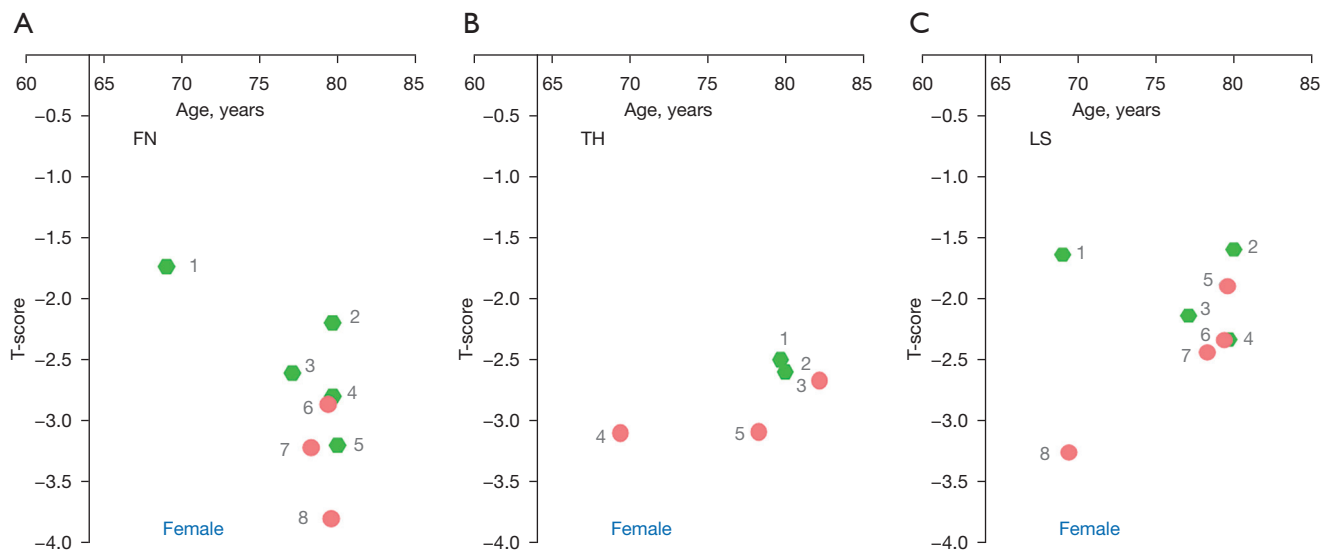
-2.77 for Hong Kong Chinese, while a lumbar spine T-score of -2.44 for Italian Caucasians is equivalent to -3.75 for Hong Kong Chinese (19). Moreover, our literature analysis suggested that, while a cutpoint T-score  $\leq -2.5$  for defining spine densitometric osteoporosis is justified for Caucasian women, for East Asian women the same cutpoint T-score much inflates the estimated prevalence of spine densitometric osteoporosis (11).

To further support our argument that the cutpoint T-score for defining femoral neck densitometric osteoporosis among East Asian populations should be lower than the conventional value of  $\leq -2.5$ , we conducted an additional literature analysis. The hypothesis is that, around the time when a proximal femur FF occurs (which is a clinical endpoint for osteoporosis), East Asians measure a lower T-score than that of Caucasians. We grouped together Chinese, Korean, and Japanese as East Asians. It has been suggested that Korean and Japanese older women have similar FF risk profiles similar to those of older Chinese women (5,13,20-23). On Dec 13th 2022, two structured literature searches on <https://pubmed.ncbi.nlm.nih.gov/> were conducted using the keywords combination of '(hip OR femur OR femoral) AND fracture) AND T-score', and '(BMD OR T-score) AND hip fracture AND (Chinese OR Korean OR Japanese)'. These searches generated 1,558 results and 492 results respectively. The results were initially screened by their titles, and then by their abstracts (when available). For potentially relevant items, the full articles were retrieved for analysis. Though Singapore is a Southeast Asia nation, data from Singapore were included as 75% of Singaporean populations are ethnically Chinese.

We only included studies on proximal femoral fractures among older subjects while excluded the studies included a significant portion of high energy trauma cases, thus included cases are assumed to be mostly FF. Efforts were made that the reported cases were only counted once in this analysis (note some authors might have used the same case materials for different types of analysis and published more than one article). We aimed to include studies concerning dual-energy X-ray absorptiometry areal BMD measured around the time of fracture, and usually the fracture was shortly followed by surgical intervention. Other excluding criteria were: (I) articles concerned with patients group-wise systematically under a specific anti-osteoporotic treatment regime, however, it was allowed when a portion of cases was under an anti-osteoporosis medication as an

usual care (as would be expected in a real-world clinic); (II) articles concerned with specific types of patients such as those with diabetes mellitus type 2, however, it was allowed for studies with a portion of their patients had a disease such as diabetes mellitus type 2 (as would be expected among general community older subjects); (III) articles only concerned with hip re-fracture patients; (IV) articles concerned with atypical femur fracture; (V) articles concerned with femoral head subchondral insufficiency fracture; (VI) articles concerned with *ex vivo* study; (VII) study cohorts with fewer than 10 cases. For articles from East Asia, we only included studies which used a local or an East Asian BMD reference. If this aspect was not specified in the published article, the authors were contacted to validate this information, and articles were excluded if this could not be validated (only one article was excluded due to this reason). Finally, we included 12 articles (n=5 for East Asians and n=7 for Caucasians) that reported women's and men's data separately, and 12 articles (n=7 for East Asians and n=5 for Caucasians) that reported women's and men's data together. The articles available for analysis were much fewer than initially anticipated. Many studies concerned with proximal femur FF only reported BMD values instead of T-score values. Some studies reported T-score classifications (such as 28% of the hip fracture patients had femoral neck T-score of  $\leq -2.5$ ) instead of the actual T-score values.

For the data in the articles included for analysis, the results are shown in *Figure 1* for female patients (24-33), *Figure 2* for male and female patients mixed (34-45), and *Figure 3* for male patients (24,28-30,32,33,46,47). For the data in *Figure 2*, females commonly constituted 2/3 of the cases, reflecting that hip fracture prevalence among older women is about double of that among older men. A trend can be seen that East Asian female patients measure a lower femoral neck and a lower total hip T-score than those of Caucasians. The same trend is also tentatively noted for female patients' lumbar spine T-score. For the data of male and female patients mixed, a trend is only noted that East Asian patients measure lower femoral neck T-score. For male patients, only a 'possible' trend is noted that East Asian patients measure lower total hip T-scores. Another point noted is that, around the timepoint of a hip fracture, at least for East Asians included in this study, male patients tend to measure higher femoral neck and total hip T-scores than those of female patients (*Figure 4*) (24,28-30,32,33).

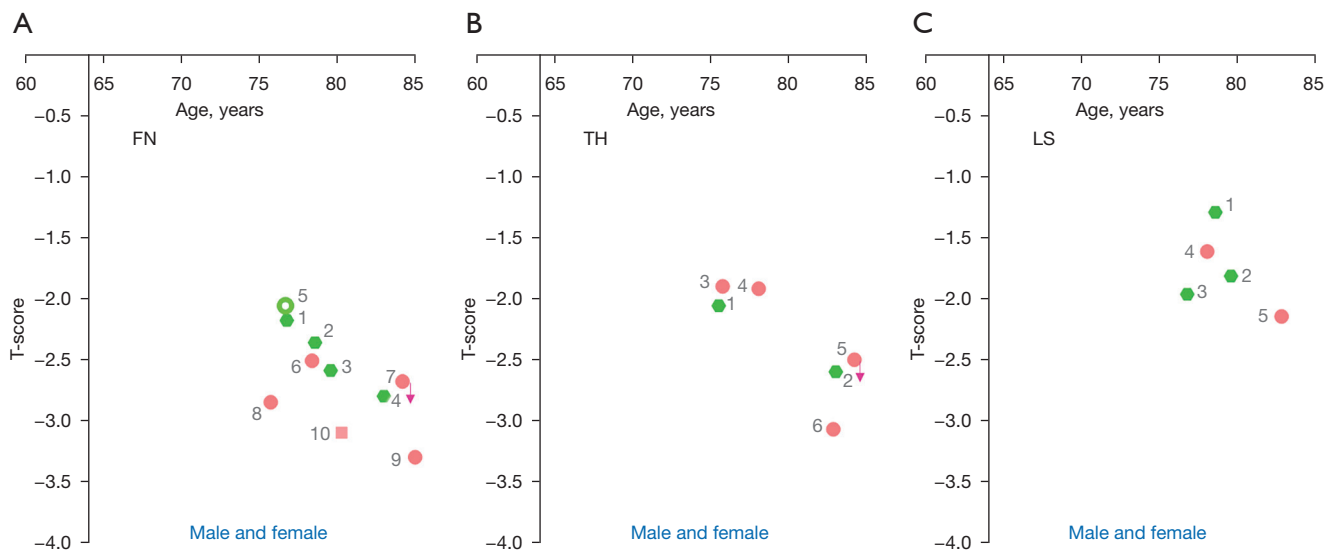


**Figure 1** Distribution of T-scores of proximal femur fracture Caucasian female patients and East Asian female patients. A trend is noted that East Asian female patients measure lower FN, TH, and LS T-scores. (A) FN data, (B) TH data, (C) LS data. A1 and C1: Wilson *et al.* (n=68 cases); A2 and C4: Olszewski *et al.* (n=37); A3 and C3: Schnabel *et al.* (n=22); A4 and B1: Di Monaco *et al.* 2020 (n=350); A5, B2 and C2: Yeo *et al.* (n=91); A6 and C6: Lee *et al.* (n=819); A7, B5 and C7: Gani *et al.* (non-diabetic group n=350, though the title of the article suggests only patients with severe osteoporotic hip fracture, however, according to the methodology and the T-score values, they included all low energy hip fracture patients); A8 and C5: Zhu *et al.* (n=24); B3: Ho *et al.* (n=167); B4 and C8: Li HL *et al.* (n=268). FN, femoral neck; TH, total hip; LS, lumbar spine.

Based on *Figure 4*, it appears that, a femoral neck T-score of  $-3.3$  in East Asian women will be approximately equivalent to a femoral neck T-score of  $-2.4$  in East Asian men (a hip T-score of  $-3.0$  in East Asian women will be approximately equivalent to a hip T-score of  $-2.4$  in East Asian men, note that femoral neck T-score and hip T-score are usually highly correlated). This may suggest that different T-score cutpoints for classifying densitometric osteoporosis should be applied for Asian men and women, on the other hand, this observation may also be coincidental. Note, the 1994 WHO Study Group did not establish any guidelines for the diagnosis of osteoporosis in men (1).

There are many limitations to the current analysis. The patient populations included in the current analysis were highly heterogeneous, while the number of studies available for analysis is small. In theory, for the studies which reported the BMD values and the specific type of bone densitometer used, we could use a suitable ethnic specific BMD reference database and perform an adjustment to count for the bone densitometers employed to derive T-scores. However, we did not choose to do this as we

consider our analysis as a ‘test-of-the-concept’ study. Since the expected trend was already shown, we did not want to further complicate our analysis, thus we chose only to use the T-score results as they were reported by the authors. The trend that older East Asian patients tend to measure lower femoral neck and total hip T-scores than older Caucasians as shown in the current analysis was not strong nor a ‘clear-cut’. This is probably not surprising. Our proposed cutpoint T-score for female femoral neck only differs by  $-0.2$  to  $-0.25$  from the conventional value of  $-2.5$  (3). However, its impact on epidemiological studies will not be trivial. As an example, using the Japanese data of Iki *et al.*, an adjustment of femoral neck T-score from  $\leq -2.5$  to  $\leq -2.75$  can lower osteoporosis prevalence for older Japanese women aged 50–79 years from 12% to 7.5% (3). Another point is that the precision of BMD measures is affected by many factors. Many reports specified that femoral neck and total hip BMD were measured using the contra-lateral non-fractured hip, while a few articles did not report such details. We can only assume the necessary steps to ensure a satisfactory level of measurement precision were taken

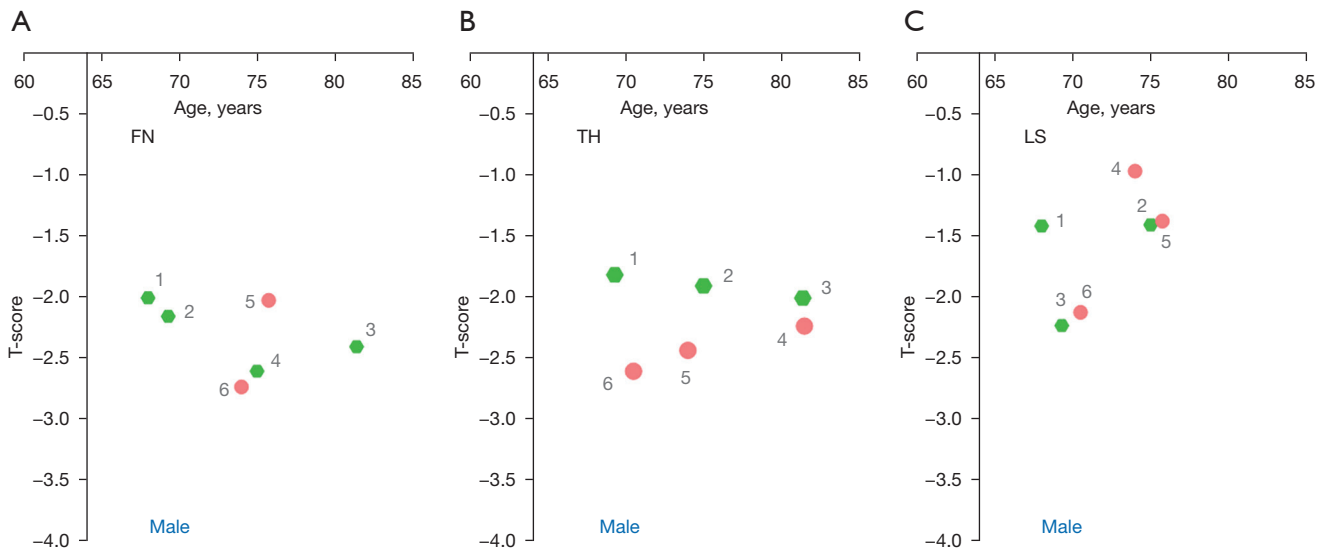


**Figure 2** Distribution of T-scores of proximal femur fracture Caucasian patients and East Asian patients. Male and female patients were reported together. A trend is noted that East Asian patients measure a lower FN T-score. (A) FN data, (B) TH data, (C) LS data. A1 and C3: Heetveld *et al.* (n=111, 68.47% females); A2, B1, and C1: Amar *et al.* (n=314, 68.8% females); A3 and C2: Valentini *et al.* (non-diabetic group n=69, assumed a mean age of 79.6 years old); A4 and B2: Ganhão *et al.* (n=214, 79.70% females); A5: Carlson *et al.* (this is from the American Orthopaedic Association's Own the Bone database. 93.3% were Caucasian and 78% were females. The mean age was 76.7 years. Hip, spine, ankle/foot, wrist and shoulder counted for 51.6%, 11.2%, 7.9%, 6.7%, and 6.1% of the fractures, respectively. Thus, this is not a pure hip fracture cohort); A6: Li XP *et al.* (n=269, 69.50% females); A7 and B5: Xu *et al.* [n=360, 51.70% females, data estimated from Fig. 5 of Xu *et al.* (34)]; A8 and B3: Hey *et al.* (n=106, 61.70% females); A9: Kanno *et al.* (n=275, 80.00% females); A10: Kang *et al.* [n=159, 69.8% females. Whether the T-score was computed using an Asian bone mineral density reference was not confirmed by us (but likely an Asian bone mineral density was used considering other publications from the same institution). Even if a Caucasian bone mineral density reference was used to compute the T-score and then T-score is adjusted according to the results of Lo *et al.* (35), the datapoint of Kang *et al.* (36) will still be closer to the Asian data cluster than to the Caucasian data cluster]; B6 and C5: Yamamoto *et al.* (n=390, 78.4% females); B4 and C4: Cha *et al.* (n=59, 72.80% females). Arrow for A7 and B5 datapoints (Xu *et al.*): most of the other data entries had approximately 2/3 of the cases being females, however for A7 and B5 approximately only 1/2 were females. As males tend to measure higher FN and TH T-scores than females, if A7/B5 had 2/3 cases being females, then the value for A7/B5 would have been measured even lower. Xu *et al.* only included those aged between 80–90 years (mean age: 84.2 years which is not very different from other studies). FN, femoral neck; TH, total hip; LS, lumbar spine.

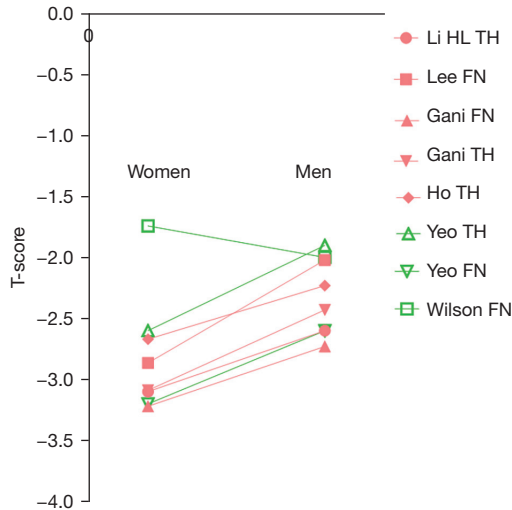
by the authors. Note the right and left hips commonly have very similar BMD values. For the current analysis, we initially anticipated a bigger difference for lumbar spine T-score between East Asians and Caucasians. The data in Figures 1–3 for lumbar spine T-score may reflect that lumbar spine T-score is not as predictive for hip fracture risk as femoral neck or total hip T-scores. The measurement of lumbar spine BMD is complicated by spine degeneration which can lead to artificially higher BMD measures, thus only a lower lumbar spine T-score is relevant rather than

the mean lumbar spine T-score. In this study, except for the data of Carlson *et al.* (41), all other Caucasian data are from Europe and Near East. The ethnicities of the patients in their studies were mostly not specified, we take it that it is a reasonable assumption that most of their older patients were Caucasians.

In conclusion, our literature analysis suggests that, around the time of a hip fracture, older East Asian female patients tend to measure lower femoral neck and total hip T-scores than older Caucasian female patients.



**Figure 3** Distribution of T-scores of proximal femur fracture Caucasian male patients and East Asian male patients. A ‘possible’ trend is noted that East Asian patients measure a lower TH T- score (however, the data certainly is not conclusive). (A) FN data, (B) TH data, (C) LS data. A1 and C1: Wilson *et al.* (n=11); A2, B1, and C3: Cesme *et al.* (n=20); A3 and B3: Di Monaco *et al.* 2018 (n=80); A4, B2 and C2: Yeo *et al.* (n=21); A5 and C5: Lee *et al.* (n=271); A6, B5, and C4: Gani *et al.* (n=162, non-diabetic group); B4: Ho *et al.* (n=72); B6 and C6 Li HL *et al.* (n=92). Note studies on Caucasian males mostly had limited sample size. FN, femoral neck; TH, total hip; LS, lumbar spine.



**Figure 4** In total six studies reported both males’ data and females’ data (24,28-30,32,33), data from all four East Asian cohorts show FN and TH T-scores of proximal femur fracture male patients measure higher than those of female patients. A trend for data of Caucasians can not be ascertained. Each line represents data from the same report. TH, total hip; FN, femoral neck.

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**Footnote**

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*Conflicts of Interest:* The author has completed the ICMJE uniform disclosure form (available at <https://qims.amegroups.com/article/view/10.21037/qims-23-65/coif>). YXJW serves as the Editor-in-Chief of *Quantitative Imaging in Medicine and Surgery*. The author has no other conflicts of interest to declare.

*Ethical Statement:* The author is 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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