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Hip structural analysis parameters are not associated with the risk of postmenopausal female second hip fracture: a retrospective study

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Abstract

Purpose Postmenopausal female patients with a history of a single hip fracture are at higher risk of a second fracture. The poorer clinical outcomes of this patient group warrants evaluating the risk of experiencing a second hip fracture. Therefore, this study aimed to investigate the effectiveness of hip structural analysis (HSA) in assessing the risk of second hip fracture in postmenopausal females.

Methods This retrospective analysis included 188 patients selected from the Chinese Second Hip Fracture Evaluation (ClinicalTrials.gov identifier: NCT03461237, first registration/posted date: 09/03/2018). They were divided into the second hip fracture (35 cases, with a mean age of 79.33 ± 7.70 years) and the control group (153 cases, with a mean age of 73.41 ± 9.56 years). Parker Mobility Score were determined via telephone follow-up, and two computed tomography scanners were used for images acquisition. All HSA and areal bone mineral density (aBMD) parameters were calculated through Mindways QCTPRO software.

Results The refracture group showed increased age, decreased cross-sectional area, total hip aBMD, trochanteric aBMD, and intertrochanteric aBMD ($p < 0.05$). Total hip and intertrochanteric aBMD have a protective effect on the occurrence of a second hip fracture in postmenopausal women, with odd ratios of 0.61 and 0.57, respectively ($p < 0.05$). Incorporating HSA parameters into the baseline model (used age, type 2 diabetes mellitus, and the PMS as parameters, AUC = 0.729) does not significantly improve the performance of second hip fracture prediction (AUC = 0.748, $p < 0.05$ in Delong's test).

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Conclusion Based on our findings, HSA does not statistically correlate with the incidence of second hip fracture in postmenopausal women. Incorporating HSA parameters into the (baseline) model does not significantly improve the pridictive capabilities.

Keywords Second hip fracture, Hip structural analysis, Areal bone mineral density, Postmenopausal females

Introduction

The incidence of hip fracture, which raises morbidity, mortality and nursing home admissions [1], tends to increase with age. Klotzbueche et al. [2] and Hagino et al. [3] reported that patients with a history of single hip fracture have a 2-4-fold higher risk of experiencing a second fracture and poorer prognosis than the general population. In particular, among the older population, a substantial reduction in bone density is widely observed in postmenopausal women, which increases their risk of low-energy osteoporotic fractures and exacerbates the severity of the condition. Since hip fracture can seriously reduce the quality of life, significantly impact hip mobility and overall body function, and have a higher mortality rate [4–6], the assessment of hip fracture risk in postmenopausal women, especially the risk of experiencing a second fracture, is crucial.

Hip structural analysis (HSA) is a method for measuring the geometry of the hip and can be performed using quantitative computer tomography (quantitative CT, QCT). HSA measurements include cross-sectional area (CSA), cross-sectional moment of inertia (CSMI), average cortical thickness (ACT), endosteal diameter (ED), buckling ratio (BR), and section modulus (Z). Although Ito et al. [7] reported that some HSA indicators could be used to assess the risk of fracture in the femoral neck and the intertrochanteric region, few studies have examined the correlation between HSA and the incidence of second hip fracture in postmenopausal women. In addition, the performance of HSA in evaluating the risk of second hip fracture in postmenopausal females also remains unclear.

Therefore, the aim of our study was to investigate the relationship between HSA and second hip fracture in postmenopausal women, and to evaluate the predictive ability of the HSA models in assessing the risk of experiencing hip refractures.

Methods

Participants

This investigation examined a total of 668 participants in the longitudinal Chinese Second Hip Fracture Evaluation study (ClinicalTrials.gov identifier: NCT03461237, first registration/posted date: 09/03/2018) [8] between May 2015 and June 2016. All subjects suffered low-energy hip fracture (defined as the 'first hip fracture') and sought medical care at the emergency department of Jishuitan hospital. They were then followed up for a median duration of 4.5 years, spanning from 2015 to 2016 until 2019 to 2020. During the follow-up period, if a participant experienced another hip fracture, it was defined as a "second hip fracture", or "refracture".

The inclusion criteria were as follows:

- Postmenopausal women aged ≥ 50 years;
- QCT examination performed < 48 h after injury;
- Unilateral hip fracture (as the 'first fracture'), due to low-energy injury limited to falls while standing or walking;
- Han Chinese ethnicity;
- Informed consent provided in writing.

The exclusion criteria were:

- Previous hip fracture (before the 'first fracture');
- Diseases causing long-term (> 3 months) limitation of mobility that Parker Mobility Score (PMS) < 3, such as paralysis, poorly healed lower extremity fractures, poorly healed hip dysplasia (includes but not limited to developmental dysplasia of the hip, spondyloepiphyseal dysplasia, etc.), and avascular necrosis of the femoral head;
- Painful diseases in the past 3 months, such as acute pancreatitis and lumbar fracture;
- Metabolic bone disease (except senile osteoporosis and postmenopausal osteoporosis);
- Inflammatory joint disease, such as rheumatoid arthritis;
- Bone tumor or tumor-like lesions in the proximal femur, such as bone metastases, chondrosarcoma, or enostoses;
- Malignancies that may metastasize to the bone;
- Administration of treatments or medications known to affect bone metabolism (e.g., glucocorticoids).

Finally, our study enrolled 188 subjects, including 35 in the refracture group and 153 in the control group; the data exclusion process was detailed in Fig. 1. This retrospective analysis (of the prospective cohort study mentioned above) was approved by the ethics committee of Beijing Jishuitan Hospital. Informed consent was obtained from each participant.

CT data acquisition

Spiral CT imaging of the hip was performed using two Toshiba Aquilion 64-row CT scanners (Toshiba Medical Systems Division, Tokyo, Japan). The patients were

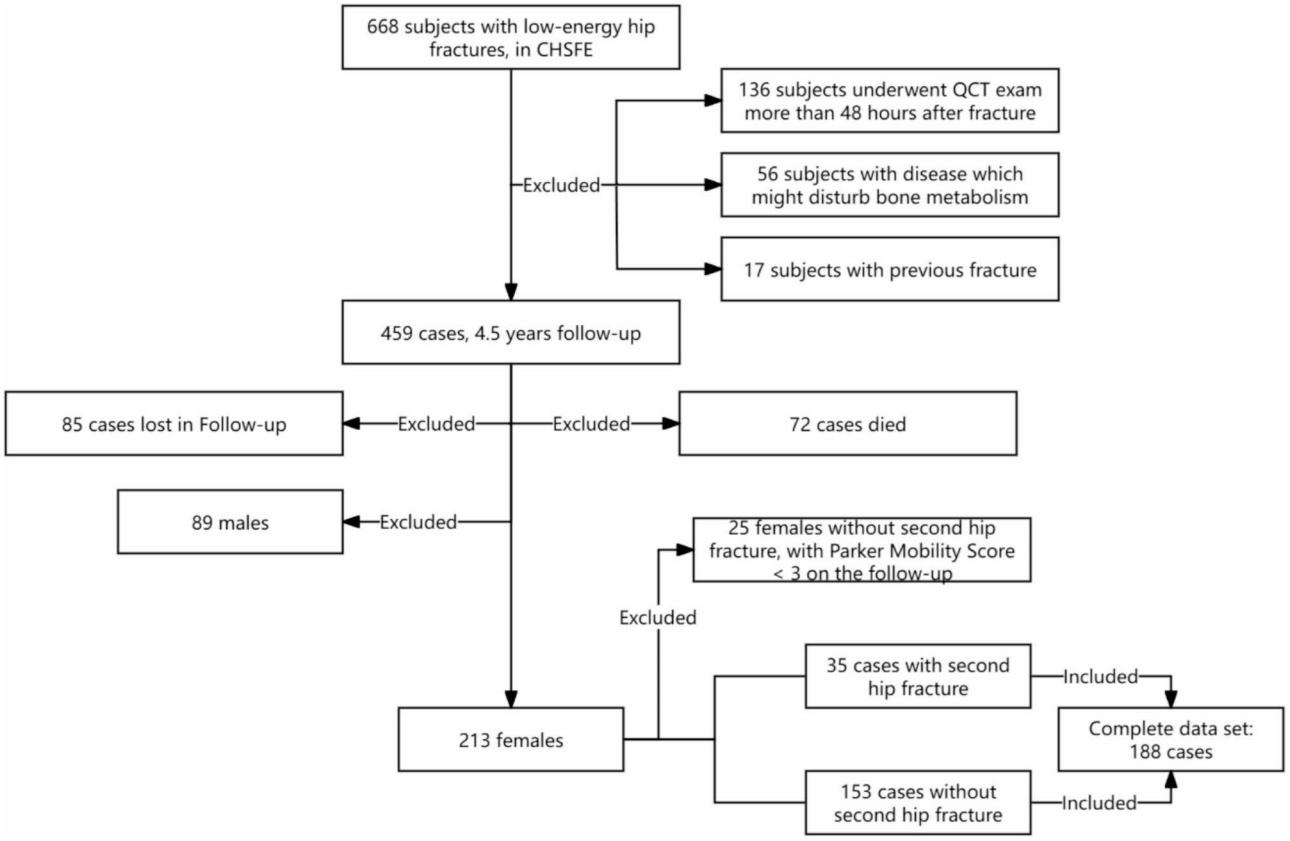

Fig. 1 Flow chart of participant selection for the study

scanned in the supine position with a tube voltage of 120 kV and an exposure dose of 250 mA·s, starting 2 cm superior to the top of the acetabulum and ending at least 3 cm inferior to the level of the lesser trochanter. The imaging matrix size was 512 × 512, and the reconstruction slice thickness was 1.0 mm.

Criteria for the PMS

The PMS is a measure of mobility. It consists of three assessment items: (a) ability to walk indoors, (b) ability to walk outside, and (c) ability to walk to nearby stores for shopping. The PMS of the patients were obtained through telephone follow-up, and each item was rated on a four-point scale: 3 for no difficulty, 2 for needing an assistive device, 1 for needing assistance from another person, and 0 for complete immobility. The total PMS ranged from 0 to 9.

In our study, to ensure that all HSA and areal bone mineral density (aBMD) analysis were focused on individuals with at least some mobility, the subjects who exhibited a PMS less than 3 were excluded.

Measurements of HSA and aBMD parameters

All HSA parameters including cross-sectional area (CSA), cross-sectional moment of inertia (CSMI), average cortical thickness (ACT), endosteal diameter (ED), buckling ratio (BR), and section modulus (Z), and aBMD parameters containing total hip (TH), femoral neck (FN), trochanteric (TR) and intertrochanteric (IT) region were calculated through QCT.

CT volumetric data were transferred to the QCTPRO software (v. 4.1.3, Mindways Software, San Francisco, CA, USA). The computed tomography X-ray absorptiometry (CTXA) and bone investigational toolkit (BIT) modules of the software were used for our analysis.

In the CTXA module, three orthogonal sets of hip images (axial, coronal, and sagittal images) were separately rotated, adjusted, and segmented such that the measurement guides in each set of images were parallel to the long axis of the femoral neck, and a 2D projection pattern of the femoral neck was obtained. The region of interest was set to a height of 5.0 mm in the pattern, and the TH, FN, TR and IT aBMD were automatically calculated by the CTXA module.

In the BIT module, the threshold for cortical bone separation was set to 120 mg/cm^3. The area of interest was centered on the narrowest cross-section of the FN (labeled Slice 6), and 11 slices of images of the area of interest in the FN were selected symmetrically upward and downward. HSA parameters were then calculated via

the BIT module (Fig. 2) using the images of slices 1–6 of the region of interest.

Statistical analysis

SPSS 19.0 software (IBM, Corporation, Chicago, IL, USA) was used for all statistical analyses. Continuous variables were analyzed using student's *t*-tests, reported as mean ± standard deviation and categorical variables were analyzed using Chi-squared tests.

We applied logistic regressions to calculate the odds ratios and 95% confidence intervals for each HSA parameter, controlling for age, incidence of type 2 diabetes mellitus (T2DM) and the PMS. The area under the receiver operating characteristic curve (Area under the ROC, AUC) was used to evaluate the performance of refracture risk assessment models, and Hosmer–Lemeshow test was used to evaluate model robustness. Statistical significance of the improvement of AUC after adding explanatory factors was evaluated by Delong's test.

In addition, we used Spearman's test to determine the degree of correlation between HSA and aBMD parameters.

$P < 0.05$ was considered statistically significant.

Results

The average ages of the refracture group and the control group were 79.33 ± 7.70 years, 73.41 ± 9.56 years, respectively.

Table 1 compares each variable between the refracture and control groups. The refracture group exhibited increased age, decreased CSA, TH aBMD, TR aBMD, and IT aBMD, and these differences were statistically significant ($p < 0.05$). Besides those mentioned above, no other significant differences were observed in any of the remaining variables.

Table 2 shows the logistic regression analysis results between the refracture and control groups. Only TH and IT aBMD have a protective effect on the occurrence of a second hip fracture in postmenopausal women, with odd ratios of 0.61 and 0.57, respectively ($p < 0.05$); other measured parameters have no significant correlation with the occurrence of hip refracture.

Figure 3; Table 3 displays the AUC for multiple ROC curves. Model 1 used age, T2DM, and the PMS as parameters, acted as the baseline; Model 2 included the parameters in Model 1 with HSA parameters; and Model 3 included the parameters in Model 2 with aBMD parameters. Each of these models passed the Hosmer–Lemeshow

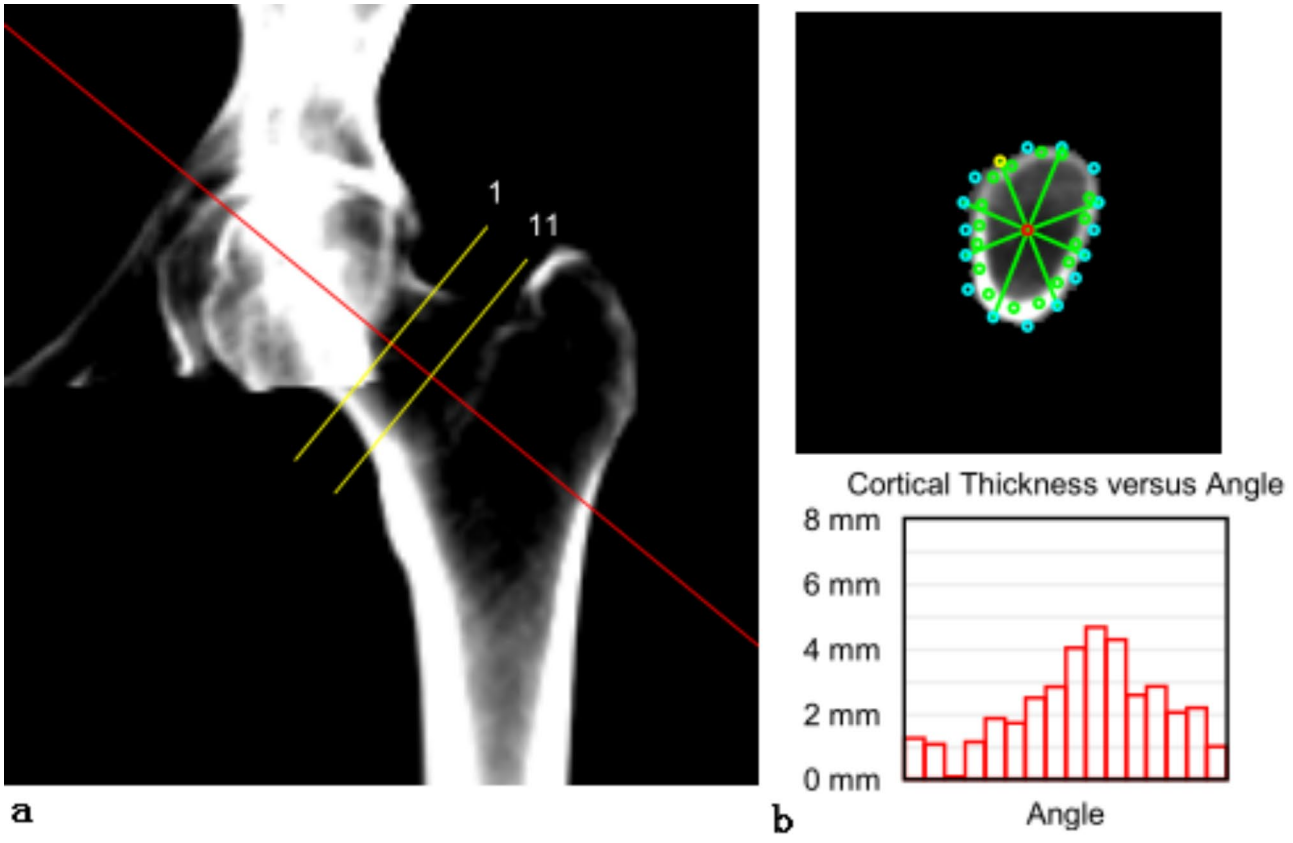

Fig. 2 (**a**) Two-dimensional projection pattern of the femoral neck; (**b**) Femoral neck cross-sectional area at the narrowest level (slice 6 of the region of interest). The central red point in the femoral neck represents the center of mass. The graph shows the cortical thickness at each measurement point at the corresponding axial angle. These parameters can be used to calculate HSA

Table 1 Comparison of differences between the refracture and control groups ($p < 0.05$ considered statistically significant)

	Group		t/χ^2	*p* Value
	Refracture	Control		
Age	79.33 ± 7.70	73.41 ± 9.56	3.91	< 0.001
Height	158.33 ± 4.68	158.50 ± 8.20	-0.10	0.919
Weight	55.98 ± 15.32	58.62 ± 9.91	-1.15	0.253
BMI	23.75 ± 4.60	23.41 ± 5.23	0.35	0.729
T2DM	12(34.3%)	79(51.6%)	3.43	0.064
PMS	8.34 ± 1.21	8.67 ± 0.89	-1.52	0.135
HSA-CSA	1.39 ± 0.22	1.51 ± 0.29	-2.73	0.008
HSA-ACT	0.11 ± 0.02	0.12 ± 0.02	-1.68	0.095
HSA-ED	2.41 ± 0.39	2.43 ± 0.33	-0.43	0.668
HSA-CSMI	1.21 ± 0.42	1.33 ± 0.65	-1.05	0.294
HSA-Z	0.72 ± 0.27	0.78 ± 0.34	-0.90	0.369
HSA-BR	16.38 ± 4.82	15.24 ± 3.68	1.55	0.122
TH aBMD	0.50 ± 0.10	0.57 ± 0.12	-3.38	0.001
FN aBMD	0.47 ± 0.14	0.49 ± 0.11	-1.20	0.232
TR aBMD	0.33 ± 0.09	0.38 ± 0.09	-2.69	0.008
IT aBMD	0.61 ± 0.11	0.70 ± 0.14	-3.60	< 0.001

Data are presented as mean ± standard deviation unless otherwise indicated

BMI, body mass index; T2DM, type 2 diabetes mellitus; PMS, Parker Mobility Score; HSA, hip structural analysis; CSA, cross-sectional area; ACT, average cortical thickness; ED, endosteal diameter; CSMI, cross-sectional moment of inertia; Z, section modulus; BR, buckling ratio; aBMD, areal bone mineral density; TH, total hip; FN, femoral neck; TR, trochanteric; IT, intertrochanteric

Table 2 Logistic regression of HSA, aBMD, and the occurrence of second fractures (per SD increase)

Variables	Odds Ratio (95%CI)			
	Unadjusted	*p* Value	Adjusted	*p* Value
HSA-CSA	0.62(0.42,0.94)	0.024	0.82(0.53,1.27)	0.370
HSA-ACT	0.71(0.48,1.06)	0.096	0.89(0.58,1.36)	0.596
HSA-ED	0.92(0.64,1.33)	0.666	0.91(0.62,1.33)	0.624
HSA-CSMI	0.77(0.46,1.27)	0.298	0.84(0.57,1.24)	0.390
HSA-Z	0.81(0.50,1.29)	0.371	0.86(0.59,1.26)	0.445
HSA-BR	1.32(0.93,1.87)	0.126	1.17(0.80,1.72)	0.419
TH aBMD	0.48(0.31,0.76)	0.001	0.61(0.38,0.97)	0.038
FN aBMD	0.78(0.51,1.18)	0.231	0.84(0.56,1.25)	0.393
TR aBMD	0.56(0.36,0.87)	0.010	0.75(0.47,1.19)	0.214
IT aBMD	0.46(0.29,0.72)	0.001	0.57(0.35,0.90)	0.017

*. Adjusted for age, PMS, T2DM

OR, odds ratio; CI, confidence interval; T2DM, type 2 diabetes mellitus; HSA, hip structural analysis; CSA, cross-sectional area; ACT, average cortical thickness; ED, endosteal diameter; CSMI, cross-sectional moment of inertia; Z, section modulus; BR, buckling ratio; aBMD, areal bone mineral density; TH, total hip; FN, femoral neck; TR, trochanteric; IT, intertrochanteric

test, suggesting the capability of the models to predict the risk of hip refracture in postmenopausal women. Among them, Model 1 had the least predictive capacity with an AUC of 0.729, and Model 3 showed the highest predictive performance with an AUC of 0.793. Delong's test suggested that the performance of Model 2 had no statistical significance compared to Model 1, while Model 3 had better predictive ability than Model 2 ($p < 0.05$).

Table 4 shows the correlation between each HSA parameter and each aBMD parameter. Only CSA was strongly correlated with TH, TR and IT aBMD (cc > 0.7, $p < 0.05$).

Discussion

To our knowledge, this is the first retrospective study to compare HSA parameters for predicting the risk of second hip fracture, in postmenopausal women. As life expectancy increases, the incidence of hip fracture has concomitantly risen. It is necessary to investigate the factors associated with the risk of second hip fracture particularly in postmenopausal females, since hip refracture brings high risk of prolonged immobility and detrimental effects [9], which impose a considerable economic burden; moreover, according to the osteoporosis guidelines [10, 11], all postmenopausal females with low-energy hip fractures should receive a second hip fracture prevention treatment, and clarifying whether certain factors are risk factors for hip refracture brings better evaluation.

In our research, no statistical differences were observed in any of the HSA parameters except for CSA, comparing the refracture and control groups; logistic regression results showed that HSA parameters were neither protective nor risk factors for a second hip fracture in postmenopausal women. HSA provides information on how the geometrical changes alter the bones' ability to resist fractures via absorbing energy through combined effects of elastic and plastic deformation [12], acting as an important role in predicting the occurrence of hip fracture and describing the characteristics of fracture sites [7, 13, 14]. However, it did not play a significant part in predicting refracture. The reasons leading to such result may be as follows. First, unlike routine low-energy hip fracture, second hip fracture has different risk factors such as lack of rehabilitation, reduced walking ability, and atrophy of muscles which make patients easily fall [15–20]. Falling plays a crucial role in second fracture, more than hip mechanical structure. What is more, dementia, cardiac disease, and a history of previous fragility fracture can also lead to an increased incidence of hip refracture [19–22], but these factors have little association with HSA. Second, a prior study has reported that the incidence of hip refracture significantly increases with a decreased TH, TR and IT aBMD, especially related to the latter two [15]. But in the present research, we found that CSA was the only HSA parameter strongly correlated with TH, TR and IT aBMD, while the correlation of other parameters was poor. That may, to some extent, explain why HSA parameters were not associated with the risk of second hip fracture in postmenopausal women. Interestingly, our study showed that the odds ratio of TR aBMD was no longer significant after controlling age, T2DM and PMS. Whether this difference was caused by the

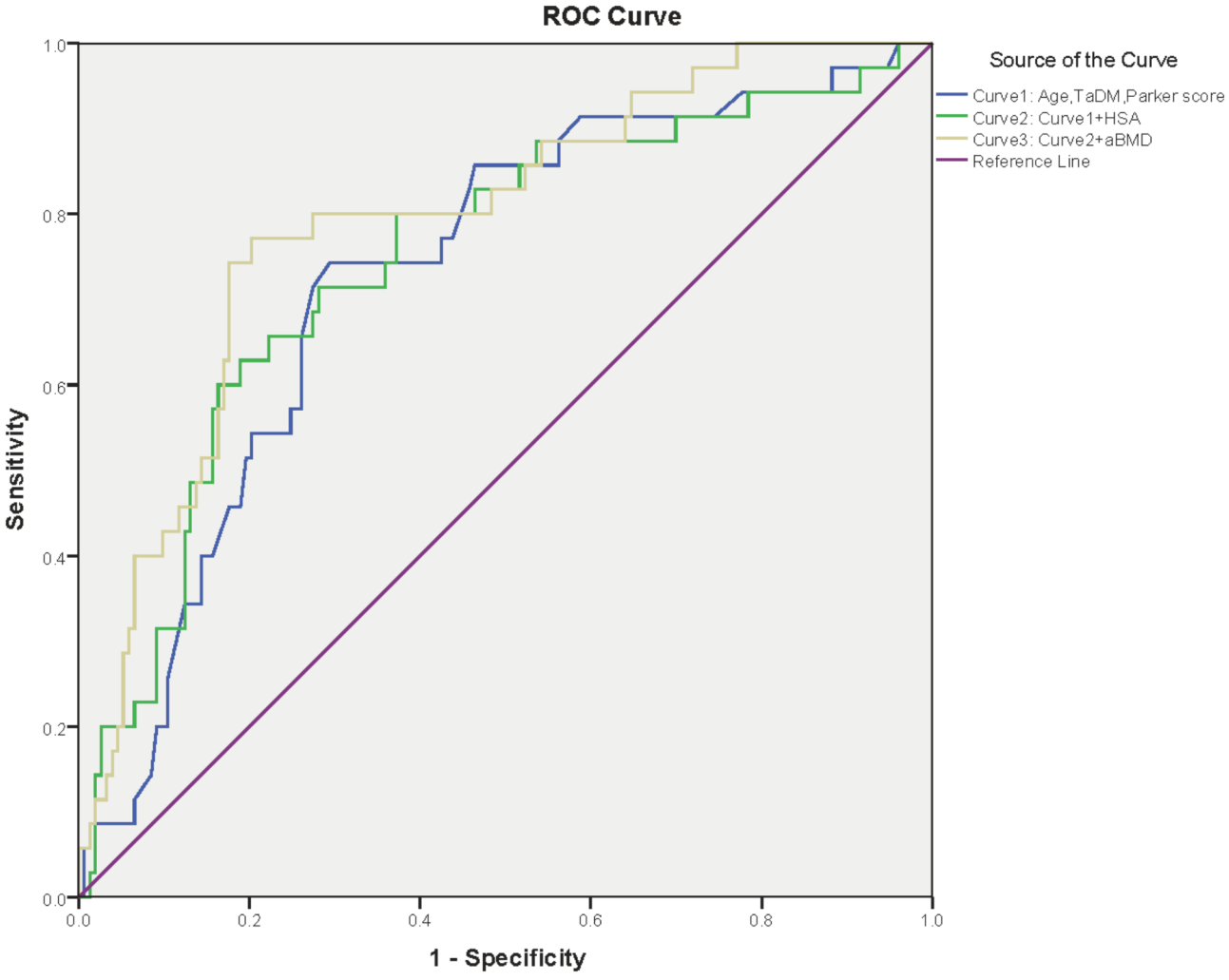

Fig. 3 ROC curves of Model 1–3 were listed above. Model 1 (as the baseline) used age, T2DM, and the PMS as parameters; Model 2 included the parameters in Model 1 with HSA parameters; and Model 3 included the parameters in Model 2 with aBMD parameters

Table 3 The AUC and Delong's test for multiple ROC curves

Test Result Variable(s)	Area (95% Confidence Intervals)	Hosmer–Lemeshow test	Delong's test	
			The differences of AUCs	*p* Value
Curve 1: Age, T2DM, PMS	0.729(0.639, 0.820)	0.267	-	-
Curve 2: Curve 1 + HSA	0.748(0.654, 0.842)	0.769	Curve2 vs. Curve1: 0.019(-0.026, 0.063)	0.409
Curve 3: Curve 2 + aBMD	0.793(0.711, 0.876)	0.270	Curve3 vs. Curve2: 0.045(0.002, 0.088)	0.039

small sample size or by the characteristics of the postmenopausal females population itself needed further research.

Our research results indicated that the performance of regression Model 2, which incorporated HSA parameters, was average in predicting the risk of hip refracture among postmenopausal women (AUC = 0.748); and its performance had not improved compared to the baseline (Delong's test, $p > 0.05$). It further proves there was no significant relation between hip refractures (in postmenopausal females) and HSA, suggesting that HSA parameters should not be taken for granted to predict the risk of hip refracture, otherwise it may mislead the judgement of radiologists and clinicians. The AUC had significantly increased (Delong's test, $p < 0.05$) when we added aBMD parameters in Model 3, due to the association between TH, IT aBMD and hip refracture [15]. However, Model 3 still performed averagely with that AUC = 0.793.

There is one thing worth mentioning that the proportion of TR fractures has increased in second hip fractures [15]. What HSA mainly evaluates is the mechanical structure of the FN region, which limits its role in predicting the risk of hip refracture.

Table 4 The correlation between each HSA parameter and each aBMD parameter

		HSA-CSA	HSA-ACT	HSA-ED	HSA-CSMI	HSA-Z	HSA-BR
TH aBMD	CC	0.770**	0.665**	0.039	0.409**	0.401**	-0.474**
	*p*Value	< 0.001	< 0.001	0.590	< 0.001	< 0.001	< 0.001
FN aBMD	CC	0.579**	0.462**	0.171*	0.367**	0.307**	-0.302**
	*p*Value	< 0.001	< 0.001	0.019	< 0.001	< 0.001	< 0.001
TR aBMD	CC	0.707**	0.596**	0.038	0.359**	0.339**	-0.410**
	*p*Value	< 0.001	< 0.001	0.606	< 0.001	< 0.001	< 0.001
IT aBMD	CC	0.743**	0.642**	0.045	0.397**	0.394**	-0.458**
	*p*Value	< 0.001	< 0.001	0.538	< 0.001	< 0.001	< 0.001

*. Correlation is significant at the 0.05 level (2-tailed)

**. Correlation is significant at the 0.01 level (2-tailed)

CC, correlation coefficient

The main clinical significance of our research is to deny the feasibility of using HSA to predict the risk of second hip fracture in postmenopausal females, which may help to reduce miscalculations. The strengths of our study are that all subjects had CT examination within 48 h after injury, minimizing fracture-related changes in bones; and the fracture they suffered were all low-energy osteoporotic type. Furthermore, the HSA and aBMD parameters we analyzed were measured by Mindways QCTPRO software, which has higher accuracy than those obtained from dual energy X-ray absorptiometry.

This study has some limitations. Our sample selection for the refracture and control groups was limited by the characteristics and incidence of related diseases, and our sample size was relatively small, which might cause bias in results. Second, CT scans of the hip were performed at baseline and were not repeated, leading to data on changes of bone after first hip fracture are lacking. In future research, we plan to include more samples and explore the correlation between hip refractures and some mobility factors.

In conclusion, while HSA is a critical parameter for predicting hip fractures, it does not statistically correlate with the incidence of second hip fracture in postmenopausal women, and incorporating HSA (and aBMD) parameters into the predictive model does not significantly improve the performance of second hip fracture prediction.

Abbreviations

ACT	Average cortical thickness
BMD	Bone mineral density
BR	Buckling ratio
CSA	Cross-sectional area
CSMI	Cross-sectional moment of inertia
ED	Endosteal diameter
FN	Femoral neck
HSA	Hip structural analysis
IT	Intertrochanteric
PMS	Parker
QCT	Quantitative computer tomography
TH	Total hip
TR	Trochanteric
Z	Section modulus

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Not applicable.

Author contributions

Authors contribution is listed as follows: Yimin Ma and Yufeng Ge contributed to the conception of the study, while writing the paper; Yimin Ma, Zhe Guo and Yongbin Su performed the data acquirement; Chao Wang and Qianqian Wang performed the data analyses and statistical works; Ling Wang, Xiaoguang Cheng, Minghui Yang and Dong Yan helped to offer constructive discussions, and revision of paper.

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Data availability

All data generated or analysed during this study are included in this published article.

Declarations

Ethics approval and consent to participate

This study was in progress after the agreement from the Medical Bioethics Committee of Beijing Jishuitan Hospital, Capital Medical University. Ethics approval No.: 202104-10. Informed consent was obtained from each participant.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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