Original Article

Quantitative computed tomography analysis of proximal femur bone mineral density and its relation to hip fracture risk

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Background: Hip fractures significantly reduce the quality of life and mobility of older adults. This study aimed to analyze the correlation between volumetric bone mineral density (vBMD) in different regions of the proximal femur as measured by quantitative computed tomography (QCT) and various subtypes of hip fractures.

Methods: This case-control study included patients over the age of 65 years admitted to Huadong Hospital Affiliated to Fudan University for hip fractures from November 2022 to December 2023; additionally, patients from the health examination center or outpatient center treated during the same period were included as a control group. Age and gender were matched to eliminate potential confounding factors. The vBMD at the femoral neck (FN), intertrochanteric (IT), and subtrochanteric (ST) regions in the hip fracture groups [FN fracture (FNF) and IT fracture (ITF)] and control group were measured using QCT.

Results: A total of 107 patients with FNF, 77 with ITF, and 72 controls were included. After matching for age and gender was completed, 48 individuals were included in each of the three groups. The vBMD at the IT, FN, and ST regions were significantly lower in patients with hip fractures compared to those in the control group for both genders ($P<0.001$). The vBMD of the FN and IT regions of females in the ITF group was lower than that of those in the FNF group ($P<0.05$). Additionally, the vBMD of the ST region in both genders was lower in the ITF group than in the FNF group (male: $P<0.05$; female: $P<0.001$). In all three groups, females had a significantly lower vBMD in all three regions compared to males ($P<0.001$). The decline in vBMD was more pronounced in the ITF group than in the FNF group for both genders, with the largest reduction compared to controls observed in the ST region of females in the ITF group.

Conclusions: Older adult individuals with a lower hip vBMD are more susceptible to experiencing osteoporotic hip fracture than are those with a normal vBMD. Reduced ST vBMD may serve as an indicator for ITF, especially among females.

Keywords: Quantitative computed tomography (QCT); volumetric bone mineral density (vBMD); intertrochanteric fracture (ITF); femoral neck fracture (FNF); subtrochanteric region (ST region)

Submitted Jun 25, 2024. Accepted for publication Oct 04, 2024. Published online Oct 28, 2024.
doi: 10.21037/qims-24-1293
View this article at: https://dx.doi.org/10.21037/qims-24-1293

Introduction

As the quality of life improves and the population ages, the prevalence of osteoporosis is likely to increase. Hip fracture is one of the more common complications of osteoporosis in older adults and significantly reduces their quality of life (1,2). It is estimated that the number of hip fractures will double annually by 2050, and approximately half of these are expected to occur in Asia, particularly in China (3,4). Hip fractures are associated with high rates of disability and mortality. According to one relevant study, the 1-year mortality rate for individuals aged 74 to 88 years with hip fractures is approximately 22% (5).

Bone mineral density (BMD) is currently used as a critical clinical marker for diagnosing osteoporosis and assessing hip fracture risk (6). Over the past three decades, dual-energy X-ray absorptiometry (DXA) has been widely applied in clinical practice for measuring BMD. However, its limitations are increasingly being recognized, as it does not clearly reflect the complex three-dimensional structure of the hip. Quantitative computed tomography (QCT), unlike traditional DXA, measures true volumetric BMD (vBMD), which is unaffected by bone size and shape (7). It can provide a three-dimensional view based on computed tomography (CT) data, which helps prevent errors due to overlapping structures, thereby enhancing the sensitivity and accuracy of measurements (8). Therefore, employing QCT for measuring hip vBMD is crucial for predicting and managing hip fractures.

This study used QCT to scan the proximal femur of individuals aged 65 years and older, including patients with femoral neck fracture (FNF), intertrochanteric fracture (ITF), and healthy controls. The QCT Pro software (Mindways Software Inc., Austin, TX, USA) was used to measure the vBMD at the femoral neck (FN), intertrochanteric (IT) region, and for the first time, the subtrochanteric (ST) region. The correlation of QCT-measured vBMD in these three regions and hip fractures was analyzed. We also evaluated the extent of vBMD reduction in these three regions in the FNF and ITF groups compared to the control group. We hope our findings can enable healthcare providers to implement more effective management and prevention strategies, potentially improving outcomes for older adults at risk of hip fractures. We present this article in accordance with the STROBE reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-24-1293/rc).

Methods

Participants

This study recruited patients aged 65 years and older with FNF or ITF who were admitted for surgery to the Department of Orthopedics at Huadong Hospital Affiliated to Fudan University from November 2022 to December 2023. Concurrently, patients from the health examination center or outpatient center who typically did not have a history of fractures were included as a control group. To minimize the potential impact of age and sex differences on the study outcomes, 1:1:1 matching by age and sex was performed among the FNF, ITF, and control groups. An allowable age difference of ±2 years was applied during the matching process.

The inclusion criteria for the hip fracture group (FNF and ITF) were as follows: (I) hip fractures caused by low-energy injury as diagnosed by X-ray or CT; (II) hospital admission within 48 hours of the injury; and (III) age ≥65 years. Meanwhile, the exclusion criteria were as follows: (I) presence of severe bone metabolic diseases such as osteomalacia, osteogenesis imperfecta, Paget disease, Cushing syndrome, or hyperprolactinemia; (II) intake of medications affecting bone metabolism, including the use of intravenous bisphosphonates, fluoride, or strontium agents within 2 years; teriparatide or denosumab for osteoporosis within 6 months, oral bisphosphonates within the previous year, or continuous use of calcitonin for more than 3 months with the last dose being taken within the previous year; (III) history of smoking or alcohol abuse; (IV) ongoing treatment for active malignancy; (V) bed rest exceeding 1 month prior to the fracture; (VI) history of hip joint replacement surgery or internal fixation for hip fractures; and (VII) hip fractures caused by high-energy injury.

For the control group, the inclusion criteria were as follows: no diagnosis of hip or vertebral fracture and age ≥65 years. Meanwhile, the exclusion criteria were as follows: (I) presence of severe bone metabolic diseases such as osteomalacia, osteogenesis imperfecta, Paget disease, Cushing syndrome, or hyperprolactinemia; (II) intake of medications affecting bone metabolism; (III) history of smoking or alcohol abuse, including the use of intravenous bisphosphonates, fluoride, or strontium agents within 2 years; (IV) use of teriparatide or denosumab for osteoporosis within the previous 6 months or oral bisphosphonates within the previous year or continuous

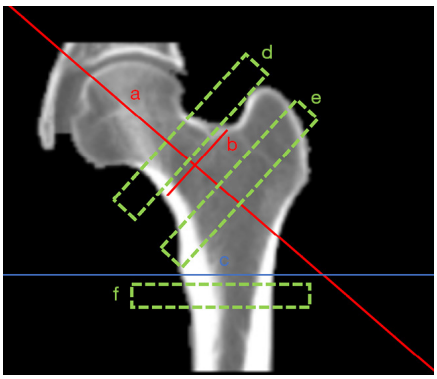

Figure 1 The ROI for vBMD measurement. Straight line a, FN long axis; straight line b, neck-shaft junction; straight line c, plane of the inferior border of the lesser trochanter; rectangular box d, FN ROI; rectangular box e, IT ROI; rectangular box f, ST ROI. ROI, region of interest; vBMD, volumetric bone mineral density; FN, femoral neck; IT, intertrochanteric; ST, subtrochanteric.

use of calcitonin for more than 3 months, with the last dose taken within the previous year; (V) ongoing treatment for active malignancy; and (VI) history of hip joint replacement surgery or internal fixation for hip fractures. The sample size was determined by the number of cases as indicated in previous studies (9,10) to ensure that it was sufficient and adequate for the detection of significant differences.

If patients with hip fractures refused surgical intervention and opted for conservative treatment, they did not undergo QCT examinations. This decision was made to minimize the patients' exposure to radiation. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The Ethics Review Committee of Huadong Hospital Affiliated to Fudan University approved the protocol (No. 2022K068), and informed consent was obtained from all participants.

Data collection

Basic demographic information, including age and gender, was collected for all patients. For the patients with hip fracture, QCT-measured vBMD at the FN, IT, and ST regions of the contralateral nonfracture hip was obtained. For the control group, QCT-measured vBMD at the same three regions on both hips was also collected, and the average of left and right hips was taken to represent the vBMD at each region. We ensured that all data were collected and recorded meticulously, resulting in a complete dataset without any missing values.

The QCT measurements were conducted using a SOMATOM Definition Flash 64-slice CT scanner (Siemens Healthineers, Erlangen, Germany), with hip scanning performed using a solid phantom (Mindways Software Inc.). The scanning parameters were as follows: tube voltage, 120 kV; tube current, 150 mAs; table height, 155.5 mm; scan field of view, 500 mm; and slice thickness, 1 mm. During the scan, the phantom was placed under the hip joint, and patients were positioned supine with arms raised and hands clasped behind the head.

Region of interest (ROI) selection was performed using the "computed tomography X-ray absorptiometry (CTXA) hip analysis" module in QCT Pro software version 4.2.3 (Mindways Software Inc.). As seen in *Figure 1*, line a represents the long axis of the FN, line b represents the neck-shaft junction, and line c represents the plane below the lesser trochanter. For the vBMD measurement of the FN, the lower edge of the ROI (green rectangular frame d) was placed just touching line b and following the direction of line a. For the IT vBMD, the ROI (green rectangular frame e) was positioned above line c and below line b, along with the direction of line a. The upper edge of the ROI (green rectangular frame f) was placed immediately below line *c* to measure the vBMD of the ST region. The actual measured images in the software are shown in *Figure 2*.

Statistical analysis

Data were presented as the mean ± standard deviation (SD) for normally distributed continuous variables, as the median and interquartile range (IQR) for nonnormally distributed variables, and as number and percentage for categorical variables. Case-control matching was performed for age and gender. The matching conditions were the same gender and an age difference less than ±2 years. The Kolmogorov-Smirnov test was applied to assess the normality and homogeneity of variance for all datasets. For comparisons involving multiple groups, P values were obtained using one-way analysis of variance (ANOVA) for continuous variables and were obtained with the least significant difference *t*-test (LSD-*t*) for multiple comparisons. Comparisons between males and females were conducted using an independent samples *t*-test. A P value of less than 0.05 was considered to indicate statistical significance in all tests. All statistical analyses were conducted using the SPSS 29.0 software (IBM Corp., Armonk, NY, USA).

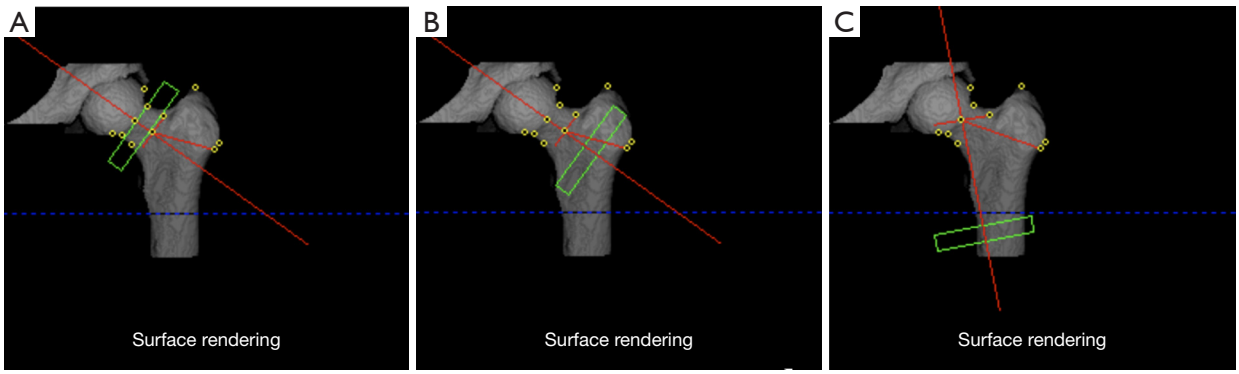

Figure 2 The regions measured in this study as they appeared in QCT Pro software. (A) The measured green ROI area is the FN region. (B) The measured green ROI area is the IT region. (C) The measured green ROI area is the ST region. QCT, quantitative computed tomography; ROI, region of interest; FN, femoral neck; IT, intertrochanteric; ST, subtrochanteric.

Table 1 Patient demographics

Group	Total, n	Male, n	Female, n	Age range (years)	Average age (years)
FNF	48	14	34	65–91	82.42±6.11
ITF	48	14	34	67–92	82.77±5.60
Control	48	14	34	67–92	83.15±5.91

Average age data are presented as the mean ± SD. FNF, femoral neck fracture; ITF, intertrochanteric fracture; SD, standard deviation.

Results

Participant demographics

A total of 256 patients aged 65 years and above were initially enrolled and included in this study. Among them, 107 had FNF, 77 had ITF, and 72 were healthy controls. After age and gender matching was conducted, a total of 144 participants were included in the study, comprising 96 patients with hip fractures and 48 health controls. The fracture group consisted of 48 patients with FNF and 48 with ITF. Each group had 14 (29.2%) males and 34 (70.8%) females. The age range of patients in the FNF, ITF, and control groups were 65 to 91 years (average age 82.42±6.11 years), 67 to 92 years (average age 82.77±5.60 years), and 67 to 92 years (average age 83.15±5.91 years), respectively (*Table 1*).

vBMD comparisons across groups and genders

The vBMD values for the FN, IT, and ST regions were compared among the FNF, ITF, and control groups using ANOVA analysis, and significant differences were found among the three groups in all regions (all P values <0.001; *Table 2*). Further gender-specific analyses revealed consistent findings. For both males and females, significant differences in vBMD values were observed across the three groups in each region (all P values <0.001; *Table 2*). Additionally, *t*-test analysis showed that, across all three groups, vBMD values in the FN, IT, and ST regions were significantly lower in females than in males (P<0.001; *Table 3*).

Post-hoc comparisons of vBMD across groups and genders

Further multiple comparisons using the LSD-*t* test after ANOVA revealed the following:

- The vBMD at all three regions (FN, IT, ST) was significantly lower in both the FNF and ITF groups compared to the control group (all P values <0.001). This pattern persisted in both the male and female subgroups (P<0.001) except for the ST region for males, where the difference between the FNF and control groups remained significant (P<0.05; *Table 4*).
- No significant differences in vBMD in the FN and IT regions were found between the FNF and ITF groups in the overall population or the male subgroup (P>0.05). However, in the female subgroup, these differences were statistically significant (P<0.05; *Table 4*).
- The vBMD in the ST region was significantly lower in the ITF group than in the FNF group (P<0.001). This pattern was also observed in both males (P<0.05) and females (P<0.001; *Table 4*).

Table 2 vBMD values in different groups and genders

Gender	Region	Group			P value
		FNF	ITF	Control	
Total	FN (mg/cm^3)	224.22±43.01	206.62±46.72	304.24±56.66	<0.001
	IT (mg/cm^3)	173.02±39.26	156.13±42.53	230.60±52.36	<0.001
	ST (mg/cm^3)	355.77±78.69	280.01±104.11	435.60±84.05	<0.001
Male	FN (mg/cm^3)	265.52±35.14	253.60±33.81	358.89±52.29	<0.001
	IT (mg/cm^3)	215.00±33.07	196.22±41.98	291.11±34.74	<0.001
	ST (mg/cm^3)	459.01±57.21	402.74±75.85	522.96±64.50	<0.001
Female	FN (mg/cm^3)	207.21±33.73	187.27±36.56	281.74±41.31	<0.001
	IT (mg/cm^3)	155.73±26.62	138.20±29.51	205.68±35.17	<0.001
	ST (mg/cm^3)	313.25±33.84	229.48±64.42	399.63±62.42	<0.001

Data are presented as the mean ± SD. FN vBMD, IT vBMD, and ST vBMD were all significantly different between the hip fracture groups (FNF and ITF groups) and the control group according to ANOVA (P<0.001). vBMD, volumetric bone mineral density; FNF, femoral neck fracture; ITF, intertrochanteric fracture; FN, femoral neck; IT, intertrochanteric; ST, subtrochanteric; SD, standard deviation; ANOVA, analysis of variance.

Table 3 Comparisons of vBMD values between genders

Region	Group		
	FNF	ITF	Control
FN	<0.001	<0.001	<0.001
IT	<0.001	<0.001	<0.001
ST	<0.001	<0.001	<0.001

The vBMD in the FN, IT, and ST regions was significantly lower in females than in males in all groups (FNF, ITF, and control groups) according to independent samples *t*-test (P<0.001). vBMD, volumetric bone mineral density; FNF, femoral neck fracture; ITF, intertrochanteric fracture; FN, femoral neck; IT, intertrochanteric; ST, subtrochanteric.

Percentage decrease in vBMD

The percentage reduction in vBMD across the three regions was compared between the ITF, FNF, and control groups. The ITF group exhibited a larger percentage decrease in vBMD across all three regions as compared to the FNF group. Both males and females in the ITF group showed a larger percentage decrease in vBMD across all regions compared to those in the FNF group. Notably, females in the ITF group demonstrated the largest decrease in vBMD in the ST region, which was more pronounced than in any other region or population (*Table 5* and *Figure 3*).

Table 4 Post-hoc comparisons (LSD-*t*) of vBMD values across groups and genders

Gender	Region	Group comparison (P value)		
		FNF *vs.* control	ITF *vs.* control	FNF *vs.* ITF
Total	FN	<0.001	<0.001	>0.05
	IT	<0.001	<0.001	>0.05
	ST	<0.001	<0.001	<0.001
Male	FN	<0.001	<0.001	>0.05
	IT	<0.001	<0.001	>0.05
	ST	<0.05	<0.001	<0.05
Female	FN	<0.001	<0.001	<0.05
	IT	<0.001	<0.001	<0.05
	ST	<0.001	<0.001	<0.001

Post-hoc comparisons of vBMD values at the FN, IT, and ST regions across the FNF, ITF, and control groups according to the LSD-*t* test. Significant differences were observed between both FNF and ITF groups compared to the control group in all regions in the overall population (P<0.001), except for the ST region in males, where the FNF *vs.* control comparison yielded P<0.05. No significant differences were found between FNF and ITF groups in the FN and IT regions for the overall population and males (P>0.05), whereas significant differences were detected in females (P<0.05). A significant difference in the ST region was found between FNF and ITF in both males (P<0.05) and females (P<0.001). LSD-*t*, least significant difference *t*-test; vBMD, volumetric bone mineral density; FNF, femoral neck fracture; ITF, intertrochanteric fracture; FN, femoral neck; IT, intertrochanteric; ST, subtrochanteric.

Table 5 Percentage reduction in vBMD

Gender	Group	FN reduction (%)	IT reduction (%)	ST reduction (%)
Total	FNF *vs.* control	−26.30	−24.97	−18.33
	ITF *vs.* control	−32.09	−32.73	−35.72
Male	FNF *vs.* control	−26.02	−26.14	−12.23
	ITF *vs.* control	−29.34	−32.59	−22.99
Female	FNF *vs.* control	−26.45	−24.29	−21.61
	ITF *vs.* control	−33.53	−32.81	−42.58

The ITF group showed a larger percentage decrease in vBMD across all regions than did the FNF group, which was consistent for both males and females. In the female ITF group, the ST region had the largest vBMD decrease compared to the control group. vBMD, volumetric bone mineral density; FN, femoral neck; IT, intertrochanteric; ST, subtrochanteric; FNF, femoral neck fracture; ITF, intertrochanteric fracture.

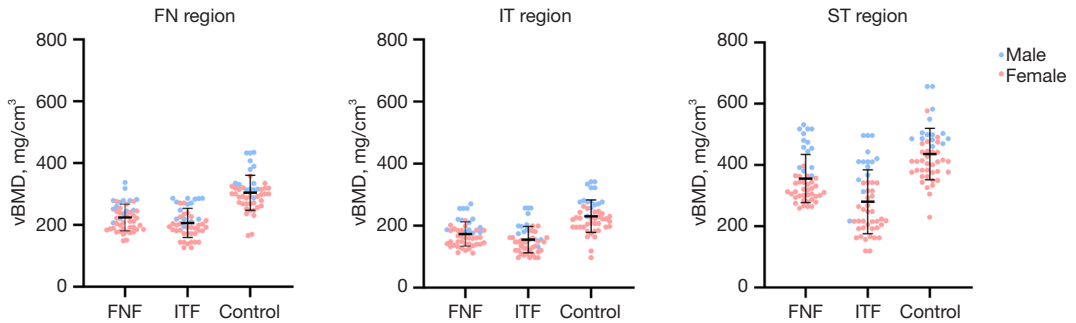

Figure 3 Comparison of the decrease in vBMD between the hip fracture group and control group in the different regions of the hip for both genders. Bars represent the mean ± SD in each group. FN, femoral neck; FNF, femoral neck fracture; ITF, intertrochanteric fracture; IT, intertrochanteric; ST, subtrochanteric; vBMD, volumetric bone mineral density; SD, standard deviation.

Discussion

Hip fractures are often caused by changes in the mechanical properties of bone, which are related to factors such as BMD, bone strength, and microarchitecture. Currently, BMD is the predominant indicator among these factors and is the standard used for diagnosing osteoporosis and predicting fracture risk (11-13). Accurate measurement of BMD in the hip is crucial for the early prevention and treatment of osteoporotic fractures in this region. Our study employed QCT to measure the vBMD of the hip, providing more precise information regarding the vBMD of the proximal femur. In addition to assessing the vBMD of the FN and IT regions, our study introduced an innovative approach of incorporating the ST region into vBMD measurements. This novel methodology offers new clinical references for evaluating hip vBMD and predicting the risk of hip fractures.

FNF and ITF are typical types of hip fractures. Hey *et al.* found through multivariate linear regression that BMD in the greater trochanter and IT regions is notably lower in patients with ITF than in those with FNF (9). However, our study found that although the vBMD at the FN and IT regions in the ITF group was lower than that in the FNF group, the differences were not statistically significant ($P>0.05$). This result is consistent with the findings of Li *et al.*, who also did not find statistically significant differences in BMD between these groups (10). However, when we analyzed the data by gender, we found that in females, the vBMD at the FN and IT regions was significantly lower in the ITF group than in the FNF group ($P<0.05$). Additionally, our study demonstrated that both the FNF and ITF groups had lower vBMD in the FN, IT, and ST regions as compared to the control group ($P<0.001$). The same pattern was observed when the data were analyzed separately for males and females. These results

indicate that vBMD values differ significantly between patients with FNF, ITF, and health controls, regardless of gender.

Previous studies of hip BMD have primarily focused on the FN and IT regions, and there has been less attention given to the ST region (14-17). However, QCT allows for the selection of a specific ROI, with the measurement of vBMD in the ST region being more convenient than that of DXA. This facilitates a more comprehensive analysis of vBMD variations in the proximal femur. The ST region generally refers to the area between the lesser trochanter and the isthmus of the femoral canal. Fractures occurring in the ST region have also been described as those occurring within the first 5 cm distal to the lesser trochanter (18). Our study not only found that the ST vBMD in the hip fracture group was lower compared to that in the control group, but we also discovered that patients with ITF had a significantly lower ST vBMD than did those with FNF ($P<0.001$). After analyzing the data separately by gender, the same results were observed for both male and female patients ($P<0.05$ and $P<0.001$, respectively). This suggests that older adult individuals with lower ST vBMD are more likely to experience ITF after a fall. The ST region is a transitional area from the FN to the shaft, where trabecular bone transitions into cortical bone, resulting in relatively thinner cortical bone in this part of the femur (19). Due to the unique anatomical structure of the hip, the ST region undergoes multidirectional stresses under load; in addition to axial stress, it also endures compressive-tensile and torsional stresses (20). Consequently, this region is a stress concentration point, making the surrounding area more susceptible to fractures when subjected to trauma.

The proximal femur exhibits unique biomechanical characteristics, and research on the mechanisms of hip fractures indicates that most of such fractures result from falls (21), the majority of which are lateral falls impacting the greater trochanter area (22). In our study, the ITF group exhibited a larger percentage decrease in vBMD across all three regions than did the FNF group. After males and females were analyzed separately, the results remained consistent. Additionally, we found that in the female ITF group, the ST region showed the largest decrease in vBMD compared to the control group across all regions and populations. These findings suggest that greater reductions in hip vBMD may increase the likelihood of ITF. Therefore, when there is a significant decrease in hip vBMD, prevention and clinical interventions should particularly focus on reducing the incidence of ITF. Particular attention should be given to preventing ITF in females with pronounced vBMD decrease in the ST region. The FN region is highly susceptible to injury during falls, while the IT region serves a buffering role, mitigating the impact forces on the FN region (23). The anatomical structure of the proximal femur influences the distribution of bone mass in the hip, and when subjected to external forces, the trabecular bone primarily resists stresses near the proximal FN, whereas the cortical bone bears more stress at the distal FN. In lateral fall experiments, the role of trabecular bone has been demonstrated to be particularly significant (24). This biomechanical interplay highlights the importance of maintaining sufficient BMD in the IT region to prevent fractures, especially in older adults who are at higher risk of falls.

Some limitations to this study warrant mention. First, the sample size and the number of hip fractures included for analysis might not have been sufficiently large but could nonetheless obtain significant results. Further research with larger sample sizes would enhance the generalizability of our findings. Second, we employed a single-center, hospital-based design, and thus further research on this topic should involve multiple centers with participants from different regions. Third, due to certain clinical workflow constraints, we were unable to obtain complete information on all patients' height, weight, or activity levels. We acknowledge that vBMD alone is not sufficient to predict fracture risk. Other critical factors, such as BMI and activity levels, also play a significant role and should be considered in future studies to develop a more comprehensive understanding of hip mechanics and fracture risk.

Conclusions

BMD gradually decreases with advancing age. Concurrently, osteoclast activity leads to the resorption of bone tissue, resulting in the development of osteoporosis. This condition weakens the structural strength of the proximal femur, thereby increasing the risk of hip fractures in older adults with osteoporosis (25). According to our findings, vBMD at the FN, IT, and ST regions was significantly lower in patients with hip fractures than in controls in both genders, indicating a strong correlation between decreased vBMD and fracture risk. Additionally, our study found that in female patients, the FN and IT regions exhibited lower vBMD in those with ITF compared to those with FNF. By assessing the vBMD of the hips of older adults, it is possible to identify specific areas of vulnerability for

different types of hip fractures. Moreover, we found that the vBMD of the ST region was lower in the ITF group than in the FNF group for both genders, and the reduction in vBMD was more pronounced across different regions of the hip in patients with ITF, particularly in females, where the decrease in the ST region was the most significant. This may suggest that a lower ST vBMD may serve as a valuable indicator for assessing the risk of extracapsular hip fractures, such as ITF, especially in women. These findings may contribute to developing more effective prevention and treatment strategies for hip fractures, particularly in women, by offering valuable insights into bone density differences and fracture risk. This approach has the potential to mitigate the risk and impact of hip fracture, ultimately improving the quality of life for older adults.

Acknowledgments

Funding: This work was supported by the National Key Research and Development Program of China (No. 2020YFC2008700), the Shanghai Municipal Commission of Health (No. 202040297), and the Clinical Research Center for Geriatric Fractures of Huadong Hospital (No. LCZX2208).

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://qims.amegroups.com/article/view/10.21037/qims-24-1293/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-24-1293/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The Ethics Review Committee of Huadong Hospital Affiliated to Fudan University approved the study protocol (no. 2022K068), and informed consent was obtained from all participants.

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Cite this article as: Xu Y, Zhu Y, Lin W, Lee DH, Yang F, Fan Y. Quantitative computed tomography analysis of proximal femur bone mineral density and its relation to hip fracture risk. Quant Imaging Med Surg 2024;14(12):9385-9393. doi: 10.21037/qims-24-1293

