



ORIGINAL ARTICLE

# Characteristics of bone biochemical indices in predicting secondary osteoporotic fracture after intertrochanteric fracture in elderly women



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## KEYWORDS

bone biochemical indices;  
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osteoporotic fractures;  
secondary fractures

**Summary** *Background:* This study aimed to explore the characteristics of bone biochemical indices, including bone mineral density (BMD), metabolic markers in elderly women with osteoporotic intertrochanteric fracture and their relevance in secondary fracture.

*Methods:* The standard for follow-up from 58 elderly women was established to analyse the BMD in the injured hip, healthy hip, and the vertebra at 1 week and 12 months after fracture. The serum levels of total procollagen type N-terminal propeptide (tPINP) and the age-related type I cross linked C-telopeptide ( $\beta$ -CTX) were recorded and compared between those patients with and without secondary fractures within 12 months.

*Results:* Twelve months after fracture, the serum levels of tPINP and  $\beta$ -CTX were significantly higher than the baseline values ( $p < 0.01$ ). The tPINP baseline in patients with secondary fracture was significantly lower than that in the rest patients without secondary fracture ( $p < 0.01$ ). The  $\beta$ -CTX baseline was notably higher than that without secondary fracture ( $p < 0.01$ ). BMD values of the three periods had no significantly difference.

*Conclusion:* The serum levels of tPINP and  $\beta$ -CTX are of great value in earlier and more sensitively reflecting the condition of bone turnover in body. Meanwhile, they can predict the subsequent fracture risk more accurately combined with a lower BMD.

*The Translational Potential of this Article:* Besides BMD, bone microstructure and remodeling levels can be accurately measured by bone biochemical indices. The main objective of this research is to explore the change of BMD and the serum level of bone biochemical indices of elderly women who suffered unilateral intertrochanteric fracture within 12 months.

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Simultaneously, with aim to better obtain bone remodeling level and predict more accurately the risk of a secondary osteoporotic fracture, bone biochemical indices of these patients, who undergo secondary osteoporotic fracture or not, are collected during follow-up and compared respectively.

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## Introduction

With the improvement of living standards in recent decades, people are living significantly longer than before. Therefore, the world is gradually developing into an ageing society and a series of resulting problems have become increasingly prominent. Owing to the weakening of body function, elderly people usually have varying degrees of osteoporosis. Particularly, postmenopausal women with dramatically decreased oestrogen have shown more severe osteoporosis [1,2].

As a systemic disease of the skeleton, osteoporosis can bring a great increase of skeletal fragility and risk of fracture [3] due to the reduced bone mass and damage to the bone microstructure [4,5]. Normally, fractures of vertebrae, proximal femur, and wrist are regarded as the typical osteoporotic fractures [4]. Proximal femur (hip) fracture is strongly related to low bone mineral density (BMD) and has become the international norm of osteoporosis and causes more disability than the other two types of osteoporosis fracture [4]. To make matters worse, 10–20% of patients die during the first year after a hip fracture according to Steven [4]. In general, BMD is merely one of the contributors to bone strength, which is also associated with other factors such as bone microstructure and remodelling levels, which can be accurately measured by bone biochemical indices [6,7]. Therefore, studying the dynamic change of BMD, the serum level of bone biochemical indices and dynamically monitoring bone mass, bone formation and bone resorption markers of postoperative elderly women with hip fracture are of significant importance for the early diagnosis and treatment of osteoporosis, as well as the predication of secondary osteoporotic fracture (SOF) and improvement of quality of life. Intertrochanteric fracture, which is a common type of hip fracture, is selected as an example in this work.

Our research aimed to explore the change in BMD and the serum level of bone biochemical indices within 12 months in elderly women with unilateral intertrochanteric fracture. Simultaneously, these biochemical indices in such women who had SOF or not during follow-up were collected and compared, which were expected to obtain better bone remodelling level and predict more accurately the risk of SOF.

## Materials and methods

The clinical study was approved by the Ethics Committee of the First Affiliated Hospital of Soochow University, and

written informed consent was obtained from all participants and was performed in accordance with the ethical standards of the Declaration of Helsinki of 1964. Fifty-eight elderly female patients (postmenopausal women with a mean age of  $80.5 \pm 7$  years; range 65–96 years) who were clearly diagnosed with unilateral intertrochanteric fracture (in accordance with fragility fracture) by radiography in our department, from March 2011 to December 2013, and treated with Gamma 3 nail fixation were selected randomly. The specific selection process was as follows: 102 patients were enrolled and 44 cases were excluded: not meeting inclusion criteria ( $n = 22$ ); declined to participate ( $n = 14$ ); and other reasons ( $n = 8$ ). The remaining 58 participants were required to meet the following criteria: (1) to eliminate the interference by oestrogen, all female patients were not less than 60 years old and had been in menopause for  $> 5$  years; (2) without antiosteoporosis treatment before fracture; (3) according to the patients' medical history, their fracture types were all conformed to first fragility fractures; SOF occurred without severe trauma, tumour, or tuberculosis and was diagnosed via computed tomography scan; (4) patients with delayed union or nonunion diagnosed by computed tomography scan were excluded; and (5) all participants were ruled out with diabetes, thyroid function hyperfunction, hyperparathyroidism, malignant tumour, and history of taking thyroid hormone or steroids. All participants were informed of the nature of this study. BMD of bilateral hip joints and lumbar vertebra of 58 participants were measured by dual energy X-ray absorptiometry before surgery. The results obtained within 1 week after fracture were set as baseline and were compared with data that were collected 12 months after fracture. Blood samples collected within 4 hours and 12 months after fracture were analysed by chemiluminescence immunoassay to acquire the two typical bone biochemical indices of total serum procollagen type N-terminal propeptide (tPINP) and age-related type I crosslinked C-telopeptide ( $\beta$ -CTX). Due to the lack of bone biochemical indices data before fracture, data collected at 4 hours after fracture were adopted as approximate baseline values as reported by Ivaska et al [8] based on the unobvious change of bone biochemical indices within 4 hours after fracture. Participants were divided into two groups (A: with SOF; B: without SOF) in accordance with whether SOF (hip, vertebral, wrist, and other fracture) occurred during 12 months follow-up. All women with SOF diagnosed clearly conformed to the following exclusion criteria: (1) traffic accident, high fall injury, and other severe trauma that led to subsequent fracture; and (2) pathological fracture. Meanwhile, the BMD of bilateral hip joints and lumbar

**Table 1** Baseline characteristics of patients with SOF.

Index	Age (y)	Time (mo)	SOF style					
			Hip	Vertebrae	Wrist	Others	Ipsilateral	Contralateral
Group A	70.41 ± 3.21	8.92 ± 3.11	3	2		7	1	4

SOF = secondary osteoporotic fracture.

**Table 2** Changes in BMD and bone biochemical indices in elderly women with intertrochanteric fracture.

Time	Affected hip	Healthy hip	Lumbar vertebrae	tPINP (µg/L)	β-CTX (µg/L)
Within 4 h/1 wk	-2.33 ± 0.56	-2.22 ± 0.41	-2.83 ± 0.40	48.3 ± 10.39	0.44 ± 0.15
12 mo	-2.40 ± 0.31	-2.31 ± 0.28	-2.99 ± 0.29	77.71 ± 8.38	0.76 ± 0.24
<i>p</i>	0.745	0.590	0.288	0.00001**	0.001**

Results for 58 patients, presented as mean ± standard deviation.

Compared with tPINP or β-CTX within 4 h.

\*\**p* < 0.01.

BMD = bone mineral density; β-CTX = age-related type I crosslinked C-telopeptide; tPINP = total procollagen type N-terminal propeptide.

vertebrae and these two typical bone biochemical indices described above in Groups A and B was collected and analysed.

Data are presented as mean ± standard deviation. The differences in BMD and serum level of tPINP and β-CTX between 4 hours and 12 months after fracture were compared by paired samples *t* test. A value of *p* < 0.05 showed that the difference was statistically significant between these groups.

## Results

Baseline characteristics of patients with SOF are shown in Table 1. The change in BMD and bone biochemical indices in elderly women with osteoporotic intertrochanteric fracture undergoing fracture healing is shown in Table 2. Twelve months after injury (namely 6 months after bone union was completed), the serum levels of tPINP and β-CTX, which represented the condition of bone formation and bone resorption, were still significantly higher than the baseline (*p* < 0.01). According to the World Health Organization osteoporosis diagnosis principles [9], the value of BMD at 12 months follow-up did not differ significantly compared with the baseline level. The baseline BMD and bone biochemical indices of patients after fracture in the two groups are summarised in Table 3. The mean tPINP in Group A

(49.90 ± 9.59 µg/L) was significantly lower than that in Group B (*p* < 0.01). The average β-CTX in Group A was 0.79 ± 0.22 µg/L, which was significantly higher than in Group B (*p* < 0.01). BMD of bilateral hip joints and lumbar vertebrae did not differ dramatically between the two groups.

## Discussion

Early research has shown that postoperative pain and immobilisation affect bone metabolism and accelerate the rate of decomposition, leading to loss of bone mass [10–12]. In addition, during the period of fracture healing, the bone turnover speeds up, which shows up as increased bone resorption and bone formation. It is well known that patients with a T score < -2.5 can be diagnosed with osteoporosis according to the World Health Organization [9]. However, bone strength was embodied in two main features: bone density and bone quality [13], indicating that BMD measurement alone is not adequate for judging fracture risk [14,15]. For example, for elderly postmenopausal women, owing to oestrogen deficiency physiologically, bone loss significantly increases. Therefore, predicting secondary fracture risk depending on higher bone loss only hides many potential secondary fracture risks and treatment efficacy [16,17]. In our study, there was no obvious difference in BMD collected at fracture

**Table 3** Baseline of BMD and bone biochemical indices of patients between two groups.

	Affected hip	Healthy hip	Lumbar vertebrae	tPINP (µg/L)	β-CTX (µg/L)
Group A	-2.40 ± 0.53	-2.26 ± 0.37	-2.83 ± 0.37	49.90 ± 9.59	0.79 ± 0.22
Group B	-2.44 ± 0.26	-2.33 ± 0.21	-2.93 ± 0.26	76.90 ± 8.43	0.43 ± 0.13
<i>p</i>	0.841	0.575	0.436	< 0.0001**	0.0001**

Results presented as mean ± standard deviation.

Compared with the other group, \*\**p* < 0.01.

BMD = bone mineral density; β-CTX = age-related type I crosslinked C-telopeptide; tPINP = total procollagen type N-terminal propeptide.

occurrence and 12 months after in elderly women with intertrochanteric fracture, further demonstrating that using BMD to reflect the real bone remodelling in elderly women after intertrochanteric fracture has a lack of specificity and sensitivity.

Bone biochemical indices are some metabolites generated in the process of bone remodelling, including two types of index of bone formation and bone resorption. The tPINP derived from collagen type I is considered to be a quantitative measure of newly formed type I collagen, which appears to be a sensitive index of bone formation rate [18]. Moreover,  $\beta$ -CTX is currently considered to be the best index for the evaluation of bone resorption [19]. Therefore, tPINP and  $\beta$ -CTX chosen in this work to assess bone remodelling are representative and significant. On the one hand, due to the healing mechanism and entering a period of active osteogenesis after fracture, bone formation index begins to rise; on the other hand, the bone resorption indices increase because of pain, immobilisation, bone decomposition, and necrotic bone resorption. Bone biochemical indices remain increased even after bone union is completed [20–23]. In our research, 12 months after fracture (namely 6 months after fracture healing), the serum level of tPINP and  $\beta$ -CTX was still significantly higher than the baseline value and the difference was consequential ( $p < 0.01$ ), suggesting that bone turnover was not complete and bone biochemical activity was still active. Garnero et al [24] have demonstrated that the combination of low BMD and high bone resorption measurement identify elderly women at higher risk of hip fracture than those identified by merely one feature. To confirm the effect of bone biochemical indices in predicting the risk of SOF, the BMD value and bone biochemical indices in these patients with or without SOF were compared. The mean tPINP in Group A was significantly lower than that in Group B ( $p < 0.05$ ). The average  $\beta$ -CTX in Group A was significantly higher than in Group B ( $p < 0.01$ ). BMD of bilateral hip joints and lumbar vertebrae did not dramatically differ between the two groups. Therefore, using BMD does not usually evaluate the real status of bone remodelling or predict SOF accurately. In this case, BMD combined with bone biochemical indices such as tPINP and  $\beta$ -CTX can achieve a more accurate and early evaluation of bone strength and bone quality, and provide more significant guidance in prevention of SOF.

The present study had several limitations. The sample size of our study was small. A larger study is needed. In addition, making a conclusion regarding predictive value of a measurement based on such uncontrolled and unadjusted analyses was risky because the results could have been influenced by known and unknown factors.

In conclusion, for elderly women with intertrochanteric fracture who have achieved clinical healing for 6 months (12 months after fracture), BMD is still lower than normal but does not differ significantly compared with at the time of fracture, and it also does not indicate change in bone strength and quality. More importantly, bone biochemical indices (tPINP and  $\beta$ -CTX) are still distinctly higher than the baseline at this period, indicating that bone remodelling still continues. Due to the lower tPINP and higher  $\beta$ -CTX at baseline in the SOF group, bone biochemical indices can earlier and more sensitively reflect the condition of bone

turnover in the body and more accurately predict the SOF risk combined with a lower BMD based on current findings.

## Conflicts of interest

The authors have no conflicts of interest relevant to this article.

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