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Ex Vivo Evaluation of Hip Fracture Risk by Proximal Femur Geometry and Bone Mineral Density in Elderly Chinese Women

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Background:
The incidence of hip fracture is steadily increasing. We aimed to establish a creative approach to precisely estimate the risk of hip fracture by exploring the relationship between hip fracture and bone mineral density (BMD)/femur geometry.

Material/Methods:
Sixteen samples of cadaveric female proximal femora were randomly selected. Experiments were performed experimental measurement of the femoral neck BMD and geometric parameters (including neck length, neck diameter, head diameter, and neck-shaft angle). In addition, the experimental measurements contain the failure load, which represents the mechanical strength of the femoral neck, and we calculated the correlation coefficient among BMD, geometric parameters, and failure load.

Results:
Significant correlations were discovered between femoral mechanical properties and femoral neck BMD ($r=0.792$, $r^2=0.628$, $P<0.001$), trochanteric BMD ($r=0.749$, $r^2=0.560$, $P=0.001$), and head diameter ($r=0.706$, $r^2=0.499$, $P=0.002$). Multiple linear regression analyses indicated that the best predictor of hip fracture was the combination of femoral neck BMD, head diameter, and neck diameter ($r^2=0.844$, $P<0.001$).

Conclusions:
The results confirmed that, compared with BMD alone, the combination of BMD and geometric parameters of proximal femur is a better estimation of hip fracture. The geometry of the proximal femur played an important role in assessing the biomechanical strength of femur. This method greatly assists in predicting the risk of hip fracture in clinical trials and will assist studies on why the incidence of hip fracture varies among races.

MeSH Keywords:
Bone Density Conservation Agents • Geography, Medical • Hip Fractures • Osteoporosis

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Background

Osteoporosis is a type of metabolic bone disorder characterized by reduced bone mass and deterioration of bone structure [1]. Bone fragility and susceptibility to fracture are increased due to resorption of bone [2] and changes in bone geometry [3,4]. Osteoporotic hip fracture is a major public health problem due to its mortality, disability, and financial costs for treatment, particularly among elderly patients. For efficient targeting of preventive care, an effective and precise method to estimate the risk of fracture would be of practical value [5,6].

A number of different techniques for the assessment of bone fracture risk have been described, such as ultrasound (US), high-resolution computed tomography (CT), and magnetic resonance imaging (MRI). However, there are inherent limitations in the application of these techniques, such as inaccuracy (US) [7], radiation dose (CT) [8], and costs (CT and MRI) [9].

Dual energy X-ray absorptiometry (DXA) of the hip is the most widely applied technique in quantitative assessment of bone mineral density (BMD) *in vivo* and is currently used as an indicator of osteoporosis by the World Health Organization (WHO) [10]. Previous *in vitro* investigations have shown that femoral neck strength is highly correlated with BMD, which is most often used as a representative measure of proximal femoral BMD to predict the risk of hip fracture [11,12]. However, DXA lacks reliability in predicting individual risk of fracture [13] because DXA cannot elucidate trabecular bone structure, which is important in maintaining bone integrity and mechanical strength [2,14].

The geometry of the proximal femur is related to mechanical strength as determined by analysis of X-ray images, which was previously proposed for measuring bone structure [15,16]. Unfortunately, some issues remain controversial when explicitly detailing such a relationship; for example, which geometric parameter of the hip has the closest association with femoral neck mechanical strength, and how it is related [3,17]. The objectives of the present research were: a) to determine how BMD is related to femoral neck mechanical strength; b) to determine which geometric parameter is most related; and c) to find the combination of BMD and some geometric parameter(s) that can best describe the risk of hip fracture.

Material and Methods

Sample preparation

The experimental sample consisted of 16 right proximal femur patients (all females, mean age 77.8±10.2 years). The samples were obtained from the Institute of Anatomy at the Fourth Military Medical University, Xi'an, Shannxi Province, China.

This study was officially approved by the institutional Ethics Committee of the Air Force Medical University (No. 033782).

The criterion for inclusion was a testamentary decree to the institute several years prior to death so that the samples could be assumed to be representative of the population of this age range in China. The individuals had a wide range of social backgrounds, with no detailed social history available. The main causes of death, obtained from autopsy reports and clinical diagnoses, were heart failure, pneumonia, stroke, and sepsis. To identify samples with bone diseases other than osteoporosis or osteopenia, biopsies were taken from the left iliac crest for histology observation. Individuals with bone diseases other than osteoporosis or osteopenia were excluded from the study [16,18].

The proximal femora were excised within 10 days after death. We cleaned the surrounding soft tissue and trimmed it with a handsaw approximately 10 cm below the lesser trochanter. All the samples were radiographed to exclude those with prior fracture or other local bone disorders. Each femur was sealed in a double-layered plastic bag and stored in a –20°C cryogenic freezer [19]. The tissues were placed in a clean lab at room temperature for 24 h to thaw naturally before any measurements or tests. All the samples were maintained moist continuously during geometry measurement, radiography, DXA measurement, and mechanical testing [18].
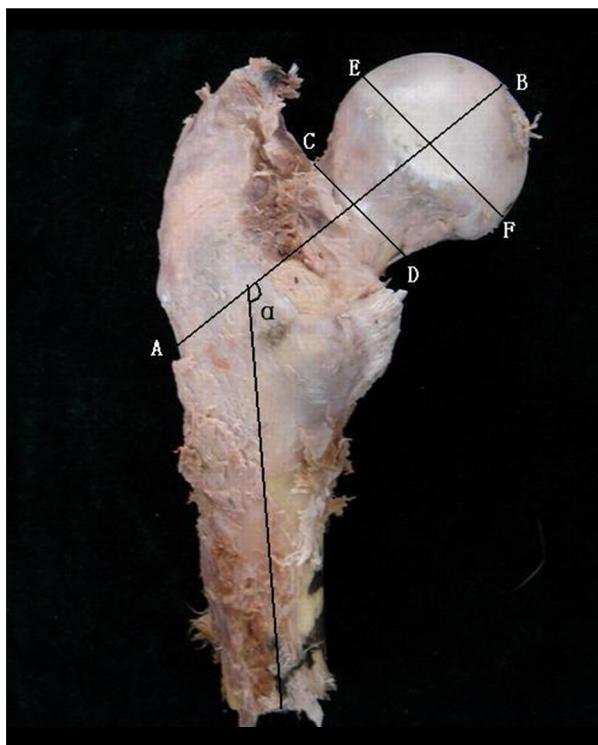
Geometry

All of the geometric parameters (including neck length, neck diameter, head diameter, and neck-shaft angle, Figure 1) of the proximal femur were measured using a vernier caliper.

Densitometry

Vitro DXA scans of the femora were obtained using a standard narrow-angle fan-beam scanner (GE Lunar Prodigy; GE Lunar Corp., Madison, WI, USA) (Figure 2). The scans were evaluated with the software provided by the manufacturer, providing results of BMD (g/cm^2) of the total proximal femur. The experimental measurements were performed independently 3 times; the average value was calculated as the result.

Biomechanical tests

The distal end of the femur and the proximal end of the femoral neck were potted into 2 specially designed mild steel cylinder connectors with dental cement at an anatomical angle of 18° from the vertical [26]. The tests were performed on the MTS 880 material testing system (MTS System Inc., Minneapolis, MN, USA). The original load was applied and gradually increased at a rate of 12.7 mm/min until failure load occurred,

Figure 1. Geometry of proximal femur ;A, B – Femoral neck axis length from the external side of the trochanter to the inner pelvic brim; C, D – Femoral neck diameter orthogonally to the hip axis at the narrow portion of the femoral neck; E, F – Femoral head diameter orthogonally to the hip axis at the wide portion of the femoral head; α – Neck-shaft angle between the femoral neck and shaft axis; G, H – femoral shaft axis.

and the values were recorded (failure criteria: occurrence of fracture, rupture in femoral head or neck) [19]. The loading signals from the testing machine were automatically recorded by a computer data acquisition system and the maximum mechanical strength was calculated with corresponding software.

Statistical analysis

All data were analyzed with SPSS version 24.0 software (SPSS, Inc., Chicago, IL) and are presented as mean value ± standard deviation. We used linear correlation regression and multiple linear regression analyses to determine the correlation between geometric parameters, BMD, and failure load of the femoral neck of each specimen. The results were used to compare different influences on the failure load of the femoral neck and to unveil the underlying relationship. Pearson's correlation coefficient (r), coefficient of determination, and P value were used to describe the relationship between BMD of the femoral neck and each geometric parameter with failure load. In addition, multiple linear regression analyses were used to determine whether certain combinations of related parameters improved the predictive ability.

Figure 2. DXA scans of the femora were obtained using a standard narrow-angle fan-beam scanner (GE Lunar Prodigy, GE Lunar Corporation, Madison, WI, USA), the proximal femur specimens being placed in the same position.

Results

The average failure load of the specimens was 8658.2N±2563.5 SD with the average trochanteric BMD 0.590 g/cm^2 ±0.139SD, the average neck BMD 0.614 g/cm^2 ±0.076 SD, the average neck length 101.9 mm ±8.8 SD, the average neck diameter 31.9 mm ±3.2 SD, the average head diameter 46.8 mm ±4.2 SD, and the average neck-shaft angle 124.5° ±6.8 SD (Table 1).

Pearson's correlation coefficient, determination coefficient, and P value between femoral neck BMD, each geometric parameter, and femoral neck failure load were calculated. By means of linear correlation regression analysis, we found that femoral neck BMD (r=0.792, r^2=62.8%, P<0.001) of the proximal femur was more strongly correlated with the failure load than any other variable. There was distinct correlation between trochanteric BMD (r=0.749, r^2=56.0%, P=0.001), head diameter (r=0.706, r^2=49.9%, P=0.002) and the failure load of the proximal femur. There is some certain correlation among the neck length (r=0.599, r^2=35.9%, P=0.014), neck diameter (r=0.516, r^2=26.6%, P=0.041) and the failure load. There was no obvious correlation between neck-shaft angle (r=0.402, r^2=16.2%, P=0.122) and the failure load (Table 2).

Multiple linear regression analyses of the combinations of the variables revealed the best combination which could predict the risk of hip fracture. We found that the best combination is that of femoral neck BMD, femoral head diameter, and femoral neck diameter (r^2=84.4%). The second best is that of femoral neck BMD and femoral head diameter (r^2=70.7%). The following combinations are "femoral neck BMD, neck-shaft angle and femoral neck length (r^2=70.5%)" and "femoral neck BMD and the femoral neck length (r^2=67.4%)" (Table 3).

Table 1. Measurement of the variables and fFailure loads.

Specimens	Femoral neck axis length (mm)	Femoral neck diameter (mm)	Femoral head diameter (mm)	Neck-shaft angle (°)	Trochanteric BMD (g/cm²)	Femoral neck BMD (g/cm²)	Failure load (N)
1	90.2	27.3	40.9	118.9	0.488	0.591	7568.7
2	116.3	37.5	52.2	123.1	0.721	0.709	9343.2
3	102.6	34.4	46.8	122.2	0.540	0.491	7260.2
4	93.5	30.8	41.6	126.6	0.569	0.574	7190.8
5	109.4	30.7	52.7	126.2	0.530	0.542	10546.3
6	94.1	31.0	45.2	127.8	0.641	0.623	8215.1
7	108.3	35.6	48.9	131.5	0.671	0.647	9947.2
8	107.9	37.1	51.8	125.7	0.989	0.776	13728.1
9	101.2	29.4	45.5	133.9	0.437	0.565	6810.4
10	97.3	30.5	44.1	119.8	0.503	0.589	5542.5
11	91.7	28.2	43.0	126.2	0.591	0.687	9317.9
12	105.1	33.4	48.3	110.8	0.480	0.539	5879.6
13	97.8	30.9	44.0	113.1	0.501	0.577	6971.7
14	101.2	28.7	45.3	133.5	0.439	0.569	6813.3
15	120.1	29.7	54.8	132.3	0.701	0.710	14497.8
16	93.6	34.9	43.3	120.0	0.636	0.641	8897.9
Mean	101.9	31.9	46.8	124.5	0.590	0.614	8658.2
SD	8.8	3.2	4.2	6.8	0.139	0.076	2563.5

Mean – mean value; SD – standard difference; BMD – bone mineral density.

Table 2. Correlation coefficients between femoral neck mechanical strength and the variables. Femoral neck BMD of the proximal femur is most strongly correlated with the failure load than any other variable. There is distinct correlation between trochanteric BMD, head diameter and the failure load of the proximal femur. There is some certain correlation between neck length, neck diameter and the failure load. There is no obvious correlation between neck-shaft angle and the failure load.

	r	r² (%)	p
Femoral neck BMD	0.792	62.8	<0.001
Trochanteric BMD	0.749	56.0	0.001
Femoral head diameter	0.706	49.9	0.002
Femoral neck axis length	0.599	35.9	0.014
Femoral neck diameter	0.516	26.6	0.041
Neck-shaft angle	0.402	16.2	0.122

BMD – bone mineral density; r – Pearson's correlation coefficient; p – value of statistical significance.

Discussion

As age increases, the risk of osteoporosis increases. Osteoporosis is an important factor that can cause hip fracture. Even slight forces can cause hip fractures in the elderly. Reduction of bone mass is an important factor that affects biomechanical strength of bone, thus making BMD an important indicator to assess hip fracture [20]. However, studies have shown that predicting hip

Table 3. Correlation coefficients between femoral neck mechanical strength and combinations of the variables. The best combination which can predict the risk of hip fracture is that of femoral neck BMD, femoral head diameter and femoral neck diameter (r^2=84.4%) and the second best is that of femoral neck BMD and femoral head diameter (r^2=70.7%).

	r^2 (%)	p
Femoral neck BMD	84.4	<0.001
Femoral head diameter		<0.001
Femoral neck diameter		0.004
Femoral neck BMD	70.7	0.004
Femoral head diameter		0.029
Femoral neck BMD	70.5	0.001
Neck-shaft angle		0.153
Femoral neck axis length		0.105
Femoral neck BMD	67.4	0.001
Femoral neck axis length		0.062
Femoral neck BMD	65.7	<0.001
Neck-shaft angle	84.4	0.092

BMD – bone mineral density; r – Pearson's correlation coefficient; p – value of statistical significance.

fracture using only BMD it is not sufficiently precise. Using the combination of BMD and geometric parameters of the proximal femur, hip fracture can be predicted more accurately [3,21]. Our findings indicate that femoral neck BMD and trochanteric BMD (r=0.792, r^2=62.8%, P<0.001; r=0.749, r^2=56.0%, P=0.001) of the proximal femur are more correlated with the failure load than other factors. This is consistent with the studies of Pulkkinen et al. [16] and LeBras et al. [19], who reported that femoral neck diameter and femoral head diameter were not factors predictive of hip fracture. However, the present study shows that there is an obvious correlation between femoral head diameter (r=0.706, r^2=49.9%, P=0.002) and failure load of the proximal femur; there is a correlation between femoral neck length (r=0.599, r^2=35.9%, P=0.014), femoral neck diameter (r=0.516, r^2=26.6%, P=0.041), and the failure load, which agrees with the conclusions of some previous studies [3,22]. Pulkkinen et al. [23] found that the femoral neck-shaft angle was the best choice for predicting hip fracture, especially the fracture type of the femoral neck, as well as for different sexes or failure loads of the specimens, and the best factor to predict the fracture type was the neck-shaft angle. However, our study shows that there is no distinct correlation between the neck-shaft angle (r=0.402, r^2=16.2%, P=0.122) and the fracture type. These conflicting results probably arise from the different sex ratios of the selected samples.

Because the biomechanical properties are affected by many factors, such as BMD and geometric parameters, we analyzed which combination of the variables contributes the most to predict the risk of hip fracture by using multiple linear regression analysis. We found that the best combination to predict the risk of hip fracture is that of femoral neck BMD, femoral head diameter, and femoral neck diameter. Furthermore, these 3 factors not only affect the mechanical properties, but also predict the risk of hip fracture when used in combination. The 2 factors (femoral neck BMD and trochanteric BMD) can affect the failure load of the proximal femur and have stronger influence than geometric parameters. But among them, femoral neck BMD with other factors is more significant. Results have shown that BMD along with geometric parameters is more effective in predicting the risk of hip fracture than BMD alone, which is in accord with studies of Pulkkinen et al. [3], Faulkner et al. [24], and Seyyed Morteza Kazemi et al. [25].

The incidence of osteoporotic fracture (OF) varies among races. Studies have shown that Caucasoids (white people) have the highest risk, Negroids (black people) have the lowest risk, and other races have medium risk [26,27]. The difference in bone geometric parameters may be one of the major reasons why the incidence of hip fracture among different races varies. Bone strength is the ultimate standard of fracture resistance, which is determined primarily by BMD and geometry [28]. A study on the risk of hip fracture among white and black females showed that black females have a higher level of peak bone mass and bone strength, which may explain why the incidence of osteoporotic fracture of black people is lower than that of white people [29]. Asian people have smaller skeletons, lower BMD value, and lower risk of hip fracture [30]. Comparing the study results, we discovered that the peak bone mass among Chinese people is approximately 15% lower than that of white people and they have thus a faster decrease in femoral neck BMD [31,32]. This indicates that the differences in incidence of hip fracture between Caucasoids and Asians may be influenced by geometry of the femoral neck rather than the BMD differences among different races. In order to reduce the effects of sex-related differences, we chose female samples for the present research.

This study provides a good example for studies on the estimation of hip fracture and reached some conclusions for clinical operation. More studies with a larger number of samples will be collected for further investigation. Due to the limitation of experimental conditions, we have no samples from races other than Chinese. Efforts will be made to collect samples from other races for a more comprehensive study in the future.

Conclusions

Compared with BMD alone, BMD along with geometric parameters of proximal femur showed higher reliability in predicting the risk of hip fracture. The geometry of the proximal femur plays an important role in assessing the biomechanical strength of the femur. This method creates a more reliable standard to predict the risk of hip fracture in clinical trials.

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Conflict of interest

None.

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