# Correlation analysis between risk factors, BMD and serum osteocalcin, CatheK, PINP, β-crosslaps, TRAP, lipid metabolism and BMI in 128 patients with postmenopausal osteoporotic fractures

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**Abstract.** – **OBJECTIVE:** Our aim is to investigate the correlation between risk factors of postmenopausal osteoporotic fracture, BMD and Bone turnover markers, lipid metabolism and BMI.

**SUBJECTS AND METHODS:** The Cox proportional hazard model was used to conduct univariate and multivariate analysis to screen the risk factors related to postmenopausal osteoporotic fractures. Blood samples were collected to detect biochemical markers of bone turnover, blood lipids content, and then measure the BMI of the survey subjects. BMD was measured and its correlation with biochemical markers of bone turnover, lipid metabolism and BMI was analyzed.

**RESULTS:** Cox univariate analysis indicated that average age, menopause, years since menopause, number of deliveries, and limb spasm are associated covariates of postmenopausal osteoporotic fractures. Where, BMD severity, history of hysterectomy or ovariectomy, and years since menopause are significant covariates for the incidence of postmenopausal osteoporotic fractures. The correlation study with lipid metabolism found that the smaller the BMI value, the greater the BMD loss; the smaller the TG value, the greater the BMD loss, exhibiting a downward trend. No difference was observed between HDL-C and LDL-C content, and the difference was not statistically significant ($p > 0.05$). Femoral neck BMD was negatively correlated with CatheK, serum osteocalcin, PINP, β-crosslaps and TRAP, and lumbar spine BMD was also negatively correlated with CatheK, serum osteocalcin, PINP, β-crosslaps and TRAP.

**CONCLUSIONS:** Biochemical markers of bone turnover are highly expressed in postmenopausal women and increase with the decrease of bone density, which can be used as markers for disease prediction. Combined with BMI, triglyceride and other related indicators, and closely related factors such as the patient's age, the number of deliveries, it is possible to predict the incidence of PMOP fractures early.

## Introduction

For postmenopausal women, due to the decline in the body's estrogen level, the bone metabolism is unbalanced, which breaks the balance between the original bone resorption and bone formation, and accelerates the bone trabecular resorption, so that the bone microstructure changes, activating osteoclast-mediated irreversible bone loss with high turnover. Decreased bone mass results in increased bone fragility, so fracture is easy. Even low energy loads in daily activities or minor trauma, such as sneezing, coughing, etc., may lead to fractures. The high incidence sites of fractures mainly include the spine, distal ulna and radius, and the hip. In particular, elderly population is prone to fracture, which is an important cause of decline in their quality of life and even death. Related epidemiology shows that among women with (PMOP) postmenopausal osteoporotic fractures, after a hip or femur fracture in the elderly population, the rate of death from related complications within 1 year is as high as 25%. Therefore, postmenopausal osteoporosis becomes the most serious chronic disease after cardiovascular and cerebrovascular diseases[1,2]. A number of studies[1-3] at home and abroad have also confirmed that the risk of postmenopausal osteoporotic fractures in women is positively correlated with the increase in the years since menopause. The BMD value of normal women reaches a peak at the age of 30-35 years old. During the perimenopausal period, BMD value shows a downward trend year by year, and af-

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ter menopause, female estrogen levels decrease significantly with age, with the activity of osteoblasts decreased and the activity of osteoclasts increased, which breaks the balance between bone resorption and bone formation, leading to reduced bone formation and enhanced bone resorption. With the increasing years since menopause, the body's estrogen levels and BMD decline faster, resulting in an increased probability of fractures[1-3]. Scholars have shown[4] that bone turnover-related biochemical markers can be detected to determine the type of clinical bone metabolism, which can accurately reflect the rate of bone formation and resorption and can be used to assess the rate of bone loss and disease progression, so that it is possible to timely select appropriate intervention measures and treatment schemes. Also, previous studies[5,6] by the research team also confirm that the intramedullary fat in patients with osteoporosis is significantly increased, while blood lipid is one of the three major substances for the body's basal metabolism. It is confirmed by more related research[5,6] that a certain relationship may exist between the two, and each lipid metabolism affects the incidence of osteoporosis in varying degrees. Based on previous literature research, this study screened out the relevant risk factors for postmenopausal osteoporotic fractures, including BMD diagnosis, number of pregnancies, years since menopause, number of deliveries, and history of ovariectomy. Cox multivariate analysis was performed with the above five risk factors and the incidence time of osteoporotic fracture as the outcome variables to analyze the related risk factors for women aged 45-65 years with postmenopausal osteoporotic fractures, and detect BMD, CatheK, serum osteocalcin, PINP, β-crosslaps, TRAP, lipid metabolism and BMI index. In this way, it is possible to investigate their risk levels and correlations, initially identify the related risk factors for fractures in women with postmenopausal osteoporosis and provide scientific basis for relevant departments and health administrative agencies to conduct follow-up early risk prediction and health education for high-risk groups with PMOP fractures.

## Subjects and Methods

### General Information

The data of 128 patients with postmenopausal osteoporotic fractures treated in our hospital and project cooperation units from January 2019 to January 2021 were collected. The average age was (54.36±5.47) years. The incidence site of fractures included: 22 cases of distal radius fractures, 11 cases of rib fractures, 32 cases of thoracic spine fractures, 39 cases of lumbar spine fractures, 10 cases of thoracolumbar multiple compression fractures, 3 cases of femoral neck fractures, 2 cases of pertrochanteric fractures, 2 cases of femoral intertrochanteric fractures and 7 cases of lateral malleolus fractures. 25 cases had intermittent oral administration of calcium and vitamin D drugs, but all did not receive systematic and regular anti-osteoporosis treatment.

### Diagnostic Criteria

Guidelines for the diagnosis and treatment of primary osteoporosis[7] was referred to for the diagnosis of postmenopausal osteoporosis.

### Inclusion Criteria

①Aged 45-65 years old, female; ②With clear consciousness, normal spirit, able to keep to the subject, communicate with staff normally and answer relevant questions; ③With no bad or special eating habits; ④Without systematic and regular anti-osteoporosis treatment in the past;⑤Agree to participate in this research project and sign the informed consent.

### Exclusion Criteria

①Unnatural menopause with a history of ovariectomy; ②Secondary osteoporosis caused by the use of glucocorticoids and other drugs, hyperthyroidism, diabetes and other related diseases; ③Super aged pregnant women; ④Mental illness or cognitive dysfunction; ⑤Patients with a history of severe cardiovascular and cerebrovascular diseases, liver and kidney failure and malignant tumor.

### Detection Indexes

Blood samples from the enrolled patients were collected to detect blood lipids (TC, TG, HDL-C, LDL-C), and immunodetection of biochemical markers of bone turnover was performed: serum cathepsin K (CatheK), type II procollagen amino-terminal propeptide (PINP), β-collagen degradation products (β-crosslaps), osteocalcin and tartrate-resistant acid phosphatase (TRAP). The body mass index (BMI) of the survey subjects was measured, the bone mineral density (BMD) was detected, and its correlation with lipid metabolism was analyzed. At the same time, based on previous literature research, the risk factors related to postmenopausal osteoporotic fractures were screened, and relevant case data were collected, including menopause, years since menopause

(years since menopause≤ 10 years, years since menopause >10 years), number of pregnancies (≤1, 2, 3, ≥4), number of deliveries (≤2, ≥3). The correlation between risk factors and postmenopausal osteoporotic fractures was analyzed.

### Statistical Analysis

SPSS 22.0 software (IBM Corp., Armonk, NY, USA), R3.0.2 software Survival software package and Cox's Proportional Hazard Model methodology were used for statistical analysis and risk factors analysis. All statistical analysis tests were two-sided hypothesis tests, and $p \leq 0.05$ was considered statistically significant.

# Results

According to the BMD results, the correlation between population with different degrees of osteoporosis and the incidence of fragility fractures is compared, as shown in Table I.

Cox proportional hazard model for postmenopausal osteoporotic fracture events is shown in Table II.

Correlation analysis between the incidence of postmenopausal osteoporotic fractures and BMI, lipid metabolism is shown in Table III.

Correlation analysis between serum biochemical markers of bone turnover and BMD, as shown in Table IV.

# Discussion

Postmenopausal osteoporotic fracture (PMOP) has many related short-term and long-term complications, which is one of the most harmful clinical outcomes for postmenopausal women, and the incidence is increasing year by year. Hence, preventing PMOP and lowering PMOP incidence has become an important public health problem in China, and early prediction is one important means to prevent PMOP and lower PMOP incidence[8,9]. So finding relevant risk factors are important methods of predicting PMOP. Based on the conclusions of this study, Through the screening of high-risk factors such as the severity of osteoporosis, years since menopause, whether there is a history of hysterectomy or ovariectomy, and combined with close factors such as the patient's age and the number of deliveries, the risk of PMOP was judged. Previous literature study[10] has shown that the fat in the medullary cavity gradually increases in the case of OP,

indicating a certain relationship between the two, with various blood lipids exerting different effect on osteoporosis[10]. Moreover, the findings are also controversial. Hsu et al[11] believed that BMD was significantly negatively correlated with TC, TG, and LDL-C levels, while Tang et al[12] believed that BMD was positively correlated with TG levels. Wang et al[13] believed that BMD was positively correlated with TG levels and negatively correlated with LDL-C, TC, and HDL-C. The findings of Cai et al[14] and Gong et al[15] are basically consistent with those Wang et al[13]. Qiu et al[16] believed that HDL-C was positively correlated with BMD. At the same time, the team has also achieved certain previous results in the mechanism of lipid metabolism and OP. Studies[16-18] show that both adipocytes and osteoblasts are differentiated from stromal cells in the bone marrow. When more adipocytes are differentiated than osteoblasts, osteoblast differentiation will be affected, thus affecting BMD value. Meanwhile, oxidized low-density lipoprotein (ox-LDL) not only directly inhibits the formation of osteoblasts, but also induces apoptosis of osteoblasts, which can indirectly destroy osteocytes by inducing inflammatory response. HDL-C can inhibit the effect of ox-LDL. TC levels affect the formation and survival of osteoclasts, and lipoproteins can indirectly affect bone remodeling by regulating cholesterol levels. Various studies[16-18] have shown that lipid metabolism substances are closely related to the incidence of osteoporosis.

Biochemical markers of bone turnover include CatheK, serum osteocalcin, PINP, β-crosslaps, and TRAP, which can not only represent osteoblast activity, but also reflect the bone turnover rate and remodeling process through mechanism, while higher bone turnover is closely related to osteoporosis[19]. Where, osteocalcin is an important index influencing bone turnover, PINP is specific and sensitive to bone formation, TRAP mainly exists in mature osteoclasts and active macrophages, β-crosslaps can reflect osteoclast activity and bone resorption, and CatheK is a protease associated with diseases like tumors, osteoporosis, all of which are closely related to the incidence of osteoporosis[20-22].

# Conclusions

Based on Cox proportional hazard model and data correlation analysis, this study aims to find the relevant risk factors for postmenopausal osteoporotic fractures and their correlation with lipid metabolism. The study finds that BMD severity,

years since menopause, history of hysterectomy or ovariectomy are the most important risk factor for osteoporotic fractures, which are closely related to factors such as age, number of deliveries. Meanwhile, data analysis shows that the smaller the BMI value, the greater the BMD loss, exhibiting a downward trend; the smaller the TG value, the greater the BMD loss, exhibiting a downward trend. No difference is observed between HDL-C and LDL-C content. In this survey, BMI=23.26±3.48 kg/m$^2$, which is between 18.5-27.9 kg/m$^2$, so it is inferred that people in Xinfan area are normal or obese. TG=1.63±1.091 mmol/L, which is normal high. Out of the three BMD content grades, no difference was observed between HDL-C and LDL-C content, with HDL-C=1.60±0.722 mmol/L, LDL-C=2.54±0.848 mmol/L, all of which were at normal levels. The TC value of osteoporosis is different from the TC value of normal bone mass. The smaller the TC value, the greater the BMD loss, exhibiting a downward trend. TC=4.47±0.998 mmol/L, which is at a normal level, so it can be inferred that the survey subjects have relatively normal blood lipid metabolism. At the same time, this study found that femoral neck BMD was negatively correlated with CatheK, serum osteocalcin, PINP, β-crosslaps, and TRAP, and lumbar spine BMD was also negatively correlated with CatheK, serum osteocalcin, PINP, β-crosslaps, and TRAP. It shows that the activity of osteoclasts in postmenopausal bone metabolism is enhanced, and postmenopausal osteoporosis is an osteoporosis with high turnover rate.

## Conclusions

This study finds that BMD severity and years since menopause are the most important risk factors inducing PMOP fractures. The smaller the BMI value and triglyceride, the greater the bone mass loss. There is no significant correlation with HDL-C, LDL-C, while the expression of biochemical markers of bone turnover is closely related to BMD. Postmenopausal osteoporosis is a high turnover bone disease, which is highly expressed in postmenopausal women, and increases with decrease of BMD. It can be used as a marker for predicting the disease. At the same time, combining the patient's age, number of deliveries, and whether there is a history of hysterectomy or ovariectomy and other closely related factors, it is possible to predict the incidence of PMOP fractures early.

However, due to the small sample size in this study, there may be certain limitations. The sample size should be expanded in the later stage to conduct stratified and further study on patients' age.

## Conflict of Interests

The authors declare that they have no conflict of interests.

## Funding

## Ethics Approval

This study was approved by the Ethics Committee of Chengdu Jinniu District People's Hospital.

## Informed Consent

The study was conducted with the informed consent of the patients.

## Availability of Data and Materials

The data are available upon reasonable request to the Corresponding Author.

## Authors' Contribution

Jia long: Design, survey, data collection, analysis and writing. Cheng Ming: Guidance and supervision.

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