


## CLINICAL ARTICLE

# Evaluation of Serum 25-Hydroxyvitamin D<sub>3</sub> and Bone Mineral Density in 268 Patients with Hip Fractures

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**Objective:** The aim of the present study was to evaluate the relationship among vitamin D nutritional status, bone mineral density, and other factors in elderly patients with brittle hip fractures.

**Methods:** The present study was a retrospective analysis of 268 patients, 102 men (38.06%) and 166 women (61.94%), with brittle hip fractures admitted to the Hip Joint Center of Tianjin Hospital from February 2016 to June 2018. The median age of the patients was 74 years (range, 50–93 years). The patients were divided into three groups based on age: ≤69 years, 70–79 years, and ≥80 years. Serum 25-hydroxyvitamin D<sub>3</sub> (25(OH)D<sub>3</sub>), parathyroid hormone (PTH), body mass index (BMI), and bone mineral density (BMD) of the lumbar spine, femoral neck, and hip were measured and statistically analyzed.

**Results:** The median serum 25(OH)D<sub>3</sub> level of patients was 9.90 (range, 2.60–42.70) ng/mL; the proportion of deficiency was 89.18% and the deficiency was severe in 136 cases (49.25%). The proportion of vitamin D deficiency was significantly lower in men than in women ( $P = 0.013$ ). With the increase of age, 25(OH)D<sub>3</sub> levels gradually decreased ( $P = 0.044$ ) and PTH levels gradually increased ( $P < 0.001$ ). There was significantly negative correlation ( $P < 0.001$ ) between the levels of serum 25(OH)D<sub>3</sub> and PTH. There were 200 cases (74.63%) in which *T-values* of BMD were less than  $-2.5$  in any part of the lumbar vertebrae, femoral neck, and hip. *T-values* in 74 cases (27.61%) were less than  $-2.5$  in all three parts. The *T-values* of BMD in men were significantly higher than those in women ( $P < 0.001$ ). With the increase of age, the femoral neck BMD in men gradually decreased ( $P = 0.016$ ), and the femoral neck and hip BMD in female gradually decreased ( $P$ -value was 0.001 and 0.003, respectively). Multivariate analysis suggested that gender and BMI were independent risk factors for BMD, and vitamin D deficiency affected BMD.

**Conclusion:** Vitamin D deficiency is common in patients with brittle hip fractures, especially in women. With the increase of age, vitamin D continues to decrease and PTH increases. The decrease of BMD in patients with hip fractures is the result of a combination of age, gender, BMI, and vitamin D content.

**Key words:** 25-hydroxyvitamin D<sub>3</sub>; parathyroid hormone; bone mineral density; hip fracture

## Introduction

The number of osteoporotic patients in China, which is now an aging society, is increasing year by year. Osteoporosis is characterized by a breakdown in the micro-architectural structure of bone, which leads to decreased bone mass and, subsequently, increased bone fragility and fracture risk. Hip fracture is a serious threat to the physical

and mental health of elderly patients. It has been estimated that one-fifth of men and one-third of women over the age of 50 years will sustain a major fragility fracture through their remaining lifetime. Among such patients, 25% have to spend time in a nursing home following the fracture and 50% of patients never reach their pre-fracture activity levels. Many countries have classified such fractures and the

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associated dysfunction as significant public issues, and the personal and societal costs of treatment are increasing.

Serum markers, including magnesium (Mg), copper, iron, and vitamins, are potential risk factors associated with the incidence of osteoporotic fractures in the elderly. Vitamin D plays an important role in increasing the intestinal absorption of calcium (Ca) and phosphorus (P) and, thus, helps to maintain a healthy musculoskeletal system. Serum 25-hydroxyvitamin D (25(OH)D) is recognized as the main circulating form of vitamin D; it accurately indicates the vitamin D concentration in the body. Gorter *et al.*<sup>1</sup> found that insufficiency and deficiency of vitamin D accounted for a considerable proportion of elderly patients with osteoporotic fractures, but information on this aspect is relatively lacking for Chinese patients. To investigate the relationship between vitamin D nutritional status and bone mineral density in elderly populations, 268 patients with brittle hip fractures in the Tianjin area were retrospectively analyzed. In these patients, the present study explores: (i) the vitamin D nutritional status; (ii) bone mineral density; and (iii) other influencing factors.

## Materials and Methods

### Demographic

A total of 268 hip fracture patients admitted to the Tianjin Hospital Hip Center were enrolled in this study from February 2016 to June 2018. All patients were of Han ethnicity and had lived in Tianjin for at least 10 years. The exclusion criteria were: (i) patients with chronic liver disease, renal insufficiency, malignant tumors, active rheumatic immune disease, active tuberculosis, thyroid and parathyroid disease, Parkinson's disease, and other metabolic bone diseases; (ii) patients with a history of surgery or disease that might cause vitamin D deficiency, including postoperative gastrectomy, postoperative bowel resection, gastrointestinal spasm, and inflammatory bowel disease; and (iii) patients who had undergone systematic anti-osteoporosis treatment before admission, including oral vitamin D, Ca tablets, and diphosphate drugs.

The median age of patients was 74 years (range, 50–93 years), including 102 men (38.06%) and 166 women (61.94%), who were postmenopausal. All patients were admitted to hospital within 24 h of the fall (non-car accident); there were 165 cases of femoral neck fractures (61.57%) and 103 cases of intertrochanteric fractures (38.43%). The following data were collected after admission: gender, age, height, weight, and body mass index (BMI). There was no significant difference in the basic clinical characteristics between male and female patients (Table 1). Patients were then divided into groups according to gender (male and female) or age ( $\leq 69$  years, 70–79 years, and  $\geq 80$  years old). Parameters were compared between groups, including 25(OH)D<sub>3</sub>, parathyroid hormone (PTH), incidence of vitamin D deficiency, and BMD. Furthermore, factors

related to vitamin D deficiency were analyzed in the current study.

### Research Methods

The patients were enrolled at the hospital early in the morning to collect fasting blood samples.

### Detection of Serum 25-Hydroxyvitamin D<sub>3</sub>

Vitamin D is a fat-soluble essential vitamin. Adequate vitamin D increases intestinal Ca absorption, promotes bone mineralization, maintains muscle strength, improves balance, and reduces the risk of fall. The serum levels of 25(OH)D<sub>3</sub> were measured using a 25-hydroxy vitamin D sample release agent kit (Guangzhou Golden Field Biotechnology) with an AB high performance liquid chromatography-tandem mass spectrometer (MPX-API 4000, Roche Molecular Systems, Switzerland) detection. Patients were divided into groups based on 25(OH) D<sub>3</sub> level: (i) vitamin D was sufficient, 25(OH) D<sub>3</sub>  $\geq 30$  ng/mL; (ii) vitamin D was insufficient, 20 ng/mL  $\leq$  25(OH) D<sub>3</sub>  $< 30$  ng/mL; and (iii) vitamin D was deficient, 25(OH) D<sub>3</sub>  $< 20$  ng/mL. If 25(OH) D<sub>3</sub>  $< 10$  ng/mL, there was a serious deficiency of vitamin D<sup>2, 3</sup>.

### Detection of Serum Parathyroid Hormone

The main effect of PTH is to increase the activity and number of osteoclasts; it increases blood calcium and promotes absorption of intestinal Ca and P. It was measured using a Roche parathyroid hormone detection kit (Mannheim, Germany).

### Detection of Serum Calcium, Phosphorus, and Magnesium

Calcium and phosphorus are important components of the human body; they are stored in bone and regulated by PTH and vitamin D. One of the physiological functions of Mg is maintaining bone growth and neuromuscular excitability. It is an essential mineral element in the human body, with 60%–65% of the body's Mg existing in bone. These electrolytes were measured. Detection was conducted using Siemens ADVIA2400 automatic biochemical analyzer (Vital Scientific B.V., Holland).

### Measurement of Bone Mineral Density

Bone mineral density is an important index of bone strength, which reflects the degree of osteoporosis. BMD in the lumbar spine, the contralateral femoral neck, and hip were measured using dual-energy X-ray absorptiometry (Hologic Discovery A, USA). According to the guidelines for the diagnosis and treatment of osteoporosis in China<sup>4</sup> and the World Health Organization diagnostic criteria<sup>5</sup>, a T-value  $\leq -2.5$  was defined as osteoporosis,  $-2.5 < \text{T-value} < -1.0$  as bone loss, and T-value  $\geq -1.0$  as normal bone mass.

### Statistical Analysis

The data were analyzed and processed using SPSS 21.0 statistical software. The measurement data were presented as

**TABLE 1** Characteristics of patients

Characteristics	Male (102 cases)	Female (166 cases)	P-value
Age [years, M (range)]	74.5 (50–92)	73 (54–93)	0.161
BMI ( $\bar{x} \pm s$ , kg/m <sup>2</sup> )	23.51 $\pm$ 3.79	23.09 $\pm$ 3.39	0.346
Comorbidity			
None	54 (20.15%)	108 (40.30%)	0.070
One kind of disease	27 (10.07%)	26 (9.70%)	
$\geq 2$ kinds of disease	21 (7.84%)	32 (11.94%)	
Type of fracture			
Femoral neck	69 (25.75%)	96 (35.82%)	0.109
Trochanteric fracture	33 (12.31%)	70 (26.12%)	

mean  $\pm$  SD or median after the normality test and the enumeration data were presented by rate (%). For the normal distribution and variance homogeneity measurement data, the parameter test was used. The two groups of measurement data were compared by *t*-test, including BMI, serum levels of P, and BMD T-values between male and female patient groups. The three age groups and the abovementioned potential risk factors were compared by one-way analysis of variance, including the serum levels of P and BMD T-values among different age groups; the non-normal distribution measurement data was analyzed by Mann–Whitney *U*-test (age, serum levels of 25(OH) D<sub>3</sub>, PTH, Ca, and Mg) and Kruskal–Wallis test (the three age groups, the abovementioned potential risk factors, and serum PTH levels between different age groups).  $\chi^2$ -tests were used to compare the incidence of vitamin D deficiency between different groups. The correlation between variables was analyzed by Spearman correlation. The risk factors in the univariate analysis ( $P < 0.2$ ) were included in the logistic regression model for the multivariate analysis.  $P < 0.05$  was considered statistically significant difference. The whole process of the research is presented in Fig. 1.

## Results

### Serum 25-hydroxyvitamin D<sub>3</sub> Outcomes

The median serum 25(OH)D<sub>3</sub> of 268 patients was 9.90 (2.60–42.70) ng/mL. According to the grading criteria, only 3 patients (1.12%) had adequate vitamin D; 25 patients (9.70%) had insufficient vitamin D. There was a lack of vitamin D in 240 cases (89.18%), of which 136 cases (49.25%) were severely deficient. Table 2 and Fig. 2 showed that the median serum 25(OH)D<sub>3</sub> in male patients was 9.80 (3.10–38.90) ng/mL and 9.90 (2.60–42.70) ng/mL in female patients. There was no significant difference between the two groups ( $P = 0.328$ ). There were 85 cases (83.33%) with vitamin D deficiency in the male group. The incidence was significantly higher in the female group (155 cases, 93.37%) ( $P = 0.013$ ). With the increase in age, the serum vitamin D levels of the three groups gradually decreased. The difference was statistically significant ( $P = 0.044$ ). The serum 25(OH)D<sub>3</sub> level of patients aged  $\leq 69$  years was significantly

higher than that of the  $\geq 80$ -year-old group ( $P < 0.05$ ) (Table 3 and Fig. 3). The incidences of vitamin D deficiency in each age group were 88.51%, 87.25%, and 92.41%, respectively; no statistically significant difference was detected ( $P = 0.526$ ).

### Parathyroid Hormone Outcomes

The median PTH of this group was 51.00 (15.7–323.9) pg/mL. There was no significant difference between men and women (see Table 2 and Fig. 2,  $P = 0.485$ ). With the increase of age, the PTH level of patients gradually increased, and the difference between the groups was statistically significant ( $P < 0.001$ ) (Table 3 and Fig. 3). Correlation analysis suggested that there was a significant negative correlation between 25(OH)D<sub>3</sub> and PTH levels ( $r = -0.310$ ,  $P < 0.001$ ).

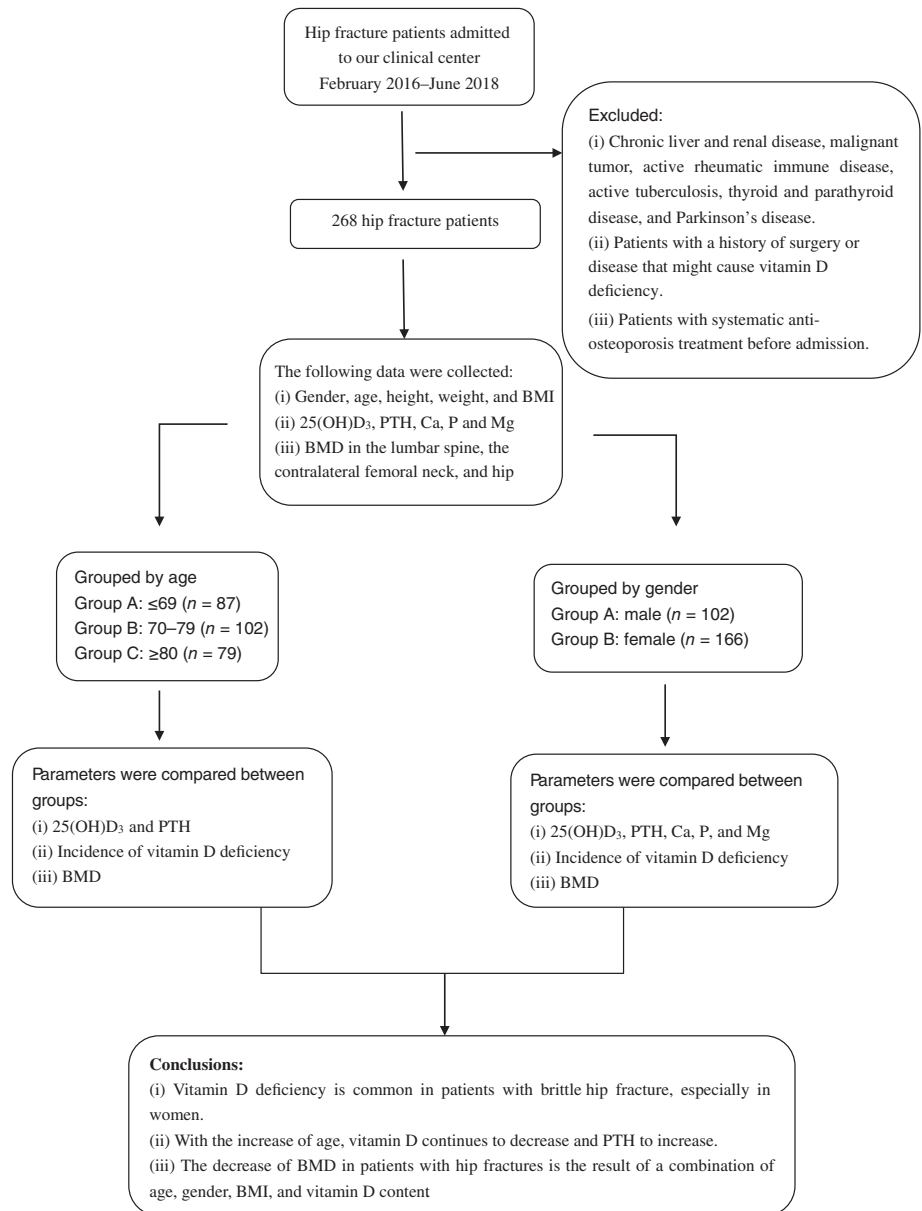
### Calcium, Phosphorus, and Magnesium Outcomes

The expression of serum phosphorus was  $0.96 \pm 0.20$  mmol/L in the male group and  $1.04 \pm 0.19$  mmol/L in the female group. The difference was significant ( $P = 0.001$ ). There was no significant difference in Ca and Mg content between men and women (see Table 2 and Fig. 2).

### Bone Mineral Density Detection

Only 4 cases (1.49%) had normal bone mass in the lumbar spine, the contralateral femoral neck, and the hip. There were 64 patients (23.88%) with reduced bone mass in any part of the patient; 200 patients (74.63%) had BMD T-values less than  $-2.5$  in any part, including 74 patients (27.61%; 12 men and 62 women) whose T-values were  $\leq -2.5$  in all three parts. The T-values of lumbar spine, contralateral femoral neck, and hip BMD in men were  $-1.70 \pm 1.24$ ,  $-2.39 \pm 0.65$ , and  $-1.73 \pm 0.77$ , respectively. The T-values of these locations in women were, respectively,  $-2.67 \pm 1.29$ ,  $-3.01 \pm 0.82$ , and  $-2.44 \pm 0.94$ . The T-values of BMD in men were significantly higher than those in women ( $P < 0.001$ ) (see Fig. 4).

There was no significant difference in BMD between lumbar vertebrae and hip in all age groups ( $P = 0.501$  and  $0.063$ , respectively). The T-values of femoral neck BMD in



**Fig 1** Patient flow diagram. Process of the research. 25(OH) D<sub>3</sub>, serum 25-hydroxyvitamin D<sub>3</sub>; BMD, bone mineral density; BMI, body mass index; Ca, calcium; Mg, magnesium; P, phosphorus; PTH, parathyroid hormone.

the three groups were  $-2.39 \pm 0.56$ ,  $-2.18 \pm 0.68$ , and  $-2.62 \pm 0.62$ , respectively, and the difference was statistically significant ( $P = 0.016$ ). The femoral neck BMD in the 70–79-year-old group was significantly higher than that in

the  $\geq 80$ -year-old group ( $P < 0.05$ ) (see Table 4 and Fig. 5). Female patients were divided into the same three groups. There was no significant difference in lumbar spine BMD among the age groups ( $P = 0.700$ ). The BMD of the femoral

**TABLE 2** Results of examination in men and women

Index	Male (102 cases)	Female (166 cases)	P-value
25 (OH)D <sub>3</sub> (M [range], ng/mL)	9.80 (3.10–38.90)	9.90 (2.60–42.70)	0.328
PTH (M [range], pg/mL)	50.25 (13.20–174.60)	51.50 (15.7–323.9)	0.485
Ca (M [range], mmol/L)	2.23 (1.96–2.99)	2.27 (1.89–2.82)	0.061
P ( $\bar{x} \pm s$ , mmol/L)	$0.96 \pm 0.20$	$1.04 \pm 0.19$	0.001
Mg (M [range], mmol/L)	0.87 (0.65–1.03)	0.88 (0.65–1.14)	0.415

PTH, parathyroid hormone; Ca, calcium; P, phosphorus; Mg, magnesium.

**TABLE 3** Relationship between age and levels of serum 25-hydroxyvitamin D<sub>3</sub> (25(OH)D) and parathyroid hormone (PTH) in serum

Groups	Cases	25(OH)D <sub>3</sub> (ng/mL)	PTH (pg/mL)
≤69 years	87	12.20 (2.60–38.90) <sup>a</sup>	44.80 (13.2–174.60)
70–79 years	102	9.65 (3.10–28.80)	49.75 (13.80–219.80)
≥80 years	79	8.70 (3.30–42.70)	65.65 (24.80–323.90)
<i>P</i> value		0.044	<0.001

<sup>a</sup> Compared with ≥80 years group, *P* < 0.05.

neck and hip showed a decreasing trend with age, and the difference was statistically significant (*P* = 0.001 and 0.003, respectively) (Table 4 and Fig. 6).

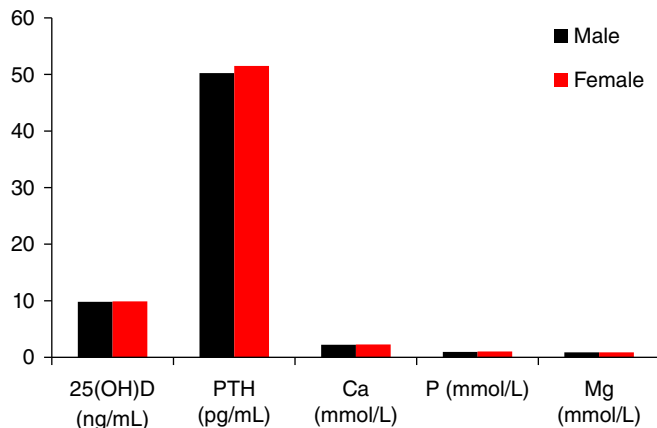
#### Analysis of Risk Factors Related to Bone Mineral Density

In the correlation analysis, decreased BMD (T-value ≤ -2.5) in any location (the lumbar vertebrae, femoral neck, and hip) was correlated with gender (*r* = 0.285, *P* < 0.001), 25(OH)D<sub>3</sub> level (*r* = -0.138, *P* = 0.023), and BMI (*r* = -0.323, *P* < 0.001). In the univariate analysis, the gender (*P* < 0.001), decreased serum 25(OH)D<sub>3</sub> level (*P* = 0.024), and BMI < 24 kg/m<sup>2</sup> (*P* < 0.001) were risk factors for reduced BMD, with T-value ≤ -2.5 in any of the lumbar vertebrae, femoral neck, and hip as a dependent variable. BMD decreased with age, but the difference was not statistically significant (*P* = 0.146). The variables with *P* < 0.2 were included in the multivariate logistic regression model (using forward LR); only the gender (OR = 0.249, 95% CI 0.137–0.454, *P* < 0.001) and BMI (OR = 3.358, 95% CI 1.838 to 6.134, *P* < 0.001) were independent risk factors for reduced BMD.

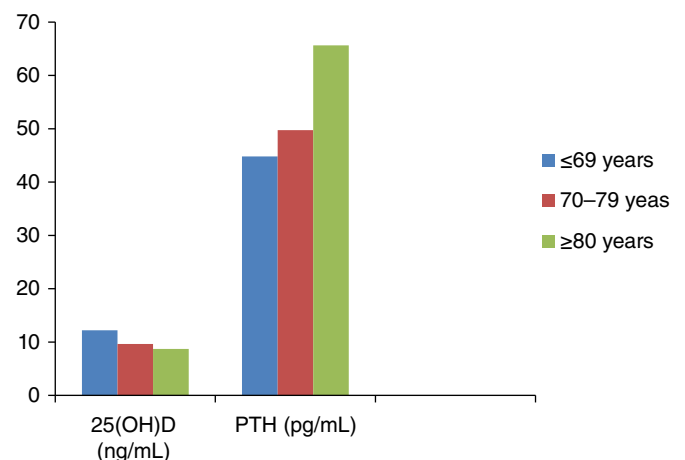
#### Discussion

##### Status of Vitamin D in Patients with Hip Osteoporosis Fractures

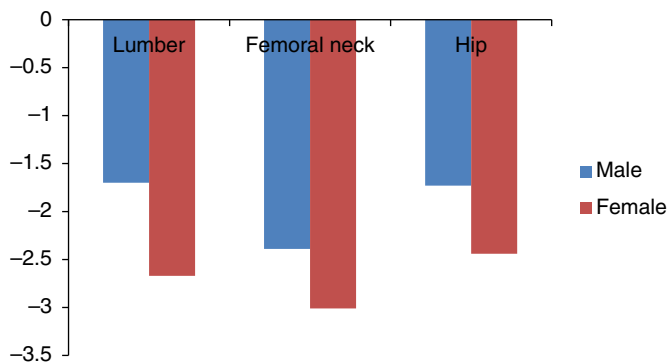
Since the 1980s, with the increasing aging of China's population, the prevalence of osteoporosis in people over 60 years of age has increased significantly<sup>6</sup>. The main cause of senile osteoporosis is the negative balance of bone formation and absorption resulting from decreased hormone levels and inflammatory factors. In addition, the elderly commonly have insufficient nutritional intake, reduced physical activity, and vitamin D deficiency, aggravating the progression of osteoporosis<sup>7, 8</sup>. According to Takiar *et al.*, approximately 1 billion people in the world have a vitamin D deficiency<sup>9</sup>. The third US Health and Nutrition Survey, in 2005, found that 41% of men and 53% of women were lacking in vitamin D<sup>10</sup>. What about vitamin D deficiency in patients with osteoporotic fractures? A group of fracture patients who underwent conservative treatment were studied by Gorter *et al.*<sup>1</sup>; vitamin D levels in 71% of the patients were abnormal, of which 40% were lacking in vitamin D and 11% were severely deficient in vitamin D. Hwang *et al.*<sup>11</sup> found that 86.6% of Taiwanese menopausal women with hip fractures were vitamin D deficient. Other scholars have revealed that 60% of



**Fig 2** Results of examination in men and women. 25(OH) D<sub>3</sub>, serum 25-hydroxyvitamin D<sub>3</sub>; Ca, calcium; Mg, magnesium; P, phosphorus; PTH, parathyroid hormone.



**Fig 3** Levels of 25(OH)D<sub>3</sub> and parathyroid hormone (PTH) in serum in three age groups.



**Fig 4** T-values of bone mineral density of lumbar spine, contralateral femoral neck, and hip in male and female groups.

patients with hip fractures have reduced vitamin D levels<sup>12-14</sup>.

This study included patients with a median age of 74 years, who were at high-risk of osteoporosis. The median serum 25(OH)D<sub>3</sub> level was only 9.90 ng/mL, significantly lower than the normal minimum limit of 30 ng/mL, and the proportion with normal vitamin D was only 1.12%. The incidence of vitamin D deficiency in our study was up to 89.18%, which indicated that vitamin D deficiency was commonly observed in elderly people in the Tianjin region. The serum vitamin D levels in such patients were significantly reduced, which patients and doctors must pay attention to.

#### Factors Related to Vitamin D Deficiency

In this study, patients were grouped according to age. Serum 25(OH)D<sub>3</sub> levels gradually decreased with age ( $P = 0.044$ ) and the proportion of vitamin D deficiency increased with age. This showed that the decrease of vitamin D was a manifestation of human aging. In addition, the proportion of men with a vitamin D deficiency was significantly lower than that of women ( $P = 0.013$ ), which might be related to the congenital differences between genders or certain acquired factors. In addition to confirming the above factors, Dam *et al.*<sup>15</sup> found that 25(OH)D<sub>3</sub> levels decreased in high BMI and heavy drinkers.

Bischoff-Ferrari<sup>16</sup> found that vitamin D levels in hip fracture patients were also related to the season and living environment: they were low in spring, highest in summer, highest at home, and lowest in nursing homes in Switzerland. In summary, the reduction of vitamin D levels in patients is caused by a combination of factors, such as age and gender, and external factors, such as diet, activity range, and living environment.

#### Relationship between Vitamin D and Parathyroid Hormone Content

Vitamin D synthesis and metabolism are associated with the dynamic balance of Ca and are regulated by PTH, serum Ca, and P levels. When hypocalcemia occurs, the concentration of PTH in the serum increases, and Ca resorption is enhanced<sup>11, 17</sup>. In this study, the PTH level gradually increased with age ( $P < 0.001$ ), while the 25(OH)D<sub>3</sub> level was negatively correlated with PTH ( $r = -0.310$ ,  $P < 0.001$ ), which was similar to the results of Marco *et al.*<sup>17</sup> Although PTH levels were elevated, only 86 patients (32.09%) had PTH values above the upper limit of normal (76.8 pg/mL), consistent with previous studies<sup>18</sup>. Monaco *et al.*<sup>19</sup> also found 148 patients (37%) with secondary PTH elevation in 405 hip patients studied; 63% had severe vitamin D deficiency, but PTH was within the normal range. He believed that it might play an important role in the consumption of Mg, because in addition to inhibiting PTH activity, Mg could reduce PTH secretion. According to some studies, Mg deficiency and decreased renal function could elevate serum PTH<sup>20, 21</sup>.

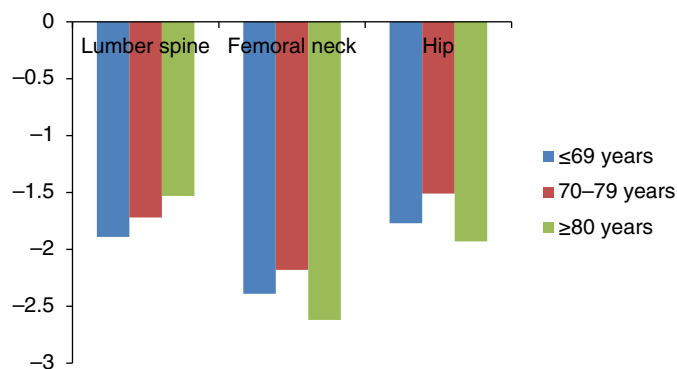
#### Harm of Vitamin D Deficiency

The main physiological function of Vitamin D is to regulate Ca and P metabolism and bone formation in the human body. It also has the effect of increasing muscle strength and maintaining neuromuscular coordination. Korean scholars<sup>11, 22</sup> demonstrated that vitamin D effects on muscle function included: one human muscle tissue containing vitamin D receptor, through which vitamin D affected muscle function by the genome path; and vitamin D deficiency could cause type 2 muscle fiber atrophy. In their study, vitamin D supplementation significantly improved grip, independent of

**TABLE 4** Relationship between age and BMD for three parts in male and female groups

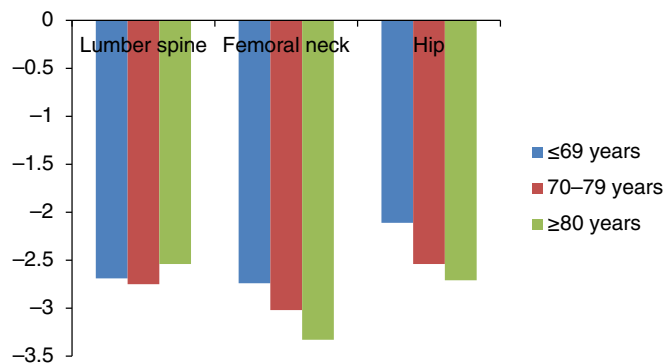
Groups	T-value of male BMD			T-value of female BMD		
	Lumber spine	Femoral neck	Hip	Lumber spine	Femoral neck	Hip
≤69 years	-1.89 ± 1.25	-2.39 ± 0.56	-1.77 ± 0.69	-2.69 ± 1.27	-2.74 ± 0.80 <sup>a</sup>	-2.11 ± 0.87
70-79 years	-1.72 ± 1.20	-2.18 ± 0.68 <sup>a</sup>	-1.51 ± 0.86	-2.75 ± 1.21	-3.02 ± 0.77 <sup>a</sup>	-2.54 ± 0.94 <sup>b</sup>
≥80 years	-1.53 ± 1.23	-2.62 ± 0.62	-1.93 ± 0.67	-2.54 ± 1.39	-3.33 ± 0.79	-2.71 ± 0.88 <sup>b</sup>
P-value	0.501	0.016	0.063	0.700	0.001	0.003

<sup>a</sup> Compared with ≥80 years,  $P < 0.05$ .; <sup>b</sup> Compared with ≤69 years,  $P < 0.05$ .  
BMD, bone mineral density.



**Fig 5** T-values of male bone mineral density for three parts in three age groups.

vitamin D levels. Snijder, in a prospective study, and others<sup>8, 20, 23, 24</sup> confirmed that when 25(OH)D<sub>3</sub> was less than 10 ng/L, the risk of falls increased in 65–75 year olds. According to Monaco *et al.*<sup>25</sup>, secondary high PTH caused by vitamin D reduction could damage bone tissue and reduce muscle mass and muscle function in the elderly, leading to the risk of falling and increased fracture probability, which could be independent of 25-hydroxyvitamin D. For patients with hip fractures, Carpintero *et al.*<sup>26, 14</sup> found that 1,25-dihydroxycholecalciferol levels were associated with all biochemical nutritional indicators (albumin, prealbumin, transferrin, and cholesterol). A reduction of these indicators could significantly predict the high rate of disability and mortality in patients with hip fractures and was also related to the degree of functional recovery at 1 year. Mak *et al.*<sup>27</sup> and Warner *et al.*<sup>28</sup> found that a decrease of vitamin D in elderly fracture patients could lead to weakened proximal muscle strength, pain, decreased dynamic balance, decreased speed of movement, and poor quality of life. Based on these mechanisms, deficiency of vitamin D (in nearly 90% of patients in this study) was one of the main reasons for hip fracture.



**Fig 6** T-values of female bone mineral density for three parts in three age groups.

### Relationship among Vitamin D, Parathyroid Hormone Levels, and Bone Mineral Density

In this study, the BMD of the lumbar vertebrae, femoral neck, and hip were measured. The results showed that the portion with T-value  $\leq -2.5$  of any location accounted for 74.63%, and T-value  $\leq -2.5$  of all parts accounted for 27.61%, which indicated that the patient's osteoporosis was extremely serious. Logistic multivariate analysis in this study revealed that gender and BMI were independent risk factors for BMD. Compared with men, the T-values of BMD in all parts of women were significantly lower, which was related to the decrease of estrogen, a hormone that inhibits osteoclast, in postmenopausal women<sup>16, 19</sup>. It might also be related to the lower proportion of vitamin D deficiency in men than in women. The correlation analysis of this study suggested that 25(OH)D<sub>3</sub> levels had an effect on BMD. The vitamin D content decreased with age, and the BMD of male and female hip and femur neck also showed a significant downward trend. The effect of PTH on bone density remains controversial. Monaco *et al.*<sup>19</sup> found that BMD values were significantly lower in the secondary high PTH group compared with the normal PTH group. However, Amouzougan *et al.*<sup>29</sup> found no significant relationship between PTH values and BMD, which was similar to the findings of this study. The negative correlation between BMI and BMD in this study was similar to that of other studies<sup>30-32</sup>. The mechanism might be the result of multiple factors, including mechanical load mechanism, hormone level, and nutritional factors. However, there is still controversy in this respect. Some scholars have suggested that when the mechanical load caused by body mass is corrected, the amount of fat is significantly negatively correlated with bone mass<sup>33, 34</sup>. These conditions indicate that the level of BMD is a result of a combination of identified and unknown factors.

This study focused on Han patients in Tianjin and had geographical limitations. Data from other regions and ethnic groups are needed, and the exploration of similarities and differences among groups may be a task for us in the future. Zheng concluded that the number of skeletal muscles was positively correlated with BMD; that is, skeletal muscle loss could lead to a decrease in bone density<sup>35</sup>. Therefore, in addition to detecting the bone mass of patients, it is necessary to measure the muscle strength of patients in the future, to investigate the living conditions of patients, including, for instance, eating habits and daily activities. The study of vitamin D deficiency in such patients should be more detailed.

### Conclusion

Patients with hip fragility fractures in Tianjin have worrying vitamin D deficiencies, with low BMD of the hip and lumbar spine. Especially in postmenopausal women, the proportion of vitamin D deficiency is higher, and the decrease in BMD is more obvious. The decrease of BMD is caused by age, sex, BMI, and vitamin D content. Anti-osteoporosis drugs such

as Ca and vitamin D should be actively supplemented to promote fracture healing and reduce the incidence of re-fracture.<sup>4, 36</sup>

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### Disclosure

The authors declare no conflict of interest.

### References

- Gorter EA, Krijnen P, Schipper IB. Vitamin D deficiency in adult fracture patients: prevalence and risk factors. *Eur J Trauma Emerg Surg*, 2016, 42: 369–378.
- Holick MF, Binkley NC, Bischoff-Ferrari HA, et al. Endocrine Society. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*, 2011, 96: 1911–1930.
- Holick MF. Vitamin D deficiency in 2010: health benefits of vitamin D and sunlight: a D-bate. *Nat Rev Endocrinol*, 2011, 7: 73–75.
- Chinese Society of Osteoporosis and Bone Miner Res. Guidelines for the diagnosis and management of primary osteoporosis. *Chin J Osteoporosis Bone Miner Res*, 2017, 10: 413–443.
- Writing Group for the ISCD Position Development Conference. Diagnosis of osteoporosis in men, premenopausal women, and children. *J Clin Densitom*, 2004, 7: 17–26.
- Editorial Committee of Chinese White Paper on Prevention and Treatment of Osteoporosis by China Health Promotion Foundation. Chinese white paper on osteoporosis. *Chin J Health Manage*, 2009, 3: 148–154.
- Orimo H, Nakamura T, Hosoi T, et al. Japanese 2011 guidelines for prevention and treatment of osteoporosis-executive summary. *Arch Osteoporos*, 2012, 7: 3–20.
- Schulman RC, Weiss AJ, Mechanick JI. Nutrition, bone, and aging: an integrative physiology approach. *Curr Osteoporos Rep*, 2011, 9: 184–195.
- Takiar R, Lutsey PL, Zhao D, et al. The associations of 25-hydroxyvitamin D levels, vitamin D binding protein gene polymorphisms, and race with risk of incident fracture-related hospitalization: twenty-year follow-up in a bi-ethnic cohort (the ARIC study). *Bone*, 2015, 78: 94–101.
- Zadshir A, Tareen N, Pan D, Norris K, Martins D. The prevalence of hypovitaminosis D among US adults: data from the NHANES III. *Ethn Dis*, 2005, 15: S5–S97.
- Hwang JS, Tsai KS, Cheng YM, et al. Vitamin D status in non-supplemented postmenopausal Taiwanese women with osteoporosis and fragility fracture. *BMC Musculoskelet Disord*, 2014, 15: 257–263.
- Alarcón T, González-Montalvo JI, Hoyos R, et al. Parathyroid hormone response to two levels of vitamin D deficiency is associated with high risk of medical problems during hospitalization in patients with hip fracture. *J Endocrinol Invest*, 2015, 38: 1129–1135.
- Sahota O, Gaynor K, Harwood RH, Hosking DJ. Hypovitaminosis D and 'functional hypoparathyroidism'-the NoNoF (Nottingham neck of femur) study. *Age Ageing*, 2001, 30: 467–472.
- Sakuma M, Endo N, Oinuma T, et al. Vitamin D and intact PTH status in patients with hip fracture. *Osteoporos Int*, 2006, 17: 1608–1614.
- Dam T-L, von Mühlen D, Barrett-Connor EL. Sex-specific association of serum vitamin D levels with physical function in older adults. *Osteoporos Int*, 2009, 20: 751–760.
- Bischoff-Ferrari HA, Can U, Staehelin HB, et al. Severe vitamin D deficiency in Swiss hip fracture patients. *Bone*, 2008, 42: 597–602.
- Dawson-Hughes B, Mithal A, Bonjour JP, et al. IOF position statement: vitamin D recommendations for older adults. *Osteoporos Int*, 2010, 21: 1151–1154.
- Nawabi DH, Chin KF, Keen RW, et al. Vitamin D deficiency in patients with osteoarthritis undergoing total hip replacement: a cause for concern? *J Bone Joint Surg*, 2010, 92-B: 496–399.
- Di Monaco M, Castiglioni C, Tappero R. Parathyroid hormone response to severe vitamin D deficiency is associated with femoral neck bone mineral density: an observational study of 405 women with hip-fracture. *Hormones*, 2016, 15: 527–533.
- Sahota O, Munday MK, San P, Godber IM, Hosking DJ. Vitamin D insufficiency and the blunted PTH response in established osteoporosis: the role of magnesium deficiency. *Osteoporos Int*, 2006, 17: 1013–1021.
- Patel S, Hyer S, Barron J. Glomerular filtration rate is a major determinant of the relationship between 25(OH)D and parathyroid hormone. *Calcif Tissue Int*, 2007, 80: 221–226.
- Lee HJ, Gong HS, Song CH, et al. Evaluation of vitamin D level and grip strength recovery in women with a distal radius fracture. *J Hand Surg*, 2013, 38A: 519–525.
- Gumieiro DN, Rafacho BPM, Pereira BLB, et al. Vitamin D serum levels are associated with handgrip strength but not with muscle mass or length of hospital stay after hip fracture. *Nutrition*, 2015, 31: 931–934.
- Snijder MB, van Schoor NM, Pluijm SM, van Dam RM, Visser M, Lips P. Vitamin D status in relation to one-year risk of recurrent falling in older men and women. *J Clin Endocrinol Metab*, 2006, 91: 2980–2985.
- Monaco MD, Vallero F, Di Monaco R, et al. 25-Hydroxyvitamin D, parathyroid hormone, and functional recovery after hip fracture in elderly patients. *J Bone Miner Metab*, 2006, 24: 42–47.
- Carpintero P, Garcia-Lazaro M, Montero M, et al. Relationship between 1,25-dihydroxycholecalciferol levels and functional outcome after hip fracture in elderly patients. *Joint Bone Spine*, 2006, 73: 729–732.
- Mak JCS, Mason RS, Klein L, et al. An initial loading-dose vitamin D versus placebo after hip fracture surgery: randomized trial. *BMC Musculoskelet Disord*, 2016, 17: 336.
- Warner SJ, Garner MR, Nguyen JT, et al. Perioperative vitamin D levels correlate with clinical outcomes after ankle fracture fixation. *Arch Orthop Trauma Surg*, 2016, 136: 339–344.
- Amouzougan A, Chopin F, Laporte S, Vico L, Thomas T. Functional hypoparathyroidism in postmenopausal women with fragility fracture. *Joint Bone Spine*, 2011, 79: 170–175.
- Hsu YH, Venners SA, Terwedow HA, et al. Relation of body composition, fat mass, and serum lipids to osteoporotic fractures and bone mineral density in Chinese men and women. *Am J Clin Nutr*, 2006, 83: 146–154.
- Salamat MR, Salamat AH, Abedi I, et al. Relationship between weight, body mass index, and Bone mineral density in men referred for dual-energy X-ray absorptiometry scan in Isfahan. *Iran J Osteoporos*, 2013, 2013: 205963.
- Ong T, Sahota O, Tan W, Marshall L. A United Kingdom perspective on the relationship between body mass index (BMI) and bone health: a cross sectional analysis of data from the Nottingham fracture liaison service. *Bone*, 2014, 59: 207–210.
- Mokdad AH, Bowman BA, Ford ES, et al. The continuing epidemics of obesity and diabetes in the United States. *JAMA*, 2001, 286: 1195–1200.
- Liu YH, Xu Y, Wen YB, et al. Association of weight-adjusted body fat and fat distribution with bone mineral density in middle-aged Chinese adults: a cross-sectional study. *PLoS One*, 2013, 8: e63339.
- Zheng F. The research and development of the senile osteoporosis and the sarcopenia. *Chin J Clinic*, 2019, 47: 144–147.
- Zhou B, Wang X-H, Guo L-Y, et al. Vitamin D deficiency in winter related to bone loss of older people in northern China. *J Clin Rehabil Tissue Eng Res*, 2011, 15: 4907–4910.