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Correlations of Serum Hormones and Bone Mineral Density with Fracture and Balance Ability of Postmenopausal Patients and Effects of Calcitriol

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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Background: The aim of this study was to analyze the correlations of serum hormones and bone mineral density (BMD) with fracture and balance ability of postmenopausal patients and effects of calcitriol on them.

Material/Methods: The clinical data of 164 postmenopausal female patients with osteoporosis (OP) treated in our hospital were retrospectively analyzed.

Results: The incidence rates of OVCF, balance index score (BIS), front-back ratio (FBR), and right-left ratio (RLR) in the normal BMD group, reduced BMD group, and OP group showed increasing trends, and there were statistically significant differences in comparisons among groups ($p<0.05$). The levels of serum estradiol (E2) and progesterone (P) in the OVCF group were lower than those in the non-OVCF group, and there were statistically significant differences in comparisons between the 2 groups ($p<0.05$). However, there was no statistically significant difference in the comparison of serum luteinizing hormone (LH) level between the 2 groups ($p>0.05$). BIS, FBR, and RLR were negatively correlated with E2 and testosterone (T) ($p<0.05$). With the prolongation of calcitriol treatment time, BIS, FBR, and RLR gradually decreased, but T value gradually increased. At 6 months and 12 months after intervention, BIS, FBR, and RLR had significant differences compared to those before the experiment ($p<0.05$). (5) Total hip BMD, height, age, and body mass index (BMI) were the independent factors affecting SDI.

Conclusions: Hip BMD, age, height, and BMI are significantly correlated with OVCF. Calcitriol treatment can increase lumbar BMD and improve balance ability, and these effects become more obvious with prolongation of intervention time.

MeSH Keywords: Bone Density • Calcitriol • Osteoporotic Fractures

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Background

Osteoporosis (OP) is systemic bone metabolic disease manifested as decreased bone mass, destruction of bone micro-structure, and increased bone fragility, thus leading to fracture. As the aging of the population increases, OP has become an epidemic disease with subtle early symptoms. It is reported that at least one-fifth of men and one-third of women aged over 50 years old suffer from OP [1]. OP is easily complicated with fractures in lumbar vertebra, hip bone, and other parts, and such fractures have not only high incidence rates, but also long treatment cycles. High fatality and disability rates of OP have become issues seriously affecting public health. The incidence rate of OP in postmenopausal women is particularly high. Effectively reducing bone loss, improving bone metabolic status, and enhancing balance are of great significance in the prevention and treatment of OP in postmenopausal women. In this study, the correlations of serum hormones and bone mineral density (BMD) with fracture and balance ability of postmenopausal patients and effects of calcitriol on them were explored, and the possible mechanisms of action were investigated, so as to provide a basis for the prevention and treatment of OP.

Material and Methods

Clinical materials

Postmenopausal female patients with OP treated in our hospital for the first time from February 2013 to June 2015 were selected. There were 164 patients meeting the requirements. They were aged 62.43±5.87 years old on average, and the average menopausal age was 49.26±4.05 years old. Inclusion criteria are as follows: patients without a history of OP treatment, and with fractures due to falling, slight trauma, or daily activity. Exclusion criteria were: patients with fractures due to falling from a height, severe trauma or violence; patients with primary hyperparathyroidism, Cushing's syndrome, thyroid disease, or other diseases that significantly affected the bone metabolism; patients with a medication history of glucocorticoid, psychotropic drugs, or anti-coagulation drugs; and patients with cerebrovascular disease, severe visual impairment, severe neuromuscular disease, or other diseases that significantly affected balance. This study was approved by the Ethics Committee of our hospital, and the patients were informed and signed the consent form.

Methods

Information on patients age, past medical history, menstrual history, and marital and reproductive history was collected and input by a specially-assigned person. The weight of patients in single-layer clothes was measured in a fasting state, and the height of patients in no shoes and hats was also measured. Body mass index (BMI) was calculated as weight (kg)/height (m^2).

Detection of serological indexes

In the early morning, 3 mL of fasting venous blood was drawn from the elbow, followed by anti-coagulation, and centrifugation. The upper-layer serum was retained and frozen for later use. Serum luteinizing hormone (LH), estradiol (E2), and progesterone (P) levels were measured via radioimmunoassay. All operations were performed strictly in accordance with the corresponding instructions.

BMD determination

Total hip BMD was determined using a dual-energy X-ray BMD measuring instrument (iDXA, GE, USA). OP diagnostic criteria [2] were: normal BMD: T>–1.0, reduced BMD: –2.5<T<–1.0, and OP: T<–2.5.

Detection of limb balance ability

The dynamic balance ability was detected using a Korebalance balancing apparatus (Sportkat, USA), and detection indexes were: 1) balance index score (BIS): the overall balance ability, 2) front-back ratio (FBR): stability and balance of center-of-gravity shift in front-back direction, and 3) right-left ratio (RIR): stability and balance of center-of-gravity shift in right-left direction. The balance index and balance ratio are negatively correlated with the balance ability of body. The higher the value is, the worse the balance ability will be, and vice versa.

Evaluation of the degree of osteoporotic vertebral compression fracture (OVCF)

The lateral thoracolumbar X-ray film was read, and the vertebral morphology was graded as follows according to the vertebral descent height or reduced area: grade 0 (normal), grade 1 (mild), grade 2 (moderate), and grade 3 (severe) fractures. In grade 1 fracture, vertebral height declined by about 20–25% or the area was reduced by about 10–20%. In grade 2 fracture, vertebral height declined by about 26–40% or the area was reduced by about 21–30%. In grade 3 fracture, vertebral height declined by more than 40% or the area was reduced by more than 40%. The vertebral morphology was scored as follows: normal (0 point), mild fracture (1 point), moderate fracture (2 points), and severe fracture (3 points). The scores of a total of 13 vertebral bodies (T4-L4) were added to obtain the spinal deformity index (SDI).

Grouping and observation indexes

Based on BMD, patients were divided into a normal BMD group (n=13), a reduced BMD group (n=82), and an OP group

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(n=69). The fracture rate and balance ability of each group were compared.

Patients were divided according to whether OVCF occurred or not, SDI was calculated, and the levels of serum sex hormones were compared.

The correlations of serum E2 and BMD with balance ability were analyzed.

A total of 82 subjects who received other treatments due to OVCF and did not receive treatment temporarily due to normal BMD were excluded, and the remaining 82 patients with reduced BMD and OP took 0.25 g calcitriol (once per day) for 12 months. The temporal changes in BMD and balance ability before treatment and at 3 months, 6 months, and 12 months after treatment were observed.

Spearman test was used to analyze the correlation between SDI and each index, and factors with significant correlations were included into regression analyses.

Statistical methods

Data were analyzed using Statistical Product and Service Solutions (SPSS) 18.0 software (SPSS Inc., Chicago, IL, USA). Normal measurement data were presented as ($\bar{\chi}\pm s$), and non-normal data were described using medians. The *t* test, chi-square test, and Wilcoxon method were used for comparisons. Correlation and linear regression analyses were performed. P<0.05 indicated that the difference was statistically significant.

Results

Comparison of incidence rate of OVCF in patients with different BMD

According to BMD, 164 postmenopausal female patients were divided into 3 groups: normal BMD group (n=13), reduced BMD group (n=82), and OP group (n=69). The incidence rates of OVCF in the normal BMD group (1/13, 7.69%), reduced BMD group (31/82, 37.80%), and OP group (38/69, 55.07%) showed increasing trends, and there were statistically significant differences in comparisons among groups (χ^2=8.675, *P*<0.05) (Figure 1).

Comparison of balance ability of patients with different BMD

BIS in the normal BMD group (1365±423), reduced BMD group (1931±518), and OP group (2435±637) showed increasing trends, and there were statistically significant differences in comparisons among groups (*P*<0.05). FBR in the normal BMD group (0.248±0.132), reduced BMD group (0.394±0.121), and OP group (0.595±0.093) also showed increasing trends, and there were statistically significant differences in comparisons among groups (*P*<0.05). RLR in the normal BMD group, reduced BMD group, and OP group was 0.248±0.132, 0.394±0.121, and 0.595±0.093, respectively, and there were statistically significant differences in comparisons among groups (*P*<0.05) (Table 1).

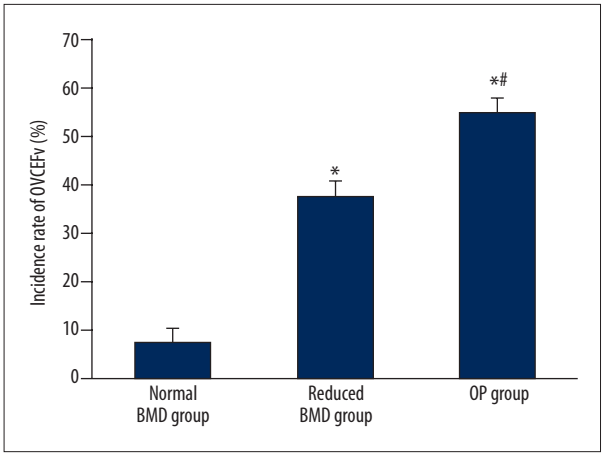

Figure 1. Comparison of incidence rate of OVCF in patients with different BMD. * Compared with that in normal BMD group, *P*<0.05. # Compared with that in reduced BMD group, *P*<0.05.

Comparisons of levels of serum sex hormones between OVCF group and non-OVCF group

The level of serum E2 was (43.21±4.37) pg/mL in the non-OVCF group and (61.34±5.48) pg/mL in the OVCF group, and there was a statistically significant difference in the comparison of serum E2 level between the 2 groups (*P*<0.05). The level of serum P was 1.62±0.42 nmol/L in the non-OVCF group and (1.43±0.31) nmol/L in the OVCF group, respectively, and there was a statistically significant difference in the comparison of serum P level between the 2 groups (*P*<0.05). The level of serum LH was 24.78±4.03 μg/L in non-OVCF group and 24.62±3.95 μg/L in the OVCF group, and there was no statistically significant difference in the comparison of serum P level between the 2 groups (*P*>0.05) (Table 2).

Correlation analyses of balance ability with serum hormones and BMD

Results of Spearman test showed that BIS was negatively correlated with E2 and testosterone (T) (*r*=–0.671 and –0.507, *P*<0.05), FBR was negatively correlated with E2 and T (*r*=–0.452 and –0.331, *P*<0.05), and there were negative correlations of RLR with E2 and T (*r*=–0.534 and –0.468, *P*<0.05) (Table 3).

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Table 1. Comparison of balance ability of patients with different BMD.

	BIS	FBR	RLR
Normal BMD group (n=13)	1365±423	0.248±0.132	0.159±0.132
Reduced BMD group (n=82)	1931±518*	0.394±0.121*	0.301±0.174*
OP group (n=69)	2435±637*,#	0.595±0.093*,#	0.537±0.206*,#

* Compared with that in normal BMD group, $P<0.05$. # Compared with that in reduced BMD group, $P<0.05$.

Table 2. Comparisons of levels of serum sex hormones between OVCF group and non-OVCF group.

	E2 (pg/mL)	P (nmol/L)	LH (μg/L)
Non-OVCF group (n=94)	61.34±5.48	1.62±0.42	24.78±4.03
OVCF group (n=70)	43.21±4.37*	1.43±0.31*	24.62±3.95

* Compared with that in non-OVCF group, $P<0.05$.

Table 3. Correlation analyses of BIS, FBR and RLR with E2 and T.

	BIS		FBR		RLR	
	r	*P*	*r*	*P*	*r*	*P*
E2	–0.671	<0.05	–0.452	<0.05	–0.534	<0.05
T	–0.507	<0.05	–0.331	<0.05	–0.468	<0.05

Comparisons of temporal changes in indexes of subjects

A total of 82 subjects who received other treatments due to OVCF and did not receive treatment temporarily due to normal BMD were excluded, and the remaining 82 patients with reduced BMD and OP took 0.25 g calcitriol (once per day) for 12 months. BIS, FBR, and RLR were decreased at 3 months after the intervention compared with those before the experiment, but there were no statistically significant differences ($P>0.05$). BIS, FBR, and RLR at 6 months and 12 months after the intervention were significantly decreased compared with those before ($P<0.05$) (Figure 2A–2C). With the prolongation of calcitriol treatment time, T value gradually increased, and it was decreased at 3 months after the intervention compared with before, but there was no statistically significant difference ($P>0.05$) (Figure 2D).

Correlation analyses of SDI with age, height, weight, BMI, and hip BMD

Spearman correlation analyses showed that SDI was significantly correlated with age ($r=0.384$), height ($r=–0.343$), BMI ($r=0.181$), and hip BMD ($r=–0.387$), but there was no significant correlation with body weight ($r=–0.022$, $P>0.05$) (Table 4).

Logistic regression analyses of factors influencing SDI

Linear regression analyses showed that total hip BMD, height, age, and BMI were independent factors affecting SDI, among which total hip BMD had the greatest impact on SDI, followed by height. Age and BMI also had different degrees of influence on SDI (Table 5).

Discussion

OP patients often have clinical symptoms of systemic pain, height decline, humpback, and fracture [3], seriously affecting quality of life. When the balance ability of the body to automatically adjust and maintain the posture is decreased, the direct manifestation is sudden or unintentional falling to the ground or to a place lower than the initial position [4]. Falling easily leads to fractures in limbs and trunk, among which hip fracture is the most severe, not only causing huge economic losses, but also directly reducing the quality of life and shortening life expectancy of the elderly. Studies have found [5] that 25% of elderly people with hip fracture die within 6 months due to the reduction of life expectancy by 10–15%. This study showed that BIS, FBR, and RLR were decreased at 3 months after administration of calcitriol compared with those before the intervention, but there were no statistically significant

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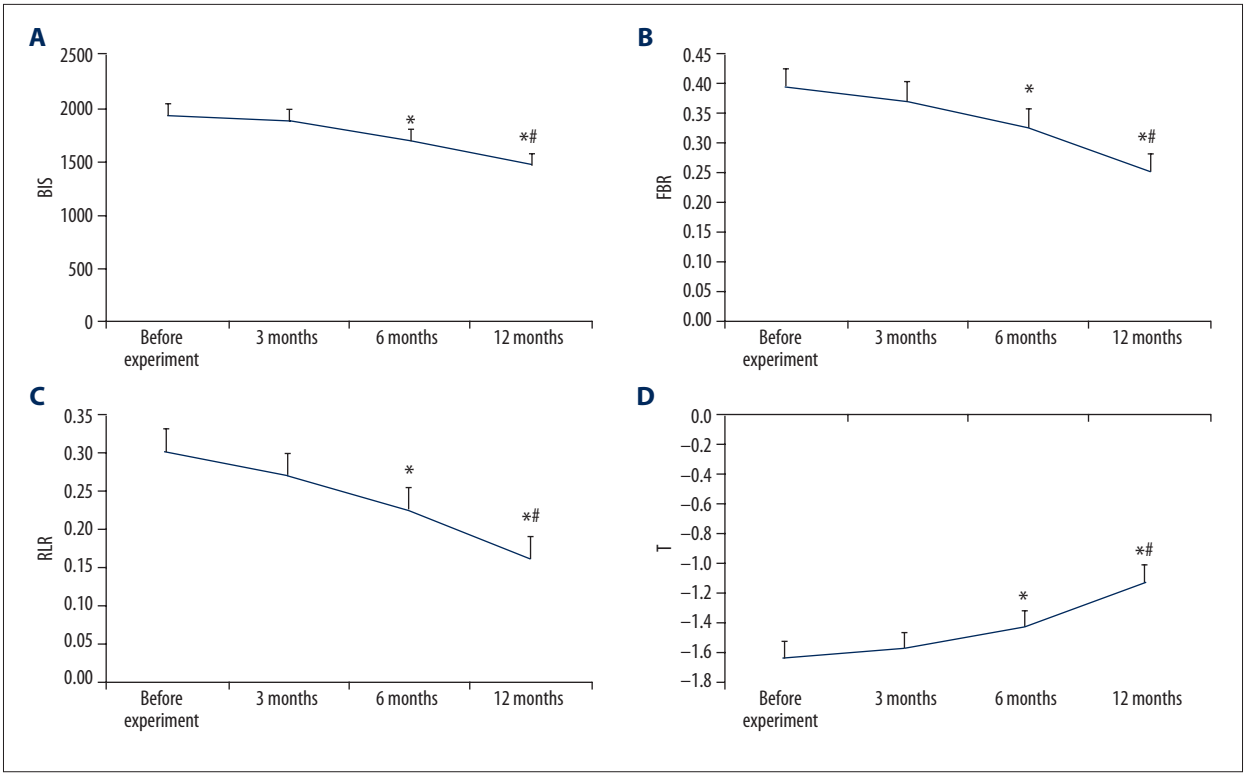

Figure 2. (**A**) Temporal change trend of BIS. (**B**) Temporal change trend of FBR. (**C**) Temporal change trend of RLR. (**D**) Temporal change trend of T value. * Compared with that before experiment, $P<0.05$. # Compared with that at 3 months after experiment, $P<0.05$.

Table 4. Correlation analyses of SDI with age, height, weight, BMI and hip BMD.

Index	Age	Height	Body weight	BMI	Total hip BMD	FI
r	0.384	–0.343	–0.022	0.181	–0.387	0.219
P	0.000	0.001	0.618	0.003	0.000	0.002

Table 5. Logistic regression analyses of influencing factors of SDI.

Factor	Non-standardized		Standardized regression coefficient	95% confidence interval		P
	Regression coefficient	Standard error		Upper limit	Lower limit	
Age	0.127	0.031	0.352	0.169	0.756	0.001
Height	–0.223	0.042	–0.387	–0.312	–0.138	0.000
BMI	0.241	0.079	0.213	0.393	0.892	0.002
Hip BMD	–12.413	2.114	–0.426	–16.509	–8.676	0.000

differences. The dynamic balance ability was not improved significantly, but BIS, FBR, and RLR at 6 months and 12 months after administration of calcitriol were significantly decreased compared with those before ($P>0.05$), suggesting that the increase and decrease of the balance ability of OP patients is slow and uncertain. Karinkanta et al. [6] reported that increasing muscle strength and improving balance are the most effective methods for the elderly to prevent falling and reduce fractures.

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In pre-menopausal and early perimenopause periods, circulating E2 is the major estrogen, which is decreased with menopause [7]. In postmenopausal OP, the level of estrogen in the body sharply declines, the bone structure is destroyed, and the bone fragility is increased, resulting in a significant increase in the incidence rate of fracture [8]. In this study, the serum E2 level in the non-OVCF group was higher than that in the OVCF group ($P<0.05$), and the E2 level was negatively correlated with indexes of balance ability (BIS, FBR, and RLR) ($P<0.05$), suggesting that estrogen plays an important role in the maintenance of a balance between bone absorption and bone formation [9]. Hays et al. [10] found that fracture risk is increased 3-fold for every one-standard-deviation drop in hip BMD. As age increases and hormone levels decline, the bones of the elderly degenerate and bone strength decreases. Moreover, the elderly are slow in reaction, and the protection capacity of hip muscles is reduced due to atrophy, so fractures can be caused easily by slight trauma [11].

OP is characterized by increased bone fragility and proneness to fractures, and vertebral fractures and spinal deformity caused by it are typical symptoms during the progression of OP [2]. BMD is the most important objective criterion for evaluating bone strength, and the decline in BMD is a major cause of OP fracture. However, OP fracture does not necessarily occur when the BMD meets the diagnostic criterion for OP. Studies have shown that approximately 50% of OP fractures occur during the BMD reduction stage. Our study also showed that the incidence rate of OVCF in subjects with reduced BMD was up to 37.80%. A large number of studies [13,14] have shown that fracture is increased by 1.5–3.0-fold for every one-standard-deviation drop in BMD of the measuring part, and BMD has a high predictive value for its measuring site but a limited value for other sites. Studies have revealed that with the decline in lumbar BMD, the incidence rate of OVCF in postmenopausal women is significantly increased, and there is a significant correlation between them. The decline in medullary BMD is also an important risk factor of OVCF. Svanhild et al. [16] showed that the hip BMD and age account for nearly 50% of the risk of OVCF [16], which are 2 major independent risk factors for OVCF. In view of the influencing factors of lumbar BMD, hip BMD, because of its most accurate response to systemic BMD, was selected as the research focus in the present study. Our study showed that the incidence rates of OVCF in the normal BMD group (7.69%), reduced BMD group (37.80%), and OP group (55.07%) had increasing trends, OVCF mostly occurred in the BMD reduction stage, and the hip BMD of more than half of the patients was in the OP stage, suggesting that bone mass loss is a high-risk factor for OVCF. The linear regression analysis results in this study showed that total hip BMD, height, age, and BMI were independent factors affecting SDI, among which total hip BMD had the greatest impact on SDI, suggesting that hip BMD can be used as an effective index for predicting OVCF. Results of this study indicate that [17–19]. OVCF affects the functions of local skeletal and muscular systems and causes lumbago and back pain and spinal deformity. Muscle disuse atrophy is caused by long-term immobilization, and the balance ability of body is decreased, significantly increasing the risk of recurrent fractures.

Besides BMD, increased age is another major and definite risk factor for the incidence of OP [20]. Epidemiological studies in China and other countries have shown that the incidence rate of OVCF in women aged 50–60 years old is about 3–10%, with an annual increase rate of 0.9%, and its incidence rate is more than 30% in people over 80 years old. The linear regression analysis results in this study showed that age was a risk factor for SDI, and the incidence rate of OVCF was increased with increased age, which were consistent with research results in China and other countries. This study also showed that height was a risk factor for SDI. Some scholars believe that OVCF should be suspected in case of height reduction by >4 cm for women and >6 cm for men compared with the peak value, while some other scholars argue that OVCF should be highly suspected in case of height reduction by >3 cm compared with the peak value [22,24]. The present study showed that there was no clear correlation between OVCF and body weight, and the relationship of body weight and BMI with OP fracture is still controversial. Most scholars believe [25] that low body weight is a secondary risk factor for OP fracture. However, some other scholars [26] found that obese patients are more prone to fractures with site specificity, which is manifested as increased risks of fractures of ankle, calf, thigh, and vertebral body, and reduced risks of pelvic and wrist fractures.

Conclusions

In conclusion, hip BMD, age, height, and BMI are significantly correlated with OVCF. Calcitriol intervention can increase lumbar BMD and improve balance ability, whose effect will be more obvious with the prolongation of intervention time. Studies [27,28] have shown that thoracolumbar lateral films combined with BMD examination can significantly improve the detection rate of OP. Therefore, thoracolumbar lateral films should be included in the routine physical examination for postmenopausal women so as to improve the detection rate of OP.

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1. Therapeutic Effect and Mechanism of GLP-1 on High Fat-Induced Bone Volume Reduction. Qingdao University Affiliated Hospital 2014 Youth Fund Project, Project Number: 2202.

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Conflict of interest

None.

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