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Correlation Between Bone Metabolism Indices and Osteoporotic Thoracolumbar Vertebrae Fracture in Postmenopausal Women

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Background: This study aims to explore the correlation between bone metabolism indices and osteoporotic thoracolumbar vertebrae fracture (OTVF) in postmenopausal women.

Methods: A total of 447 female patients with postmenopause and underwent OTVF in our hospital were selected as group A. Three hundred eighty-seven out-patients without fractures were selected as group B. Bone metabolism index including the serum levels of total Serum procollagen type N-terminal propeptide (tPINP), the age-related type I cross linked C-telopeptide (β-CTX) and 25-hydroxyvitamin D (25-OHD) were collected and compared. The relation between bone metabolism indices and OTVF was analyzed.

Results: The mean tPINP in group A was 61.72 ± 28.43, which was notably higher than group B ($P < 0.01$). Meanwhile, greater β-CTX were higher founded in group A than group B (0.778 ± 0.316 vs 0.669 ± 0.303 μg/l). However, the 25-OHD in group A was significantly lower than that in group B ($P < 0.05$). Multivariate logistic regression analysis revealed that the serum level of tPINP (OR: 0.008, $P = 0.011$), the serum level of β-CTX (OR: 0.805, $P = 0.002$) and the serum level of 25-OHD (OR: −0.029, $P = 0.003$) were independently correlated with postmenopausal OTVF.

Conclusion: Bone metabolic markers play an important role in predicting OTVF. As a reflection of bone mass and bone strength, BMD is inadequate in predicting OTVF. High expression of bone metabolism indicators β-CTX, tPINP and relatively low expression of 25-OHD suggest an increased risk of OTVF. Early detection of postmenopausal bone metabolism abnormalities can be used for early intervention to reduce the incidence of OTVF.

Keywords: bone metabolism indices, osteoporotic thoracolumbar vertebrae fracture, correlation, risk, postmenopausal women

Introduction

As the improvement of living standards in the past decades, people have significantly longer life than before. Due to the weakening of the body function, the elderly usually present varying degrees of osteoporosis. Particularly, postmenopausal women with dramatically decreased estrogen have shown severe osteoporosis.[1,2] Osteoporosis is characterized by the destruction of bone microstructure and reduction of bone mass, resulting in reduced bone strength and increased bone fragility, increasing the risk of fractures in patients. Postmenopausal osteoporosis mostly occurs in women about 10 years after menopause, and 50–70 years old women are the high-risk groups of postmenopausal osteoporosis, which is also known as type 1 osteoporosis. According to the 2013 report of the International Osteoporosis Foundation, there is 1 case of osteoporosis fracture every 3s in the world, about 50% of women and 20% of men will experience the first osteoporotic fracture after the age of 50, and 50% of patients with the first osteoporosis fracture may have the second one. Women with osteoporotic vertebral fractures are four times more likely to have a secondary fracture than those without.[3–6]

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Osteoporosis has been recognized as a serious social and public health problem due to its high incidence and great harm. As the most common injury in primary osteoporosis, fracture is often the first symptom and the reason for the treatment of osteoporosis patients. Normally, fracture of vertebrae, proximal femur and wrist are regarded as the typical osteoporotic fractures.[7] It is, therefore, especially important that prediction of osteoporotic fracture risk and early intervention in patients with high fracture risk. Bone tissue content is usually assessed by bone mineral density (BMD), but BMD testing is not suitable for short-term follow-up monitoring. Serum bone metabolism biochemical index (serum levels of total Serum procollagen type N-terminal propeptide (tPINP), the age-related type I cross linked C-telopeptide (β-CTX) and 25-hydroxyvitamin D (25-OHD)) detection is a convenient and sensitive method.[8]

The biochemical index of bone metabolism is an important index for dynamic monitoring of human bone metabolism. Its expression level can reflect the increase or decrease of bone turnover and future bone loss, and can monitor the risk of osteoporotic fracture.[8] This study aims to investigate the correlation between biochemical indicators of bone metabolism and the risk of postmenopausal osteoporotic vertebrae fractures.

Materials and Methods

The clinical study was approved by the Ethics Committee of the first affiliated hospital of Soochow University, and written informed consents were obtained from all participants and was performed in accordance with the ethical standards of the Declaration of Helsinki of 1964. In total, 834 female patients who were clearly diagnosed as postmenopausal osteoporosis at the First Affiliate Hospital of Soochow University from September 2014 to June 2020 were selected to perform a retrospective study. All participants were divided into two groups (group A: with OTVF; group B: without OTVF) in accordance with that whether OTVF occurred. All cases met the following criteria: (1) all female patients were not less than 55 years old and have been in menopause for more than 5 years; (2) without anti-osteoporosis treatment before fracture; (3) conformed to first fragility fracture occurred without violent trauma; (4) accord with BMD standard of the diagnosis of osteoporosis;[9] (5) diabetes, thyroid function hyperfunction, hyperparathyroidism, malignant tumor diseases and medical history of taking thyroid hormone or steroids were ruled out.

The age, height, weight, body mass index (BMI) and T-score of lumbar BMD in group A and group B were collected and calculated, respectively. Blood samples in group A collected within 4 hours OTVF were analyzed by enzyme-linked immunosorbent assay to acquire the three typical bone metabolic indices of tPINP, β-CTX and 25-OHD.[10] Blood samples in group B were collected in the clinic. The kits used in group A and Group B are identical.

SPSS 20.0 statistical software was used for analysis. The measurement data of normal distribution were expressed as mean ± SD, the difference between groups was tested by *t* test of independent samples, and correlation analysis between bone metabolic indices and OTVF was performed by binary logistic regression. $P < 0.05$ was considered statistically significant.

Results

The baseline characteristics of all patients in group A and group B were summarized in Table 1. Comparison of the general characteristics showed that there were no statistically significant in age, height, weight, BMI and BMD. Results of bone metabolism index of patients between two groups were collected in Table 2. The mean tPINP in group A was

Table 1 Baseline Data of Patients Between Group A and Group B (Mean ± SD)

Index	Group A	Group B	P value
Age (years)	68.39 ± 9.26	66.45 ± 7.02	0.76
Height (cm)	160.91 ± 6.20	162.23 ± 7.01	0.54
Weight (kg)	52.02 ± 10.11	50.84 ± 8.99	0.26
BMI (kg/m^2)	21.85 ± 3.68	22.17 ± 2.48	0.19
BMD (SD)	−2.84 ± 0.38	−2.76 ± 0.27	0.68

Abbreviations: BMI, body mass index; BMD, bone mineral density.

Table 2 Bone Metabolism Index of Patients Between Two Groups (Mean ± SD)

Index	Group A	Group B	P value
tPINP (μg/l)	61.72 ± 28.43	52.92 ± 25.52	0.0034**
β-CTX (μg/l)	0.778 ± 0.316	0.669 ± 0.303	0.0059**
25-OHD (μg/l)	15.762± 6.895	17.659 ± 10.27	0.021*

Note: *p<0.05, **p<0.01.
Abbreviations: tPINP, total Serum procollagen type N-terminal propeptide; β-CTX, the age-related type I cross linked C-telopeptide; 25-OHD, 25-hydroxyvitamin D.

Table 3 The Results of Logistic Regression Analysis Between Bone Metabolic Indices and OTVF

Index	OR	95% CI	P value
tPINP (μg/l)	0.008	1.002–1.014	0.011
β-CTX (μg/l)	0.805	1.337–3.739	0.002
25-OHD (μg/l)	−0.029	0.952–0.990	0.003

Abbreviations: OTVF, osteoporotic thoracolumbar vertebrae fracture; OR, odds ratio; CI, confidence interval; tPINP, total Serum procollagen type N-terminal propeptide; β-CTX, the age-related type I cross linked C-telopeptide; 25-OHD, 25-hydroxyvitamin D.

61.72 ± 28.43, which was notably higher than group B (P < 0.01). Meanwhile, greater β-CTX were founded in group A than group B (0.778 ± 0.316 vs 0.669 ± 0.303 μg/l). However, the 25-OHD in group A was significantly lower than that in group B (P < 0.05). The results of Logistic regression analysis between bone metabolic indices and OTVF was showed in Table 3. Multivariate logistic regression analysis revealed that the serum level of tPINP (OR: 0.008, P = 0.011), the serum level of β-CTX (OR: 0.805, P = 0.002) and the serum level of 25-OHD (OR: −0.029, P = 0.003) were independently correlated with postmenopausal OTVF.

Discussion

Osteoporosis is characterized by the destruction of bone microstructure and reduction of bone mass, resulting in reduced bone strength and increased bone fragility, increasing the risk of fractures in patients. Osteoporotic vertebral compression fracture is the most serious consequence of osteoporosis. Postmenopausal osteoporosis mostly occurs in women about 10 years after menopause, and 50–70 years old women are the high-risk groups of postmenopausal osteoporosis, which is also known as type 1 osteoporosis. As the globally recognized gold standard for osteoporosis, diagnosis, it is well known that the patient with the T-score of lower than −2.5 can be diagnosed as osteoporosis.[9] Due to its large limitations, BMD is not well applied in the prediction of osteoporotic fractures alone. In order to maximize the accuracy of fracture risk prediction, BMD should be combined with other clinical indicators. Although bone metabolic biochemical indices cannot be served as the gold standard for diagnosis of osteoporosis, but the levels of bone metabolic biochemical index in blood and urine can assess the situation of the metabolism of bone tissue, which is used in the evaluation of bone metabolic state, osteoporosis diagnosis classification, fracture risk prediction, curative effect evaluation of osteoporosis treatment, and the differential diagnosis of metabolic bone disease. Therefore, the focus of this study is to reveal correlation between bone metabolism indices and osteoporotic vertebrae fracture in postmenopausal women and to further predict osteoporotic fracture risk.

After the occurrence of vertebral fracture, osteocytes at the broken end, damaged periosteum and surrounding cells undergo necrosis, while osteoclasts clean the above residual dead bone and form new bone from osteoblasts to promote fracture healing.[11] In the process of physiological changes at the fracture end mentioned above, bone metabolism markers

reflect the change process of the whole fracture healing. Bone metabolic indices are some metabolites generated in the process of bone remodeling including two kinds index of bone formation and bone resorption. As markers of bone formation and bone resorption, the serum concentration of reaction activity of bone remodeling and bone remodeling activity, often increased risk of fracture. Previous studies have showed that bone metabolism index can predict osteoporotic fracture in postmenopausal patients with 2 ~ 5 years of fracture risks in the future.[12]

At present, there are a variety of biochemical indicators of bone metabolism used to clinically assess the risk of osteoporotic fracture, including 25-OHD, β-CTX and tPINP. 25-OHD, β-CTX are closely related to bone resorption and tPINP is closely related to bone resorption. The tPINP concentrations in the blood is mainly used to reflect the bone transformation and type I collagen synthesis speed, when there is a rising phenomenon, suggesting that bone collagen type conversion and I synthetic accelerated significantly.[13] In addition, tPINP has a high specificity and sensitivity in predicting the occurrence of osteoporosis, evaluating bone mass, and monitoring the effect of anti-osteoporosis. The tPINP is particularly obvious and is not affected by hormones,[14] which is of great significance in clinical research and application. Therefore, fasting serum PINP is recommended as a marker of high sensitivity of bone formation.[14] The level of CTX reflects the bone resorptive activity of osteoclasts, and CTX is an effective marker of metabolic bone disease characterized by significantly enhanced osteoclast activity. The detection of serum CTX level can predict the active degree of bone conversion and serve as an important reference index for clinical evaluation of bone conversion related bone metabolic diseases. Fasting serum CTX is recommended as a marker reflecting high bone resorption sensitivity.[14]

In this study, the mean tPINP in group A was 61.72 ± 28.43, which was notably higher than group B ($P < 0.01$). Meanwhile, greater β-CTX were founded in group A than group B (0.778 ± 0.316 vs 0.669 ± 0.303 μg/l). However, the 25-OHD in group A was significantly lower than that in group B ($P < 0.05$), which can be concluded that patients in group A with postmenopausal OTVF performed significantly stronger bone cells and faster bone turnover than that in group B. Multivariate logistic regression analysis revealed that the serum level of tPINP (OR: 0.008, $P = 0.011$), the serum level of β-CTX (OR: 0.805, $P = 0.002$) and the serum level of 25-OHD (OR: −0.029, $P = 0.003$) were independently correlated with postmenopausal OTVF. It is showed that there is a positive correlation between postmenopausal OTVF and serum tPINP and β-CTX ($P < 0.05$), suggesting that the risk of secondary fracture would increase with the increase of serum tPINP and β-CTX concentration. There is a negative correlation between postmenopausal OTVF and 25-(OH)D. The correlation between bone metabolism and osteoporotic fracture has previously been reported. Johansson, et al[15] reported that the PINP and CTX were associated with the risk of fractures, every increase of one standard deviation PINP and CTX, there was a 20% increased risk of fracture. Dai, et al[16] also concluded that PINP and CTX were significantly correlated with the risk of hip fracture, and the odds ratios (OR) were 6.63 (95% CI: 2.02–21.18) and 4.92 (95% CI: 1.67–14.51), respectively. Thus, bone metabolic markers plays an indispensable role in predicting postmenopausal osteoporotic fractures. Meanwhile, osteoporotic older women, with lower bone density and higher β-CTX, are more likely to incur osteoporotic fracture. β-CTX is better than BMD at predicting osteoporotic fracture.[17]

This study still has some shortcomings. As a retrospective study, the single-center sample size is small, and there is a certain analysis bias. In addition, due to the limitation of clinical data, the included analysis indicators are limited, so the impact of bone metabolism indicators on postmenopausal osteoporotic fractures cannot be fully explored. The correlation between biochemical results and BMD assessment was not analyzed. In the future clinical work, a prospective controlled study will be designed to improve the level of evidence-based research and provide stronger evidence for clinical decision-making.

Conclusions

Bone metabolic markers play an important role in such patients, and are significantly associated with OTVF. As a reflection of bone mass and bone strength, BMD is inadequate in predicting OTVF. In clinical work, high expression of bone metabolism indicators β-CTX, tPINP and relatively low expression of 25-OHD suggest an increased risk of OTVF. Early detection of postmenopausal bone metabolism abnormalities can be used for early intervention to reduce the incidence of OTVF.

Data Sharing Statement

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

Approval was obtained from the ethics committee of Soochow University. The procedures used in this study adhere to the tenets of the Declaration of Helsinki. Informed consent was obtained from all individual participants included in this study.

Consent for Publication

Informed consent obtained from all the participants to publish the information/image(s) in an online open-access publication.

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Disclosure

The authors report there are no competing interests to declare.

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