



Calcaneal quantitative ultrasound–bone mineral density value for evaluating bone metabolism and bone turnover in patients with osteoporotic fracture

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ABSTRACT

Objective: To study the calcaneal quantitative ultrasound-bone mineral density (QUS-BMD) value for evaluating bone metabolism and bone turnover in patients with osteoporotic fracture.

Methods: A total of 150 patients who were diagnosed with osteoporotic fracture in Nuclear Industry 417 Hospital between January 2010 and March 2017 were selected as the fracture group of the research, and 70 subjects with normal bone mineral density confirmed by physical examination during the same period were selected as the control group of the research. QUS-BMD apparatus was used to measure bone mineral density of calcaneus, and the serum was collected to determine the biochemical indexes of bone metabolism and bone turnover.

Results: QUS-BMD value as well as serum BALP, OC, OPG levels of fracture group was significantly lower than those of control group while serum TRACP5b, RANKL, PINP, PICP, CTX and NTX levels were significantly higher than those of control group; serum BALP, OC, OPG levels of patients with osteoporosis and osteopenia were significantly lower than those of subjects with normal bone mass while TRACP5b, RANKL, PINP, PICP, CTX and NTX levels were significantly higher than those of subjects with normal bone mass; serum BALP, OC, OPG levels of patients with osteoporosis was significantly lower than those of patients with osteoporosis while TRACP5b, RANKL, PINP, PICP, CTX and NTX levels were significantly higher than those of patients with osteoporosis. **Conclusion:** Calcaneal QUS-BMD is valuable for evaluating the bone metabolism activity and bone turnover process in patients with osteoporotic fracture.

1. Introduction

Osteoporosis is a systemic bone metabolism disorder characterized by bone loss, decreased bone mineral and bone matrix as well as increased bone fragility, osteoporotic fracture is the most serious complication in osteoporosis, and it will seriously affect patients' daily life and is with high mortality and morbidity[1]. In recent years, with the aggravated aging of the population in our country, the incidence of osteoporosis and its complication osteoporotic fracture are rising year by year, which not only causes adverse effects on the patient's physical and mental health, but also brings economic burden to family and society. In clinical practice, accurate measurement of bone density, early screening for osteoporosis

patients and timely intervention are the effective means to reduce osteoporotic fracture. Dual energy X-ray absorptiometry (DXA) is the gold standard to measure bone mineral density and diagnose osteoporosis, but the instrument is expensive and difficult to be popularized in disease screening[2]. Quantitative ultrasound-bone mineral density (QUS-BMD) is a method of bone density detection in recent years, and the test instrument is cheap, easy to carry, and more suitable for disease screening[3]. The calcaneal QUS-BMD value for evaluating bone metabolism and bone turnover in patients with osteoporotic fracture was analyzed in the following study.

2. Research subjects and research methods

2.1. General information of research subjects

A total of 150 patients who were diagnosed with osteoporotic fracture in Nuclear Industry 417 Hospital between January 2010 and March 2017 were selected as the fracture group of the research, all patients are with history of osteoporosis and had new fracture

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without trauma, and the patients with fracture caused by trauma and those complicated by thyroid or parathyroid dysfunction were ruled out. 70 subjects with normal bone mineral density confirmed by physical examination during the same period were selected as the control group of the research, they were without history of fractures or the history of taking anti-osteoporosis drugs, and those complicated by thyroid or parathyroid dysfunction were ruled out. Fracture group included 62 men and 88 women that were 53-76 years old; control group included 31 men and 39 women that were 50-73 years old. There was no significant difference in general data between the two groups ($P>0.05$).

2.2. Clinical research methods

2.2.1. Ultrasonic calcaneus bone mineral density measurement

Quantitative ultrasound-bone mineral density instrument from OsteoSys company was used for bone mineral density measurement, the instrument was corrected with a standard module after start-up, then the patient's left calcaneus was placed between the ultrasonic probes, the position was adjusted to make the calcaneus in the middle of both sides of probes, and the T value of bone mineral density was measured. The method of bone mineral density estimation was as follows: T value $>-1.0SD$ indicated normal bone mass, $-2.5SD<T$ value $-1.0SD$ indicated osteopenia, and T value $\leq -2.5SD$ indicated osteoporosis.

2.2.2. Serum biochemical index detection

About 5-6 mL of peripheral venous blood was collected from the fracture group immediately after admission, and 5-6 mL of venous blood was collected from control group during physical examination. The venous blood was let stand at room temperature for about 30 min and then centrifuged in the centrifuge for 20 min at a speed of 3 000 r/min to separate serum, and the BALP, OC, TRACP5b, RANKL, OPG, PINP, PICP, CTX and NTX levels were detected by enzyme-linked immunosorbent assay kits.

2.3. Statistical processing methods

SPSS 23.0 software was used to statistically process the data, the data comparison between two groups were by t test, data comparison among three groups was by variance analysis, and $P<0.05$ indicated statistical significance in differences in test and analysis results.

3. Results

3.1. QUS calcaneus bone mineral density value

QUS-BMD value of fracture group was $-(2.03\pm0.35)$ and QUS-BMD value of control group was (0.82 ± 0.11) . After t test analysis, QUS-BMD value of fracture group was significantly lower than that of control group ($P<0.05$).

3.2. Serum bone metabolism biochemical index levels and their correlation with QUS calcaneus bone mineral density value

Analysis of serum osteoblast biochemical indexes BALP (pg/mL) and OC (pg/mL) as well as osteoclast biochemical indexes TRACP5b (ng/mL), RANKL (pg/mL) and OPG (ng/mL) between fracture group and control group was as follows: serum BALP, OC, OPG levels of fracture group was significantly lower than those of control group while serum TRACP5b, RANKL levels were significantly higher than those of control group. Differences in serum BALP, OC, TRACP5b, RANKL and OPG levels were statistically significant between fracture group and control group ($P<0.05$).

According to the QUS calcaneus bone mineral density value, the subjects were divided into osteoporosis, osteopenia and normal bone mass group, and further analysis of osteoblast biochemical indexes BALP, OC, OPG as well as osteoclast biochemical indexes TRACP5b, RANKL and OPG levels showed that serum BALP, OC, OPG levels of subjects with osteoporosis and osteopenia were significantly lower than those of subjects with normal bone mass while TRACP5b, RANKL levels were significantly higher than those of subjects with normal bone mass; serum BALP and OC levels of subjects with osteoporosis was significantly lower than those of patients with osteoporosis while TRACP5b, RANKL levels were significantly higher than those of patients with osteoporosis. Differences in pair-wise comparison of serum BALP, OC, TRACP5b, RANKL and OPG levels were statistically significant among subjects with osteoporosis, osteopenia and normal bone mass ($P<0.05$).

Table 1.

Comparison of serum bone metabolism biochemical indexes between two groups of subjects.

Groups	n	BALP	OC	TRACP5b	RANKL	OPG
Fracture group	150	13.41±1.88	11.25±1.64	3.52±0.52	242.5±32.5	1.52±0.22
Control group	70	22.42±3.49	25.68±3.27	2.11±0.34	94.5±10.2	2.89±0.36
T		8.947	12.482	7.686	15.298	9.028
P		<0.05	<0.05	<0.05	<0.05	<0.05

Table 2.

Relationship between QUS calcaneus bone mineral density value and serum bone metabolism biochemical indexes.

Bone mineral density	n	BALP	OC	TRACP5b	RANKL	OPG
Osteoporosis	88	10.11±1.48 ^{ab}	10.49±1.35 ^{ab}	4.27±0.59 ^{ab}	296.5±34.5 ^{ab}	1.41±0.19 ^{ab}
Osteopenia	60	14.89±1.94 ^a	17.68±2.32 ^a	3.32±0.44 ^a	221.2±26.9 ^a	2.31±0.35 ^a
Normal bone mass	72	22.54±4.03	26.41±3.62	2.03±0.34	113.2±14.5	3.13±0.42
F		12.192	15.683	11.938	17.583	12.857
P		<0.05	<0.05	<0.05	<0.05	<0.05

^a: compared with normal bone mass group, $P<0.05$; ^b: compared with osteopenia group, $P<0.05$.

Table 3.

Comparison of serum bone turnover biochemical indexes between two groups of subjects.

Groups	n	PINP	PICP	CTX	NTX
Fracture group	150	72.51±9.35	57.21±6.72	0.69±0.09	1.25±0.15
Control group	70	44.25±6.45	30.24±4.95	0.32±0.05	0.54±0.08
T		8.384	9.215	11.283	12.598
P		<0.05	<0.05	<0.05	<0.05

Table 4.

Relationship between QUS calcaneus bone mineral density value and serum bone turnover biochemical indexes.

Bone mineral density	n	PINP	PICP	CTX	NTX
Osteoporosis	88	80.33±10.25 ^{ab}	61.24±7.02 ^{ab}	0.81±0.11 ^{ab}	1.21±0.14 ^{ab}
Osteopenia	60	57.85±8.34 ^a	43.34±5.96 ^a	0.42±0.06 ^a	0.88±0.11 ^a
Normal bone mass	72	41.24±5.96	31.24±4.95	0.28±0.06	0.52±0.07
F		9.985	10.284	18.955	12.512
P		<0.05	<0.05	<0.05	<0.05

^a: compared with normal bone mass group, $P < 0.05$; ^b: compared with osteopenia group, $P < 0.05$.

3.3. Serum bone turnover biochemical index levels and their correlation with QUS calcaneus bone mineral density value

Analysis of serum bone turnover biochemical indexes PINP, PICP, CTX and NTX between fracture group and control group was as follows: serum PINP, PICP, CTX and NTX levels of fracture group were significantly higher than those of control group. Differences in serum PINP, PICP, CTX and NTX levels were statistically significant between fracture group and control group ($P < 0.05$).

According to the QUS calcaneus bone mineral density value, the subjects were divided into osteoporosis, osteopenia and normal bone mass group, and further analysis of bone turnover biochemical indexes PINP, PICP, CTX and NTX levels showed that serum PINP, PICP, CTX and NTX levels of subjects with osteoporosis and osteopenia were significantly higher than those of subjects with normal bone mass; serum PINP, PICP, CTX and NTX levels of subjects with osteoporosis were significantly higher than those of patients with osteoporosis. Differences in pair-wise comparison of serum PINP, PICP, CTX and NTX levels were statistically significant among subjects with osteoporosis, osteopenia and normal bone mass ($P < 0.05$).

4. Discussion

Osteoporosis is a common systemic bone metabolism disorder in the elderly population. The incidence of osteoporosis has been increasing in recent years. In the course of osteoporosis, the bone mass of the bones in the whole body reduces and the bone brittleness increases, which will increase the risk of osteoporotic fracture. Thoracolumbar spine, hip and distal radius are the commonly involved areas of osteoporotic fracture, and both treatment difficulty and recurrence risk are bigger. In clinical practice, accurate measurement of bone mineral density, early screening for osteoporosis and timely treatment intervention are the effective ways to prevent osteoporotic fractures[4]. DXA is the gold standard for measuring bone density and diagnosing osteoporosis, but the test instrument is expensive and difficult to be used for large-scale screening[5]. QUS-BMD is a newly developed means of bone mineral density measurement, ultrasonic instrument costs less, is

easy to carry and can avoid the ionizing radiation, and compared with DXA, it is more suitable for mass screening for disease[6,7]. It has been confirmed that the QUS-BMD measurement has a good correlation with DXA measurement, DXA measurement results are the gold standard, and the QUS-BMD measurement has a better sensitivity and specificity for diagnosis of osteoporosis. In the above studies, QUS-BMD instrument was used to evaluate the bone mineral density of patients with osteoporotic fracture, and the results showed that QUS-BMD value of fracture group was significantly lower than that of control group. This preliminarily confirms that the QUS-BMD measurement is quite valuable for evaluating the bone mineral density in patients with osteoporotic fractures.

In the development of osteoporosis, the bone metabolism mediated by osteoblasts and osteoclasts is disturbed and unbalanced. BALP and OC are molecules that are closely related to the metabolic activity of osteoblasts, and they are synthesized and secreted by mature osteoblasts. BALP has the effect of promoting bone mineralization and increasing the deposition of bone matrix. OC is an important non-collagen component in bone matrix and participates in the process of bone matrix mineralization[8-10]. In the study, analysis of the above osteoblast biochemical indexes in serum of patients with osteoporosis confirmed that serum BALP and OC levels of fracture group were significantly lower than those of control group. TRACP5b, RANKL and OPG are molecules closely related to the metabolic activity of osteoclasts. Both RANKL and TRACP5b are synthesized and secreted by osteoclasts, the former can promote bone degradation after combined with receptor RANK, and the latter is involved in the degradation of calcium phosphate mineralizer in bone matrix[11]; OPG is secreted by osteoblasts and is able to compete with the RANK on the surface of osteoclasts to be combined with RANKL and thus inhibit the activity of osteoclasts[12]. In the study, analysis of serum levels of these osteoclast biochemical indexes in patients with osteoporotic fracture showed that serum OPG level of fracture group was significantly lower than that of control group while TRACP5b and RANKL levels were significantly higher than those of control group. This indicates that osteoblasts activity weakening and osteoclast activity enhancing

can lead to bone metabolism disorder, which leads to the bone mass loss and the occurrence of osteoporosis and osteoporotic fracture. Further analysis of the correlation between QUS-BMD value and bone metabolism indexes showed that serum BALP, OC, OPG levels of subjects with osteoporosis and osteopenia were significantly lower than those of subjects with normal bone mass while TRACP5b, RANKL levels were significantly higher than those of subjects with normal bone mass, and the changes of above bone metabolism indexes in patients with osteoporosis were more significant than those in patients with osteopenia. This means that QUS-BMD value is correlated with bone metabolism in patients with osteoporotic fractures, and QUS-BMD measurement can assess the activity of osteoblasts and osteoclasts in the course of osteoporosis.

Changes of osteoblast and osteoclast activity will further cause the change of bone turnover process, the overall performance is the increase of both bone turnover rate and bone loss, and there is the change in serum levels of various biochemical markers. Type I collagen is the most abundant component in bone matrix, and accounts for more than 90% of the bone matrix. In the transformation from type I procollagen to type I collagen, the elongation polypeptides in the carboxyl terminal and amino terminal of the type I procollagen are lysed by protease, and the products are PINP and PICP respectively. Therefore, the PINP and PICP released into the blood circulation can reflect the synthesis rate of type I collagen[13,14]. CTX and NTX are the pyrolysis products of carboxyl terminal and amino terminal in the degradation process of type I collagen, and they can reflect the degradation rate of the type I collagen after released into the blood circulation. The deposition and degradation of type I collagen in bone is a dynamic change process. When the degradation rate exceeds the deposition rate, osteoporosis occurs[15,16]. In the study, analysis of serum levels of these bone turnover biochemical indexes in patients with osteoporotic fracture showed that serum PINP, PICP, CTX and NTX levels of fracture group were significantly higher than those of control group. This means that intensified bone turnover process and the type I collagen degradation rate exceeding the deposition rate in the bone matrix are closely related to the course of osteoporosis and the occurrence of osteoporotic fracture, and the exorbitant bone turnover rate can cause bone loss and bone mineral density decrease. Further analysis of the correlation between bone mineral density value and bone turnover indexes showed that serum PINP, PICP, CTX and NTX levels of subjects with osteoporosis and osteopenia were significantly higher than those of subjects with normal bone mass, and the changes of above bone turnover indexes in patients with osteoporosis were more significant than those in patients with osteopenia. This indicates that the QUS-BMD value is correlated with the bone turnover process in patients with osteoporotic fractures, and the activity of bone turnover in osteoporosis can be assessed by QUS-BMD measurement.

Calcaneal QUS-BMD is consistent with the metabolism activity of osteoblasts and osteoclasts activity as well as the bone turnover processes of bone matrix deposition and degradation in patients with osteoporotic fracture, and it can accurately assess the bone metabolism activity and bone turn over process.

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