Analysis of combined indicators for risk of osteoporotic hip fractures in elderly women

Jinhui Zhao
Shanghai 6th Peoples Hospital Affiliated to Shanghai Jiaotong University School of Medicine
Department of Orthopaedic Surgery

Huipeng Shi
Shanghai 6th Peoples Hospital Affiliated to Shanghai Jiaotong University School of Medicine
Department of Orthopaedic Surgery

Dajun Jiang
Shanghai 6th Peoples Hospital Affiliated to Shanghai Jiaotong University School of Medicine
Department of Orthopaedic Surgery

Lingtian Wang
Shanghai 6th Peoples Hospital Affiliated to Shanghai Jiaotong University School of Medicine
Department of Orthopaedic Surgery

Shengbao Chen
Shanghai 6th Peoples Hospital Affiliated to Shanghai Jiaotong University School of Medicine
Department of Orthopaedic Surgery

Weitao Jia (jiaweitao@shsmu.edu.cn)
Shanghai 6th Peoples Hospital Affiliated to Shanghai Jiaotong University School of Medicine
Department of Orthopaedic Surgery
https://orcid.org/0000-0001-9363-5598

Research article

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Abstract

Background

Hip fractures in the elderly population has become a global issue due to its high morbidity and mortality. Although an increasing number of researchers are devoting attention to identify risk factors in attempts to reduce the incidence of hip fractures in the elderly, only few studies have investigated combined indicators in elderly hip fractures. The objective of the present study was to compare the accuracy of combined independent risk factors in assessing the risk of hip fractures in elderly women.

Methods

Ninety elderly females who sustained hip fractures and 110 female outpatients who fulfilled the inclusion criteria were included in our cross-sectional study. Bone mineral density (BMD), Beta-carboxy terminal telopeptide ($\beta$-CTX), N-terminal/mid region (N-MID), and 25(OH)D levels were analyzed. A novel evaluation model was established to evaluate combined indicators in assessing hip fractures in elderly women.

Results

Compared with the control group, taller height, higher levels of $\beta$-CTX, and lower levels of total hip BMD, femoral neck BMD, and 25(OH)D were found in the fracture group. After adjustment for confounding factors, logistic regression analysis revealed that 25(OH)D, femoral neck BMD and height remained risk factors for hip fractures in elderly women. Then a model including independent risk factors was established. DeLong test showed the area under the ROC(AUC) of 25(OH)D was significantly greater than that for femoral neck BMD ($p < 0.01$) and height ($p < 0.01$). AUC of model including 25(OH)D and height was significantly greater than that of other combinations ($p < 0.01$).

Conclusion

25(OH)D, femoral neck BMD and height were associated with the occurrence of hip fractures in elderly women even after adjustment for confounding factors, and model including 25(OH)D and height could provide better associated power than other combinations in the assessment of elderly hip fractures. $\beta$-CTX and N-MID were not independent risk factors for hip fractures in elderly women.

Background

With aging societies around the world, the incidence of hip fractures in elderly populations is also increasing. In fact, the number of hip fractures in the elderly is expected to reach 6.3 million in 2050.[1] Additionally, it is estimated that medical expenditures for hip fractures in China will reach $60 billion USD in 2020 and $240 billion USD by 2040, which results in enormous burden to individuals, families and
society. Hip fractures in the elderly are defined as those involving the femoral neck and intertrochanter in patients ≥ 65 years of age, which are frequently caused by low-energy trauma (such as fall from standing height). These fractures have also been termed “osteoporotic fractures” and characterized by bone mass reduction and microstructural destruction. Such changes are likely to lead to decreasing bone strength and consequent increases in fracture risk. Due to poor physical conditioning and more underlying disease and co-morbidity, treatment of these fractures in this population remain a clinical dilemma given that on one hand, prolonged time in bed brought by non-operative treatment is disastrous for an increased number of complications and mortality and, on the other, operative treatment (including internal fixation and arthroplasty) is also prone to various failures owing to osteoporosis, which in turn exacerbates damage.

To prevent or, at least mitigate, risk for fractures, it is crucial to identify indices most associated with hip fractures. Although bone mineral density (BMD) has been verified to be related to osteoporotic fractures in the literature,[2] osteoporosis (T-score < -2.5) is frequently absent in the majority of elderly individuals who sustain hip fractures.[3–6] Additionally, BMD is a static indicator, which cannot reflect bone turnover status at the time of measurement.[7][8] As such, BMD is clearly not suitable as a sensitive indicator in monitoring fractures. In recent years, investigators have devoted more attention to bone turnover markers (BTMs), which have been demonstrated as potential indicators of the risk for hip fractures in elderly patients because they are easy to measure and can reflect bone metabolic status in real time. Bone turnover comprises two processes: bone formation of osteoblasts; and bone resorption of osteoclasts. During resorption, the components of bone tissue are metabolized and released into the bloodstream and urine. Osteoblasts then secrete small osteoid molecules to start the process of bone formation. The level of bone turnover activity can be assessed by measuring the concentration of such metabolites in the blood. [9] Beta-carboxy terminal telopeptide (β-CTX) is a special product of cathepsin K-mediated osteolysis and released during the direct digestion of bone with cathepsin K.[10] Osteocalcin is the most abundant non-collagen protein in bone matrix, and is secreted into the systemic circulation by osteoblasts during the process of bone formation. However, the half-life of osteocalcin is very short; as such, its degradation form, N-terminal/mid region (N-MID), is more clinically useful.[11] Higher levels of BTMs, particularly levels of resorption markers, are usually considered to be associated with increased fracture risk.[12, 13] Vitamin D (25[OH]D) status is also closely related to bone turnover.[14] Vitamin D deficiency may lead to secondary hyperparathyroidism, which accelerates bone remodeling and bone loss and subsequent increased fracture risk.[15] Many studies have determined that adequate vitamin D levels could prevent—or at least mitigate—the incidence of fractures.[16, 17] Although previous studies have confirmed many risk factors that are associated with the incidence of hip fractures in the elderly, but limited study has investigated the relationship between combined indicators and hip fractures in elderly women. The purpose of the present study, therefore, was to identify the independent indicators for elderly hip fractures first, and then combine them to evaluate their accuracy in the incidence of hip fractures in Chinese elderly women.

Methods
Subjects

The “Real World-based Evaluation and Optimization study on the treatment Management Model of elderly Hip Fractures” database was reviewed from November 24, 2017 to May 20, 2019. Inclusion criteria were as follows: age ≥ 65 years; hip fractures (including those of the femoral neck and the intertrochanter); those without metabolic-related diseases (including thyroid disease, renal insufficiency, diabetes); fractures caused by low-energy trauma (e.g., accidental falls); no history of hip fracture; and good levels of activity before fracture. Individuals who sustained high-energy injury (such as motor vehicle accidents), pathological fractures (i.e., those caused by tumors), supplementary history of calcium, vitamin D and anti-osteoporosis drugs, or a history of dementia or stroke, were excluded. Elderly patients (age ≥ 65 years) who presented to orthopedists for physical examination and fulfilled the inclusion criteria were included in the control group. Because there are no significant differences in BTMs among male patients among varying age groups, and BTMs in females increase with age, male patients were excluded from the present study. Ultimately, 90 female patients who sustained hip fractures were included in the case group and 110 female outpatients without hip fractures were included in the control group. All patients were educated about the purpose of the study and provided informed consent to participate. The study protocol was reviewed by the Ethics Committee of Shanghai Sixth People's Hospital (Shanghai, China; approval number, 2017 – 152), and successfully registered with the China Clinical Trial Center, registration number ChiCTR-ONC-17013389(Registered 15 November 2017, http://www.chictr.org.cn/edit.aspx?pid=22827&htm=4).

Assays

BTMs were measured the morning at fasting status after patients were admitted to hospital.[13, 19, 20] BTMs of control group were also measured at fasting status in the morning. BTMs selected in the present study included the bone resorption marker β-CTX and the bone formation marker N-MID. The active form of vitamin D (i.e., 1,25(OH)2D) is synthesized from 25(OH)D in the kidney. However, the half-life of 1,25(OH)2D is extremely short and is not suitable for assessing vitamin D status in the body.[21] Because 25(OH)D is believed to reflect the activity of 1,25(OH)2D, 25(OH)D was measured to represent vitamin D status in the body. Serum concentrations of β-CTX, N-MID and 25(OH)D were estimated using a commercially available electrochemiluminescence kit (E601, Roche Diagnostics, Basel, Switzerland).

Areal BMD of the lumbar spine and proximal femur were measured using dual-energy X-ray absorptiometry (Lunar Corp, Madison, WI, USA).

Statistical analysis

Data are expressed as mean and standard deviation (SD). First, however, data normality of each group was tested. The variables were then tested using the independent samples t-test or Mann–Whitney test, and qualitative data were compared using the chi-squared test. The paired t-test was performed on BMD data from the femoral neck and intertrochanteric region in patients with femoral neck or intertrochanteric fractures, and those in the control group. Spearman’s correlation analysis was then performed on the total
sample to analyze possible relationships between the variables. Logistics regression analysis was performed to determine independent risk factors (use BTMs, 25[OH]D and BMD as continuous variables). Finally, risk factors were analyzed using ROC curve analysis. The accuracy of each indicator was judged according to the AUC. The DeLong test was used to compare AUC values for the different variables. An evaluation model was then established by combining independent indicators in attempts to achieve better performance. Data analysis was performed using SPSS (IBM Corporation, Armonk, NY, USA) and MedCalc (MedCalc Software bv, Ostend, Belgium); differences with p < 0.05 were considered to be statistically significant.

**Results**

Demographic information for the case and control groups and baseline data of the test variables are summarized in Tables 1. Analysis revealed that individuals in the case (i.e., fracture) group were significantly taller than those in the control group (155.68 cm versus [vs.] 150.97 cm; p < 0.01). The mean level of 25(OH)D in the case group was significantly lower than in the control group (15.67 ng/ml vs. 29.53 ng/ml; p < 0.01). Regarding BTMs, the concentration of the osteoclast indicator β-CTX in the case group was significantly higher than in the control group (525.91 ng/L vs. 330.94 ng/L; p < 0.01). In terms of BMD and T-score, mean total hip BMD and femoral neck BMD of the case group were significantly lower than in the control group (0.662 g/cm² vs. 0.699 g/cm², p = 0.022 and 0.598 g/cm² vs. 0.637 g/cm², p < 0.01, respectively). T-scores for overall hip and femoral neck in the case group were also significantly lower than in the control group (-2.4 vs. -2.1, p = 0.012 and -2.6 vs. -2.3, p < 0.01, respectively). The chi-squared test revealed that the percentage of patients with vitamin D deficiency in the case group was significantly higher than that in control group (78.89% vs. 20.00%, p < 0.01). There were no significant differences between the case and control groups in terms of the osteoblast indicator N-MID, lumbar spine BMD, lumbar T-score, age, body weight, and body mass index (15.21 ng/ml vs. 14.47 ng/ml, p = 0.435; 0.831 g/cm² vs. 0.829 g/cm², p = 0.940; -2.3 vs. -2.2, p = 0.872; 78.73 vs. 78.09, p = 0.500; 54.04 kg vs. 52.79 kg, p = 0.340; and 22.29 kg/m² vs. 23.15 kg/m², p = 0.101, respectively).
| characteristic | Fracture group (N = 90) | Control group (N = 110) | P value |
|----------------|-------------------------|-------------------------|---------|
| Age (y)        | 78.73 (7.77)            | 78.09 (5.03)            | 0.50    |
| Height (cm)    | 155.68 (6.40)           | 150.97 (6.23)           | 0.01    |
| Weight (kg)    | 54.04 (8.65)            | 52.79 (9.66)            | 0.340   |
| BMI            | 22.29 (3.25)            | 23.15 (3.97)            | 0.101   |
| β-CTX (ng/L)   | 525.91 (307.38)         | 330.94 (289.71)         | 0.01    |
| N-MID (ng/ml)  | 15.21 (6.09)            | 14.47 (7.11)            | 0.435   |
| 25(OH)D (ng/ml)| 15.67 (7.23)            | 29.53 (10.57)           | 0.01    |
| ≥20 ng/ml      | 71 (78.89%)             | 22 (20.00%)             | 0.01    |
| ≥20 ng/ml      | 19 (21.11%)             | 88 (80.00%)             | 0.01    |
| Total hip BMD (g/cm²) | 0.662 (0.117)       | 0.699 (0.111)           | 0.022   |
| Femoral neck BMD (g/cm²) | 0.598 (0.106)       | 0.637 (0.100)           | 0.009   |
| Intertrochanteric BMD (g/cm²) | 0.506 (0.107)   | 0.518 (0.099)           | 0.01    |
| (N = 85)       | (N = 87)                |                        |         |
| Lumbar spine BMD (g/cm²) | 0.831 (0.148)      | 0.829 (0.183)           | 0.940   |
| Total hip T-score | -2.4 (0.91)         | -2.1 (0.87)             | 0.022   |
| Femoral neck T-score | -2.6 (0.82)         | -2.3 (0.80)             | 0.001   |
| Lumbar spine T-score | -2.3 (1.26)         | -2.2 (1.55)             | 0.872   |

The paired samples t-test revealed that BMD of the femoral neck in the femoral neck fracture group (0.601 g/cm² vs. 0.508 g/cm², p < 0.01), intertrochanteric fracture group (0.609 g/cm² vs. 0.511 g/cm², p < 0.01), and control group (0.640 g/cm² vs. 0.518 g/cm², p < 0.01) was always greater than that for the intertrochanteric region (Fig. 1).

Considering overall data of the case and control groups, Spearman correlation analysis revealed that 25(OH)D was significantly correlated with marker of bone resorption (β-CTX) (r = -0.425, p < 0.01), marker of bone formation (N-MID) (r = -0.237, r = 0.001), and overall hip (r = 0.189, p = 0.007) and femoral neck (r = 0.211, p = 0.003) BMD. Moreover, age was also significantly correlated with femoral neck (r = -0.303, p < 0.01) and total hip (r = -0.348, p < 0.01) BMD. In addition, there was also a significant correlation between
the osteoclast indicator $\beta$-CTX and osteoblast indicator N-MID ($r = 0.697$, $p < 0.01$), and total hip BMD ($r = -0.277$, $p < 0.01$) (Table 2).

| Variables | Age | $\beta$-CTX | N-MID | 25(OH)D | Femoral neck BMD | Total hip BMD | Lumbar spine BMD |
|-----------|-----|-------------|--------|---------|-----------------|--------------|-----------------|
| Age       | –   | 0.114       | 0.068  | -0.109  | -0.303**        | -0.348**     | -0.014          |
| $\beta$-CTX | 0.114 | –           | 0.697** | -0.425** | -0.072          | -0.219**     | -0.083          |
| N-MID     | 0.068 | 0.697**     | –      | -0.237** | -0.122          | -0.277**     | -0.122          |
| 25(OH)D   | -0.109 | -0.425**    | -0.237** | –       | 0.211**         | 0.189**      | -0.037          |
| Femoral neck BMD | -0.303** | -0.072    | -0.122 | 0.211** | –              | 0.798        | 0.551**         |
| Total hip BMD | -0.348** | -0.219** | -0.277** | 0.189** | 0.798**        | –            | 0.573**         |
| Lumbar spine BMD | -0.014 | -0.083    | -0.122 | -0.037 | 0.551**        | 0.573**      | –              |

The results of binary logistics regression revealed that 25(OH)D (crude odds ratio [OR] 0.838 [95% confidence interval 0.797–0.880]; $p < 0.01$), $\beta$-CTX (crude OR 1.002 [95% CI 1.001–1.003]; $p < 0.01$), femoral neck BMD (crude OR 0.025 [95% CI 0.001–0.421]; $p = 0.01$) and height (crude OR 1.127 [95% CI 1.072–1.186]; $p < 0.01$) were risk factors for hip fractures in elderly women. After adjustment for confounding factors, 25(OH)D (adjusted OR 0.837 [95% CI 0.790–0.886]; $p < 0.01$), femoral neck BMD (adjusted OR 0.009 [95% CI 0.000–0.969]; $p = 0.048$) and height (adjusted OR 1.207 [95% CI 1.116–1.306]; $p < 0.01$) remained risk factors for hip fractures in elderly women (Table 3).
Table 3
logistic regression of each indicator.

|                  | Model 1 (crude) | Model 2 (adjusted) |
|------------------|-----------------|--------------------|
|                  | OR (95% CI) P value | OR (95% CI) P value |
| Height βCTX      | 1.127 (1.072 ~ 1.186) P = 0.01 | 1.207 (1.116 ~ 1.306) P = 0.01 |
|                  | 1.002 (1.001 ~ 1.003) | 1.001 (1.000 ~ 1.002) |
| N-MID            | 1.017 (0.975 ~ 1.061) P = 0.435 | 0.948 (0.896 ~ 1.004) P = 0.068 |
| 25(OH)D          | 0.838 (0.797 ~ 0.880) P = 0.01 | 0.837 (0.790 ~ 0.886) P = 0.01 |
| Femoral neck BMD | 0.025 (0.001 ~ 0.421) P = 0.01 | 0.009 (0.000 ~ 0.969) P = 0.048 |

Finally, a novel evaluation model was established by combining independent indicators in attempt to achieve better performance (Model 1: 25(OH)D; Model 2: Femoral neck BMD; Model 3: Height; Model 4: 25(OH)D and height; Model 5: 25(OH)D and femoral neck BMD; Model 6: 25(OH)D, height and femoral neck BMD). ROC curve analysis was used to compare the accuracy of indicators in elderly women who sustained fractures, with AUCs for models 1, 2, 3, 4, 5 and 6 were 0.867, 0.586, 0.706, 0.898, 0.867 and 0.905 respectively (Table 4). The DeLong test revealed that the AUC for Model 1 was significantly greater than for Model 2 (p < 0.01) and Model 3 (p < 0.01). There was no significant difference in AUC between Model 2 and Model 3 (p = 0.06). AUC for Model 4 was significantly greater than for Model 1 (p = 0.02) and Model 5 (p = 0.03). There was no significant difference in AUC between Model 4 and Model 6 (p = 0.36) (Table 5). The cut-off value for 25(OH)D was calculated to be 19.21 ng/ml.
### Table 4
Correlation models of elderly hip fracture

| Model | Included indicators                | Sensitivity(%) | Specificity(%) | AUC(95%CI)          |
|-------|-----------------------------------|----------------|----------------|---------------------|
| 1     | 25(OH)D                           | 77.8           | 81.8           | 0.867(0.818–0.916)  |
| 2     | Femoral neck BMD                  | 53.3           | 63.6           | 0.586(0.507–0.665)  |
| 3     | Height                            | 63.3           | 71.8           | 0.706(0.633–0.778)  |
| 4     | 25(OH)D and height                | 86.7           | 78.2           | 0.898(0.856–0.940)  |
| 5     | 25(OH)D and Femoral neck BMD      | 70.0           | 88.2           | 0.867(0.818–0.916)  |
| 6     | 25(OH)D, height and Femoral neck BMD | 84.4           | 79.1           | 0.905(0.865–0.945)  |

### Table 5
Pairwise comparison of ROC curves

|                      | Z statistic | P value |
|----------------------|-------------|---------|
| Model 1 ~ Model 2    | 6.438       | <0.01   |
| Model 1 ~ Model 3    | 3.454       | <0.01   |
| Model 2 ~ Model 3    | 1.871       | 0.06    |
| Model 1 ~ Model 4    | 2.351       | 0.02    |
| Model 1 ~ Model 5    | 0.027       | 0.98    |
| Model 1 ~ Model 6    | 2.571       | <0.01   |
| Model 4 ~ Model 5    | 2.163       | 0.03    |
| Model 4 ~ Model 6    | 0.917       | 0.36    |
| Model 5 ~ Model 6    | 2.611       | <0.01   |

**Abbreviations:** AUC, area under the curve; β-CTX, C-terminal telopeptide of type-1 collagen; N-MID, N-MID fragment. Model 1: 25(OH)D; Model 2: Femoral neck BMD; Model 3: Height; Model 4: 25(OH)D and Height; Model 5: 25(OH)D and Femoral neck BMD; Model 6: 25(OH)D, Height and Femoral neck BMD.
Discussion

BMD has long been considered to be an important indicator of hip fracture risk in elderly women. The present study demonstrated that total hip BMD, femoral neck BMD, and corresponding T-score in elderly women with hip fractures were significantly lower than those in the control group, while no significant difference was detected in lumbar BMD, which is consistent with previous meta-analysis.\(^\text{22}\) This indicated that, in elderly women who sustained hip fractures, BMD of the hip was significantly reduced, which in turn, led to a predisposition to hip fractures.\(^\text{23}\) Therefore, it is necessary to devote close attention to the local changes in hip BMD in elderly women, which may prevent or, at least mitigate, the occurrence of hip fractures in the elderly. However, it is less likely to be associated with the exact type of hip fractures because BMD of the intertrochanteric region was always significantly lower than that of the femoral neck in all three groups (i.e., femoral neck, intertrochanter, and control).

Controversy, however, persists about whether BTMs are associated with hip fractures in the elderly.\(^\text{13, 24–30}\) The reasons for this controversy may be attributed to study design (i.e., prospective or retrospective), sample size, differences in metabolic indices selected, and whether a sufficient number of confounding factors of bone metabolism have been taken into account. As a blood-based biochemical index, BTMs can be affected by many factors including age, sex, drug use, metabolic disease, circadian rhythm, and exercise level, among others. Results of the present study revealed that neither β-CTX nor N-MID was related to the incidence of hip fractures in the elderly after adjustment for confounding factors, which is consistent with previous prospective study.\(^\text{26}\) However, our result was inconsistent with that of Fan et al.\(^\text{24}\) One possible reason for the differences may be the sampling time. In our patients, blood samples were all obtained on the next morning at fasting status after fractures, while theirs were collected within one week after admission in the study by Fan.\(^\text{24}\) As time progresses, the impact of fracture on bone turnover is increasingly obvious.\(^\text{19}\) Therefore, the concentration of BTMs may be severely affected by fracture status, which would lead to an acceleration in the bone turnover process, resulting in an increase in β-CTX and N-MID levels. Our results do not support the use of β-CTX and N-MID as independent risk factors in elderly hip fractures.

Vitamin D deficiency is very common in postmenopausal women. Vitamin D status can be classified as deficient (< 20 ng/ml), insufficient (20–30 ng/ml) or sufficient (≥ 30 ng/ml) according to serum 25(OH)D concentration.\(^\text{31}\) The present study demonstrated that of 25(OH)D levels in the case group were significantly lower than those in the control group, which suggests that 25(OH)D level is also associated with hip fractures in elderly women.\(^\text{21, 24, 32, 33}\) In addition, the AUC for 25(OH)D was significantly higher than that of femoral neck BMD and height, indicating that 25(OH)D may be a more dependable and effective indicator in the assessment of hip fractures in elderly Chinese women. In our present study, we selected participants with age paired to eliminate the impact of age on each indicator. We found that height of people in case group was significantly taller than that in control group, and weight was similar between groups, which is consistent with previous study.\(^\text{34}\) The association between body height and elderly hip fractures may be due to the risk of hip fracture was increased by the great potential energy of the fall.\(^\text{35}\) Furthermore, femoral moment arm of a taller person is greater than that of a shorter person,
which might result in less force needed to break the hip. When we combined independent indicators in attempts to achieve better evaluative power, we found that accuracy was significantly improved when 25(OH)D was combined with height. Based on the indicators we studied, Combined indicator of 25(OH)D and height were more reliable than other combinations in assessing the risk of hip fractures in elderly women.

The relationship between vitamin D and BTMs or vitamin D and BMD has been explored in many studies. Spearman correlation analysis was used because some variables in the present study (e.g., β-CTX) were not normally distributed. The results revealed that 25(OH)D was negatively correlated with β-CTX and N-MID, which suggests that 25(OH)D levels could affect the levels of relevant BTMs. In addition, the present study also found that 25(OH)D was positively correlated with total hip and femoral neck BMD, which is consistent with previous studies. These results demonstrated that 25(OH)D is more associated with hip fractures in the elderly women. However, Garnero et al. and Seamans et al. found no correlation between vitamin D levels and BTMs in their research. This can partially be explained by racial differences in vitamin D status. In a study investigating vitamin D status among Chinese, Indians, and Malays living in Malaysia, researchers found that Malays and Indians are more vulnerable to vitamin D deficiency than the Chinese, which is possibly because darker-skinned individuals require more sunlight to synthesize vitamin D in the skin. The study subjects in the present study were all elderly Chinese women, which is completely different from that in the studies by Garnero et al. and Seamans et al. Therefore, further studies are needed to explore the actual relationship between vitamin D and BTMs (i.e., vitamin D and BMD) in different ethnic groups.

The aim of the present study was to compare the accuracy of combined independent risk factors in assessing the risk for hip fractures in elderly women. Here, we presented indicators associated with elderly hip fractures and established an evaluation model combined independent indicators. According to the evidenced-based evaluation model, model including 25(OH)D and height may be clinically useful in the assessment of elderly hip fractures even without BMD of hip. Strengths included the fact that indicators were measured within 24 h after fractures to eliminate the possible impact of fracture on each indicator. Different from previous research, our group took into account a large number of factors affecting the accuracy of BTM measurement (see the “Subjects” section for details). Limitations of this study include those inherent to cross-sectional study designs and the relatively small sample size. Furthermore, parathyroid hormone, which may affect the status of 25(OH)D, was not taken into account in the present study. Therefore, larger, multicenter studies including individuals of different ethnicities are necessary to confirm our results.

Conclusion

Based on the results of the present study, BMD of the hip in elderly women with hip fractures was significantly lower than that of control patients without hip fracture, while no significant difference about lumbar spine BMD was found between them. 25(OH)D, femoral neck BMD and height were associated with the occurrence of hip fractures in elderly women, and model including 25(OH)D and height were
more reliable than other combinations in the assessment of elderly hip fractures even without total hip BMD. β-CTX and N-MID proved not to be independent risk factors for hip fractures in elderly women. The relationship between vitamin D and BTMs is still controversial, further studies are needed to explore the actual relationship in different ethnic groups.

**Abbreviations**

**BMD**
Bone mineral density

**BTMs**
Bone turnover markers

**β-CTX**
Beta-carboxy terminal telopeptide

**N-MID**
N-terminal/mid region

**AUC**
Area under the ROC curve

**SD**
standard deviation

**vs.**
versus

**Declarations**

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**Author information**

Jinhui Zhao and Huipeng Shi are co-first authors.
Affiliations

Department of Orthopedic Surgery, Shanghai Jiaotong University Affiliated Sixth People's Hospital, Shanghai, 200233, P.R.China.

Jinhui Zhao, Huipeng Shi, Dajun Jiang, Lingtian Wang, Shengbao Chen and Weitao Jia

Authors’ contributions

Jinhui Zhao and Huipeng Shi searched the literature, performed the statistical analysis, drafted the manuscript. Weitao Jia and Shengbao Chen conceived of the study, participated in the entire process of drafting and revised the manuscript. Dajun Jiang and Lingtian Wang contributed to data collection and revisions of the manuscript. All authors have contributed significantly. All authors read and approved the final manuscript.

Corresponding author

Weitao Jia and Shengbao Chen are corresponding co-authors.

Ethics declarations

Ethics approval and consent to participate

The study protocol was reviewed by the Ethics Committee of Shanghai Sixth People’s Hospital (Shanghai, China; approval number, 2017-152).

Consent for publication

Written informed consent for publication was obtained from all participants.

Competing interests

The author reports no conflicts of interest in this work.
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**Figure 1**

Paired t test between BMD of femoral neck and BMD of intertrochanteric region in different groups.

Notes: *p<0.01; FNF: Femoral neck fracture; ITF: Intertrochanteric fracture; CG: Control group.