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## Original article

# Does serum calcium relate to different types of hip fracture? A retrospective study

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## ABSTRACT

**Purpose:** To investigate the potential correlation between two different types of hip fractures and serum calcium levels.

**Methods:** We consecutively studied 101 cases of femoral neck fracture and 95 cases of femoral intertrochanteric fracture between January 2011 and December 2013. Fasting blood samples were taken and serum calcium measurements were performed respectively in three periods: the time of admission, postoperation, and discharge. Creatinine, alkaline phosphatase and albumin were also analyzed.

**Results:** Considering the levels of serum calcium between two groups at the time of admission, post-operation and discharge, there was significant difference at admission and discharge ( $p < 0.05$ ), while there was no significant difference at the time of postoperation ( $p > 0.05$ ). The magnitude of serum calcium fluctuation was larger in femoral neck group than femoral intertrochanteric group. Concerning alkaline phosphatase and albumin levels at admission, there was no significant difference between two groups ( $p > 0.05$ ).

**Conclusion:** The capability of reservation and restoration of serum calcium in patients with femoral neck fracture is better than that in patients with femoral intertrochanteric fracture. A low serum calcium level may be susceptible to femoral intertrochanteric fracture.

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## Introduction

Aged-related and osteoporotic fracture, especially hip fracture, is one of the most common injuries in the elderly population. It is more prominent as the increase of China's aging population, accounting for 9.76% of the whole population in China. The number of hip fractures throughout the world is estimated approximately to 2.6 million by the year 2025, and 4.5 million by the year 2050.<sup>1</sup> Because of high mortality and morbidity<sup>2</sup> and high socioeconomic costs,<sup>3</sup> hip fracture has been studied in many aspects ranging from its mechanism and treatment, as well as the concerns to minimize medical expense. There are two main types of hip fractures according to the involved anatomic site: femoral neck fracture and femoral intertrochanteric fracture. They may have different characteristics and outcome.<sup>4</sup> Some factors may induce different types of hip fractures. Some authors have attempted to identify the different characteristics between femoral neck fracture and

femoral intertrochanteric fracture, and suggested that old age is more common in patients with femoral intertrochanteric fracture and low bone mineral density is more strongly related to femoral neck fracture.<sup>5</sup> Calcium has anti-fracture effect based on its key structural role in bone and metabolic balance.<sup>6,7</sup> Serum calcium level shows some changes in different periods of fracture healing process<sup>8</sup> and serum lactate is a prognostic indicator for patients with hip fracture.<sup>9</sup> The fluctuation of serum calcium levels may represents the capability of calcium transportation, reservation, metabolism, and restoration. We attempted to investigate the correlation between two different types of hip fractures and the fluctuation of serum calcium levels in a retrospective study.

## Patients and methods

This series included all the patients who were admitted to our hospital for hip fracture between January 2011 and December 2013. Inclusion criteria were: (1) femoral neck fracture and femoral intertrochanteric fracture diagnosed by imaging; (2) acute and primary unilateral fracture; (3) receiving operative treatment; (4) no parathyroid and thyroid diseases. Exclusion criteria were: (1) recurrent hip fracture; (2) pathological fracture; (3) a history of

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primary or metastatic tumor, tuberculosis, or chemoradiotherapy; (4) fractures caused by local and direct trauma; (5) a history of stroke and poliomyelitis; (6) a history of anti-osteoporosis treatment.

The subjects corresponding to the study criteria were divided into femoral neck fracture group (101 cases) and femoral intertrochanteric fracture group (95 cases). The age, gender, and unilateral lesion were collected from all patients. Fasting blood samples were measured using automatic biochemical analyzer (Cobas 8000, Germany) in three periods: the time of admission, postoperation and discharge. The time of admission and postoperation refers to the first day after admission or operation, while the time of discharge means the day of discharge. Neither special diet nor calcium was applied to patients after surgery. Low albumen is a sign of systemic inflammation as well as potentially chronic nutritional insufficiency. Therefore, serum calcium, creatinine, BUN, alkaline phosphatase, and albumin were evaluated in the three periods. Our research was approved for the ethic consents by the department concerned in our hospital.

The gender and injured side in two groups were compared by  $\chi^2$  test. The age is expressed by mean  $\pm$  standard deviation ( $\bar{x} \pm s$ ), and compared by *t*-test. Analysis of variance (ANOVA) was used to compare serum calcium, creatinine, and BUN levels of three different periods.

## Results

A total of 196 hip fractures were included in this study. The femoral neck fracture group consisted of 101 cases, in which 81 cases (80.20%) were female, and 20 (19.80%) were male. Right side lesions were found in 52 cases (51.49%), and left lesions in 49 cases (48.51%). The mean age was 73.85 years. The femoral intertrochanteric fracture group consisted of 95 cases. Over half of the cases (55 cases, 57.89%) were female, and 40 cases (42.11%) were male. Left side lesions were found in 49 cases (51.58%), and right side lesions in 46 cases (48.42%). The mean age was 76.27 years. In femoral neck fracture group, the mean time from injury to admission was ( $26.3 \pm 22.4$ ) hours, mean time from admission to surgery was ( $41.7 \pm 22.5$ ) hours, and mean length of surgery was ( $1.6 \pm 0.7$ ) hours. Surgical fixation procedures were compressed hollow screws in 5 cases, dynamic/sliding hip screw with long plate in 2 cases, and total hip replacement in 94 cases. The mean time from operation to discharge was ( $7.4 \pm 2.1$ ) days. In femoral intertrochanteric fracture group, the mean time from injury to admission was ( $20.9 \pm 15.1$ ) hours, mean time from admission to surgery was ( $39.3 \pm 19.4$ ) hours, and mean length of surgery was ( $1.4 \pm 0.8$ ) hours. Surgical fixation procedures were proximal femoral nail antirotation (PFNA) in 81 cases, dynamic/sliding hip screw with long plate in 9 cases, and intramedullary nail in 5 cases. The mean time from operation to discharge was ( $8.7 \pm 2.2$ ) days. There was significant difference in gender between two groups ( $p < 0.05$ ). As to lesions region, there was no significant difference ( $p > 0.05$ , Table 1).

**Table 1**  
Comparison of the characteristics of two groups.

Group	Cases	Gender (n, %)		Unilateral lesion (n, %)		Age ( $\bar{x} \pm s$ )
		Male	Female	Left	Right	
A	101	20 (19.80)	81 (80.20)	49 (48.51)	52 (51.49)	73.85 $\pm$ 11.88
B	95	40 (42.11)	55 (57.89)	49 (51.58)	46 (48.42)	76.27 $\pm$ 11.93
$\chi^2/t$ value		11.464		0.184		1.422
<i>p</i> value		0.001		0.668		0.157

A: femoral neck fracture group, B: femoral intertrochanteric fracture group.

Comparison of the levels of serum calcium between two groups is displayed in Table 2. Alkaline phosphatase and albumin levels are shown in Table 3.

**Table 2**

Serum calcium levels at the time of admission, postoperation and discharge in two groups.

Group	Serum calcium levels ( $\bar{x} \pm s$ )		
	Admission	Postoperation	Discharge
A	2.19 $\pm$ 0.12	2.01 $\pm$ 0.12	2.15 $\pm$ 0.13
B	2.13 $\pm$ 0.15	2.01 $\pm$ 0.14	2.10 $\pm$ 0.16
$\chi^2/t$ value	3.080	0.000	2.372
<i>p</i> value	0.002	1.000	0.019

A: femoral neck fracture group, B: femoral intertrochanteric fracture group.

**Table 3**

ALP and albumin levels at admission in two groups.

Group	Alkaline phosphatase ( $\bar{x} \pm s$ )	Albumin ( $\bar{x} \pm s$ )
A	79.88 $\pm$ 40.36	39.34 $\pm$ 30.55
B	89.38 $\pm$ 65.76	40.54 $\pm$ 31.38
<i>t</i> value	1.2269	0.2712
<i>p</i> value	0.2213	0.7865

A: femoral neck fracture group, B: femoral intertrochanteric fracture group.

## Discussion

In this study, we found that patients with femoral neck fractures were generally younger and involved in more women than those with intertrochanteric fractures, and those with intertrochanteric fractures had lower serum calcium values at the time of admission and discharge. Hip fracture is a complex fracture involved in many factors.<sup>10–14</sup> A strategy to secure adequate and standardized perioperative treatment is important. Age, injury mechanism, local anatomic factor, insulin-like growth factor and static balance ability are factors potentially inducing different types of hip fractures. Calderazzi et al<sup>15</sup> found that osteoarthritis strongly affects the location of the fracture in the proximal femur. In our other biomechanics study, we collected 16 patients' images (8 femoral intertrochanteric and 8 femoral neck fractures), and analyzed the lateral lesion by finite element analysis, and found that the type of hip fracture may be influenced by different densities of fractured region, namely, bony mineral density may predict the location of hip fracture. Larrosa et al<sup>4</sup> compared 128 patients with femoral neck fractures and 196 patients with femoral intertrochanteric fractures. No difference was found in the age, sex, calcium level, nutritional, healthy, and functional status or presence of previous fractures between groups. Since these data obtained were only from admission to surgical intervention, it did not represent the whole dynamic changes of serum calcium levels in two different types of hip fractures, which may not indicate the capability of calcium transportation, reservation, metabolism, and restoration.

Calcium balance refers to the state of the body stores up calcium at equilibrium over some extended period (usually days, weeks or months).<sup>16</sup> This study is the first one to observe serum calcium levels in patients at three periods, i.e. admission, postoperation, and discharge. Since all these fractures were acute injury cases and the blood samples were drawn at the time of admission when the fracture healing process had not yet started, admission sample would roughly predict the basic level of serum calcium (calcium reservation). Postoperative sample would roughly show the accommodated level of serum calcium under the condition of stress reaction to trauma (calcium transportation and metabolism). Discharge sample would roughly reflect the

resilience level of serum calcium in the recovery process (calcium restoration). Concerning the albumin level at admission between two groups, the difference was not statistically significant, indicating that the situation of the nutritional status of the patients in two groups is similar. The levels of serum calcium from admission to discharge were higher in femoral neck fracture group than femoral intertrochanteric fracture group. The magnitude of serum calcium fluctuation was larger in femoral neck group than femoral intertrochanteric group, indicating that the capability of reservation, restoration of serum calcium is better in patient with femoral neck fractures than those with femoral intertrochanteric fractures.

Calcium plays a key role in a wide range of biologic functions, either in the form of its free ion or bound complex. One of the most important functions as bound calcium is skeletal mineralization, which accounts for more than 99% in proportion of total body calcium. Serum calcium represents ionized calcium, which represents less than 1% of total body calcium. Among them, 35% combine with albumin, the other 60% exist as activated ions, and the remaining 5% become citric acid, carbonic acid or phosphoric acid complex. Serum calcium homeostasis has evolved to simultaneously maintain extracellular ionized calcium levels in the physiologic range, allowing the flow of calcium to and from essential stores. Biological calcium, especially ionized calcium, has important significance in the body's physiological function to maintain the body's normal life activities. With regard to the signal transduction factor that most commonly used in an organism, calcium plays an important role in the process of cellular division, growth and apoptosis, regulating the life process from fertilization, development, reproduction to nerve excitement and conduction.<sup>17</sup>

Physiological functions of serum calcium are generally divided into five aspects. (1) Calcium is an important factor in the process of coagulation: ionized calcium prompts prothrombin into thrombin that turns fibrinogen into fibrin in order to make blood clotting. (2) Calcium can maintain a normal permeability inside and outside of blood vessels to reduce the permeability of cell membrane of capillaries. (3) Calcium participates in the activation of many enzymes and enhancement of the activity in the body. Calcium in the cytoplasm regulates all sorts of physiological activities of cells as a messenger. When intracellular ionized calcium concentration increases, it activates a variety of protease and finishes all kinds of the body physiological activities by combination with CaM protein. (4) The contraction of cardiac muscle and skeletal muscle relies on by calcium transportation and metabolism. (5) Because it can reduce the excitability of nerve muscle, ionized calcium is of important significance in the biology of neuromuscular excitement and transmission of nerve impulse.

We hypothesized that two potential mechanisms may correlate with the type of hip fracture. (1) Elderly individuals are typically in a negative bone balance, which leads to age-related bone loss. Though bone mineral density can not be totally measured by serum calcium level, ionized calcium can relatively reflect body calcium (calcium reservation) to some extent, and reveal bone mineral density based on its key structural role in the bone. Bone strength is not only related with bony mineral density, but also with bone ultrastructure, which has a close relationship with the mechanical properties.<sup>7</sup> The level of serum calcium may affect bone ultrastructure. Thus, different types of hip fractures are induced by anatomic specificity of the bone, i.e. mineral density. We hypothesized that compared with femoral neck fracture, femoral intertrochanteric fracture belongs to extracapsular hip fractures. The capsular ligament of hip joint (iliofemoral ligament, pubofemoral ligament, and ischiofemoral ligament) may provide relative stability, preventing femoral neck from torsional displacement of three axes. (2) A mechanism by which serum calcium might influence fracture type is via its binding to the

calcium-sensing receptor because these receptors are expressed on vascular smooth muscle cells. Serum calcium fluctuation can reveal the ability of calcium transportation and restoration, which affects the number and sensitivity of calcium-sensing receptor in the lower limb muscle. Lower limb muscle strength, especially the iliopsoas and gluteus, play an important role in the process of maintaining posture balance. Lower limb muscle strength decline is the main factor for oscillation amplitude increase of standing posture in old people, damaging the elderly to correct body gravity swings. Therefore standing ability decline can lead to increased risk of falls. In addition, as the serum calcium decreases, neurotransmitter release is affected, so did excitement and inhibition function of the nervous system. As a result, a performance of neurasthenia and low nervous adjustment appear in old-aged persons. In our series, serum calcium values maintained at a critical low level in the two groups after operation, suggesting that the transportation ability of serum calcium under stress is similar in two groups. We regard it as a self-protective reaction to avoid the danger of calcium deficiency.

The limitation in our study is its small number of samples. Whether the surgical intervention would influence serum calcium is not fully considered in this study. In addition, the mechanisms by which serum calcium fluctuation may induce two different hip fracture types need further research including experimental and randomized controlled trials.

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