

Sex-related variations in cortical and trabecular bone of the femoral neck in an elderly Chinese population

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Abstract

Summary Quantitative computed tomography (QCT) was used to investigate sex-related variations in cortical and trabecular bone of the femoral neck. Cortical bone thickness of women in the superior quadrant was thinner than that of men, and the cortex in all four quadrants was negatively associated with age in women.

Introduction This cross-sectional study aimed to investigate sex-related similarities and differences in femoral neck structure in an elderly Chinese population by QCT bone investigational toolkit (BIT) analysis.

Methods This study included 207 male (67.9 ± 7.7 years; range, 55–87 years) and 400 female subjects (68.0 ± 8.7 years; range, 55–96 years). BIT module was used to measure cortical and trabecular bone in anatomic quadrants of the femoral neck. Measurements of cortical thickness (Ct.Th), cortical vBMD (Ct.vBMD), trabecular vBMD (Tb.vBMD), and integral vBMD (It.vBMD) at the femoral neck were determined in four anatomical sectors.

Results The greatest difference between sexes, after adjusting for age, height, and weight, was in Ct.Th of Quadrant Supero-anterior (SA), which was 27.4% lower in women ($p < 0.001$). Ct.Th of Quadrant Supero-posterior (SP) was 15.1% lower in women ($p = 0.027$). Ct.Th and Tb.vBMD in all four quadrants

appeared to be negatively associated with age in females, whereas no significant relationship was observed in males, except Ct.Th of Quadrant SP.

Conclusions The superior femoral neck geometry between males and females was significantly different, even after adjustment for body size and age, and the sub-regional cortical and trabecular bone negatively age-related changes in women indicated that women apparently have a more vulnerable geometrical outcome with age for fractures than men.

Keywords Cortical bone · Femoral neck · QCT · Sex · Trabecular bone

Introduction

Hip fracture, increasing exponentially with age, is the most severe clinical consequence of osteoporosis and causes a huge burden on public medical system [1–3]. Despite the fact that hip fractures are the most severe fragility fracture associated with increased mortality, the structural basis of the fractures remains obscure. Areal bone mineral density (aBMD) is used to evaluate hip fracture risk based on observed associations between decreasing aBMD and increasing fracture risk. However, aBMD alone measured by dual-energy X-ray absorptiometry (DXA) or computed tomography X-ray absorptiometry (CTXA) of quantitative computed tomography (QCT) has been suggested to not be an ideal fracture predictor [4]. The utility of aBMD in etiologic studies is limited because of the confounding effect of skeletal size on aBMD measurement and the inability of the projection measurement to separately depict the metabolically distinct trabecular and cortical bone compartments [5]. With the development of QCT, not only the aBMD of the proximal femur but also the anatomical morphology and structural mechanical properties of the

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proximal femur in hip fracture patients can be derived from a three-dimensional CT dataset. The anatomic distribution of cortical and trabecular bone in the mid-femoral neck (FN) may be a determinant of fracture risk. Moreover, most of the compressive and bending strength of a long bone is in its cortical shell; the trabecular bone contributes to the understanding of bone modeling [6]. In the FN, both cortical and trabecular bone contribute to bone strength.

Women are more likely to experience osteoporotic fractures than men are. The greater prevalence of bone fragility fracture in women could be attributed to the smaller skeletal size and lesser bone mineral content or to the more profound effect of aging in women. A better understanding of the interplay of sex in the development of fragility femur fractures is essential for the management and possible selective monitoring for fracture prevention [5]. Sex-related differences in geometry of the FN may help explain the higher hip fracture rates in women. Studies in a North American population have demonstrated that elderly males had a larger cross-sectional area of the FN than elderly women [5, 7], and Scandinavian women had 5% lower mean integral volumetric BMD (vBMD) at the mid-FN ($p = 0.01$) and 15% thinner mean cortical thickness ($p = 0.001$) than men [8].

Hip fracture incidence is lower in the Asian population [9]. Osteoporotic hip fractures are less prevalent in the Chinese population than in Caucasians [1] despite the fact that the former may have lower bone mineral density (BMD) [10]. However, relatively little information on the distribution of cortical and trabecular bone of the FN exists. To the best of our knowledge, no study on the sub-regional cortical and trabecular bone of the mid-FN in a large Chinese cohort, using QCT, has been conducted. Thus, this study aims to investigate the geometry of the FN and compare sex-related variations in an elderly Chinese population by QCT bone investigational toolkit.

Methods

Subjects

This cross-sectional study is part of the China Action on Spine and Hip Status (CASH) study and included 639 subjects enrolled between December 2012 and April 2015. The CASH study, registered in clinicaltrials.gov (NTC 01758770), is an ongoing study led by Cheng and colleagues at Beijing Jishuitan Hospital, Peking University Fourth School of Clinical Medicine, China, that utilized the large-scale population-based Prospective Urban Rural Epidemiology (PURE) population. The PURE study has been reported previously [11]. In the CASH study, PURE study subjects, comprising elderly Chinese individuals willing to participate and undergo spine and hip QCT and/or DXA to investigate the prevalence

of osteoporosis and osteoarthritis, were enrolled. In our study, 532 subjects were from PURE study in Mainland China. All eligible individuals in the selected communities and households, who were willing to participate in the study, were enrolled and were asked to sign the consent form. One hundred seven subjects >60 years old who are in good health (determined based on the questionnaires filled out by the subjects) from communities near Beijing Jishuitan Hospital were also included in this study. These study participants were not for clinical CT scan. All subjects of this study were independently community-dwelling elderly men and women. Participants on medications that have an influence on bone metabolism were excluded. The exclusion criteria also included diabetes, thyroid and parathyroid disease, or other chronic illnesses affecting the bone. Thirty-two subjects were excluded from the study because of missing height or weight information or sub-optimal image quality (i.e., artifacts) for measurement. Consequently, a total of 607 individuals were included in the final sample size, including 207 males (55 to 87 years old) and 400 females (55 to 96 years old). Institutional Review Board (IRB) approval was obtained from the ethics committee of Beijing Jishuitan Hospital, and signed informed consent form was obtained from the participants before the scan.

QCT scans and bone segmentation

QCT scans were obtained using two Toshiba Aquilion 64-slices CT scanners (Toshiba Medical Systems Corp., Tokyo, Japan) with a solid phantom (Mindways Software Inc., Austin, TX, USA). Both hips were scanned in the supine position from the top of the acetabulum to 3 cm below the lesser trochanter. The scan parameters were as follows: 120 Kvp, 125 mAs, 1-mm thickness, 50-cm field of view (SFOV), and 512×512 matrix in spiral reconstruction and standard reconstruction. Images were subsequently transferred to a QCT workstation and analyzed using the CTXA hip function version 4.2.3 of Mindways QCT pro software (Mindways Software Inc., Austin, TX, USA). After image segmentation and manipulation of proximal femur rotation, two-dimensional projection images were generated from three-dimensional CT dataset, as previously described [11].

Cortical thickness estimation

QCT bone investigational toolkit analysis (BIT 2.0, Mindways Software Inc., Austin, TX, USA), which uses a script written to automatically extract 11 contiguous 1-mm-thick cross-sectional slices perpendicular to the FN axis, was performed with a fixed bone threshold for inner cortical separation. The threshold for cortical thickness estimation was set to 450 mg/cm^3 for all of the CT images to minimize differences from the cortical thickness estimates by a higher resolution CT with 1-mm thickness. The BIT

processing was contained in the CTXA Hip module (Fig. 1). The minimum cross-sectional area of the FN (min-CSA FN) placement was automatically directed perpendicular to the FN axis. Ten further slices were extracted medially at 1-mm intervals (Fig. 1). Only the first six slices were used in the BIT analysis, and the geometric variables were derived from the average of the six slices. The interpolated pixel size of the extracted cross-sectional images was 0.488 mm. The cross-sectional femur image was subdivided into 16 sectors, referred to as BIT sectors. The BIT sectors were defined by a constant perimeter, not chosen by a constant angle, resulting in sector angles being slightly less than the average angle (22.5°) for regions with perimeters relatively far from the center of the bone. The measurements of cortical thickness (Ct.Th), cortical vBMD (Ct.vBMD), trabecular vBMD (Tb.vBMD), and integral vBMD (It.vBMD) at the FN were determined in BIT sectors. This resulted in four anatomical quadrants as follows (Fig. 1):

- Quadrant SA (Supero-anterior)—sectors 2, 3, 4, 5
- Quadrant IA (Infero-anterior)—sectors 6, 7, 8, 9
- Quadrant IP (Infero-posterior)—sectors 10, 11, 12, 13
- Quadrant SP (Supero-posterior)—sectors 14, 15, 16, 1

The BIT module also allowed measurements of CSA of the FN and average cortical thickness (as the mean across the four quadrants).

Statistical analysis

The baseline characteristics of the subjects were calculated as means and standard deviations (SD). Scans with measurement values greater or less than 3 SD from the mean values were examined for sources of error. Inappropriate scan data (i.e., artifacts or image segmentation failure) were

removed and other data were reanalyzed by BIT. To compare age differences in geometric variables, we defined three age groups, 55–64, 65–74, and ≥ 75 years, and performed linear regression analysis on the measurements of the different age groups. Unpaired Student's *t* test was performed to compare unadjusted differences between sexes in age, height, weight, body mass index (BMI), and each geometric measurement. Cross-sectional properties of the FN, which are at least partly dependent on body size, of each measured parameter (Ct.Th, Ct.vBMD, Tb.vBMD, It.vBMD, CSA) were compared between males and females, using generalized linear models (GLMs) with adjustment for age, height, and weight. Differences associated with age between men and women were tested using an age-sex interaction term in a GLM. If the age-sex interaction was significant, simple main effect tests were used to examine differences between the groups. Statistical analysis was performed using IBM SPSS Statistics for Windows version 20.0 (IBM SPSS Inc., Chicago, IL) and GraphPad Prism software for Windows version 6.0 (GraphPad Software, San Diego, Calif). Differences were considered significant at $p < 0.05$.

Results

Study population characteristics

Characteristics of the subjects are shown in Table 1. There were 240 participants in the 55–64-year-old age group, (86 men, 154 women) and 213 in the 65–74-year-old age group (71 men, 142 women). No age difference between the two sex groups was found ($p = 0.78$). As expected, males on average were taller and heavier than females; however, no differences between sexes in BMI were noted (Table 2). The average BMI of the sample and each age group was $< 28 \text{ kg/m}^2$.

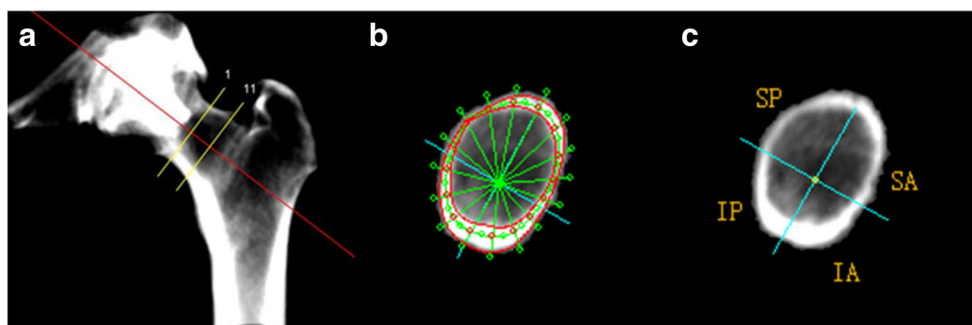


Fig. 1 QCT bone investigation toolkit (BIT) was analyzed using CTXA Hip module, and the ROI was placed automatically at the minimum cross-sectional area of the femoral neck (FN) with 11 continuous slices at 1-mm intervals medially (a). The cross-sectional femur was

subdivided into 16 sectors (b), and all the sectors were divided into four anatomical quadrants (c): SA (Supero-anterior), IA (Infero-anterior), IP (Infero-posterior), SP (Supero-posterior)

Table 1 Characteristics and measurement parameters of the subjects

Group	Male				Female			
	55–64 years (n = 86)	65–74 years (n = 71)	≥75 years (n = 50)	p value	55–64 years (n = 154)	65–74 years (n = 142)	≥75 years (n = 104)	p value
Age (years)	60.7 ± 2.5	69.6 ± 2.9	79.0 ± 3.2	<0.001	59.1 ± 3.0	69.3 ± 2.9	79.5 ± 3.9	<0.001
Height (cm)	161.7 ± 6.7	168.5 ± 4.6†	168.8 ± 6.0†	0.66	158.9 ± 5.0	157.6 ± 5.7	154.5 ± 16.2	0.001
Weight (kg)	72.4 ± 11.6	69.4 ± 8.5	69.8 ± 8.9	0.22	61.8 ± 8.8	61.9 ± 8.5	56.54 ± 10.61	<0.001
BMI (kg/m ²)	25.2 ± 3.4	24.4 ± 8.4	24.5 ± 2.9	0.30	24.5 ± 3.4	24.9 ± 3.1	23.2 ± 4.1	0.01
Ct.Th (mm)								
Quadrant SA	1.2 ± 0.8	1.2 ± 0.7	1.0 ± 0.7	0.22	1.0 ± 0.7	0.7 ± 0.6	0.7 ± 0.6	<0.001
Quadrant IA	2.3 ± 0.7	2.1 ± 0.6	2.3 ± 0.7	0.75	2.3 ± 0.7	2.0 ± 0.7	1.9 ± 0.7	<0.001
Quadrant IP	3.6 ± 0.7	3.6 ± 0.7	3.4 ± 0.8	0.22	3.8 ± 0.6	3.4 ± 0.7	3.1 ± 0.8	<0.001
Quadrant SP	0.9 ± 0.6	0.9 ± 0.6	0.6 ± 0.5	0.033	0.9 ± 0.6	0.5 ± 0.5	0.5 ± 0.4	<0.001
Ct.vBMD (mg/cm ³)								
Quadrant SA	551.1 ± 43.8	553.1 ± 43.3	549.1 ± 40.0	0.86	538.0 ± 43.6	522.7 ± 72.7	528.9 ± 69.5	0.18
Quadrant IA	697.5 ± 48.5	702.2 ± 45.5	708.9 ± 49.4	0.18	711.7 ± 51.2	711.8 ± 57.1	727.7 ± 52.9	0.029
Quadrant IP	791.3 ± 41.1	804.3 ± 54.4	797.7 ± 58.2	0.35	805.4 ± 53.4	799.1 ± 54.2	809.9 ± 62.8	0.64
Quadrant SP	539.8 ± 35.2	540.8 ± 31.9	520.4 ± 23.3	0.002	549.9 ± 37.3	527.7 ± 32.9	524.1 ± 32.6	<0.001
Tb.vBMD (mg/cm ³)								
Quadrant SA	111.7 ± 27.0	104.7 ± 26.5	106.0 ± 26.2	0.16	120.4 ± 24.9	101.0 ± 26.8	84.9 ± 28.1	<0.001
Quadrant IA	114.3 ± 29.3	108.7 ± 29.2	114.9 ± 24.0	0.92	117.3 ± 27.5	102.4 ± 34.6	85.7 ± 37.5	<0.001
Quadrant IP	119.8 ± 28.3	109.8 ± 27.9	118.5 ± 25.2	0.52	109.4 ± 29.2	92.8 ± 33.8	76.6 ± 32.7	<0.001
Quadrant SP	119.0 ± 25.9	112.3 ± 28.8	116.1 ± 26.5	0.41	121.3 ± 26.7	100.12 ± 28.39	81.4 ± 28.1	<0.001
It.vBMD (mg/cm ³)								
Quadrant SA	158.7 ± 49.2	151.2 ± 47.8	146.0 ± 45.7	0.13	161.5 ± 49.4	130.7 ± 40.9	115.8 ± 46.4	<0.001
Quadrant IA	251.2 ± 53.3	239.5 ± 51.0	254.2 ± 50.3	0.95	269.4 ± 55.7	241.4 ± 60.7	220.8 ± 63.1	<0.001
Quadrant IP	352.8 ± 54.1	351.4 ± 63.2	344.7 ± 58.6	0.46	387.8 ± 57.1	345.9 ± 62.7	321.1 ± 73.6	<0.001
Quadrant SP	158.1 ± 41.3	155.2 ± 42.5	142.1 ± 36.5	0.036	167.3 ± 46.2	130.0 ± 41.2	106.9 ± 38.8	<0.001
Ave. Ct.Th (mm)	2.0 ± 0.6	2.0 ± 0.5	1.8 ± 0.6	0.15	2.0 ± 0.6	1.7 ± 0.5	1.5 ± 0.5	<0.001
CSA (cm ²)	10.1 ± 1.6	10.1 ± 1.4	10.3 ± 1.5	0.49	8.1 ± 1.2	8.3 ± 1.3	8.3 ± 1.4	0.319

p values were for the differences among sex-specific age groups analyzed using linear regression model

BMI body mass index, Ct.Th cortical thickness, Ct.vBMD cortical volumetric bone mineral density, Tb.vBMD trabecular volumetric bone mineral density, It.vBMD integral volumetric bone mineral density, CSA cross-sectional area

Sex-related similarities and differences in cortical and trabecular bone in anatomic quadrants

Table 2 illustrates the proportional differences between women and men in cross-sectional cortical and trabecular bone in the four quadrants of the FN after adjusting for age, height, and weight. Using regression analysis to control for anthropometric variables (Table 2), we found that the greatest difference between sexes after adjustment was in Ct.Th of Quadrant SA, which was 27.4% lower in women ($p < 0.001$). The estimated Ct.Th of Quadrant SP was 15.1% lower in women than in men ($p = 0.027$). Women had a higher vBMD in the cortical bone than men did in Quadrant IA, and men had a higher Ct.vBMD in Quadrant SA. The thickest Ct.Th was in Quadrant IP for both sexes

(men 3.6 ± 0.7 mm, women 3.5 ± 0.7 mm). In the unadjusted comparison, CSA in women was 19.2% lower than that in men; interestingly, after adjusting for age, height, and weight, CSA in females was still significantly lower than in males.

Sex-related differences in sub-regional cortical and trabecular bone associated with age

Table 1 shows that Ct.Th of the superior-posterior FN, i.e., Quadrant SP, was negatively associated with age in both sexes, whereas Ct.Th of other sub-regional regions, which included Quadrants SA, IA, and IP, showed no relationship with age in men (Table 1, Fig. 2). Moreover, Tb.vBMD in all four quadrants appeared to have a significantly negative

Table 2 Sex-related differences in variables of sub-regional geometry by quadrant and demographics of the subjects

Variables	Male	Female	Unadjusted F. vs M. dif. (%)	<i>p</i> value	Adjusted F. vs M. dif. (%)	<i>p</i> value	Sex × age interaction (<i>p</i> value)
Ct.Th (mm)							
Quadrant SA	1.2 ± 0.7	0.8 ± 0.7	−28.5	<0.001	−27.4	<0.001*	0.22
Quadrant IA	2.2 ± 0.6	2.1 ± 0.8	−	−	−	−	0.002
Quadrant IP	3.6 ± 0.7	3.5 ± 0.7	−	−	−	−	<0.001
Quadrant SP	0.8 ± 0.6	0.7 ± 0.6	−17.2	0.003	−15.1	0.027*	0.069
Ct.vBMD (mg/cm³)							
Quadrant SA	551.3 ± 42.6	530.2 ± 62.3	−3.8	<0.001	−3.6	0.001*	0.55
Quadrant IA	701.9 ± 47.7	715.9 ± 54.1	2.0	0.002	2.3	0.003*	0.53
Quadrant IP	797.3 ± 50.4	804.4 ± 56.3	0.9	0.13	1.6	0.029*	0.27
Quadrant SP	535.5 ± 32.6	535.3 ± 36.4	−0.03	0.96	0.2	0.73*	0.45
CSA (cm ²)	10.1 ± 1.5	8.2 ± 1.3	−19.2	<0.001	−14.8	<0.001*	0.56
Tb.vBMD (mg/cm³)							
Quadrant SA	107.9 ± 26.7	104.3 ± 30.0	−	−	−	−	<0.001
Quadrant IA	112.5 ± 28.1	103.8 ± 35.1	−	−	−	−	<0.001
Quadrant IP	116.1 ± 27.7	95.0 ± 34.3	−	−	−	−	<0.001
Quadrant SP	116.0 ± 27.1	103.4 ± 31.9	−	−	−	−	<0.001
It.vBMD (mg/cm³)							
Quadrant SA	153.1 ± 47.9	138.7 ± 49.4	−	−	−	−	<0.001
Quadrant IA	247.9 ± 51.9	246.8 ± 62.5	−	−	−	−	<0.001
Quadrant IP	350.3 ± 58.3	355.6 ± 69.1	−	−	−	−	<0.001
Quadrant SP	153.2 ± 40.9	138.4 ± 49.1	−	−	−	−	<0.001
Ave. Ct.Th (mm)	1.9 ± 0.5	1.8 ± 0.6	−	−	−	−	0.002
Age	67.9 ± 7.7	68.0 ± 8.7	0.1	0.78	−	−	−
Height	168.9 ± 5.9	157.3 ± 9.6	−6.9	<0.001	−	−	−
Weight	70.4 ± 9.6	60.4 ± 9.5	−14.2	<0.001	−	−	−
BMI	24.7 ± 3.0	24.3 ± 3.6	−1.5	0.78	−	−	−

BMI body mass index, *Ct.Th* cortical thickness, *Ct.vBMD* cortical volumetric bone mineral density, *Tb.vBMD* trabecular volumetric bone mineral density, *It.vBMD* integral volumetric bone mineral density, *CSA* cross-sectional area, *F.* female, *M.* male, *dif.* Differences

Unadjusted and adjusted F. vs M. dif. (%) defined as (female − male) × 100/male

*Adjusted for age, weight, and height

association with age in females, whereas no significant relationship was observed in males. This observation was consistent with the result of sex-age interaction analysis for *Tb.vBMD* in this study. Of interest, no relationship with age was observed in *CSA* in either sex (Table 1).

Table 2 demonstrates that age-sex interaction was significant in Ave. *Ct.Th*, and *Ct.Th* of the inferior quadrants, and *Tb.vBMD* and *It.vBMD* in all four quadrants ($P < 0.01$) in regression models. Table 3 shows the results of the simple main effect tests of age level and sex for these measures. *Ct.Th* of Quadrant IA differed between sexes only in the Elder-Elder group ($P < 0.001$). Both *Tb.vBMD* and *It.vBMD* differed between sexes in all quadrants in the Elder-Elder group ($P < 0.05$). Ave. *Ct.Th* differed between sexes in the Elder and Elder-Elder groups ($P < 0.001$).

Discussion

This is the first study to report on the sub-regional cortical and trabecular bone of the FN measured in a large Chinese population by QCT. We hypothesized that sex differences in the geometry of the FN are a key to the difference in fracture rates between women and men. However, this is just an inference from a geometrical perspective, and a case-control or prospective study on fracture risk assessment on both sexes in a Chinese cohort may provide a more accurate insight on the association of hip geometry and fractures. The relationship with age in *Ct.Th* of the anatomic quadrants between females and males revealed similarity only for Quadrant SP. Differences in the relationship with age were observed in *Ct.Th* between male and female subjects and were markedly different according to anatomic

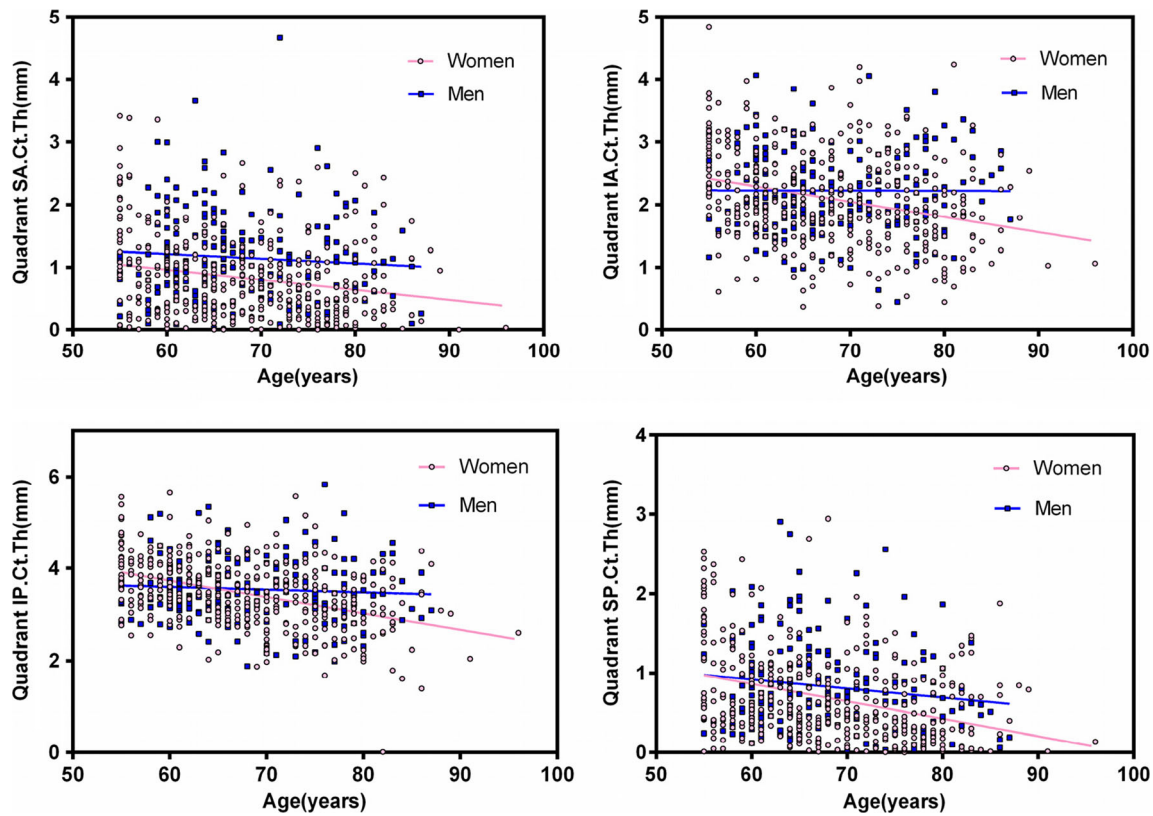


Fig. 2 Plots of sub-regional cortical thickness parameters (unadjusted data) with age in an elderly Chinese cohort. Quadrant SA. Women: $Y = -0.016 * X + 1.94, p < 0.001$ vs Men: $Y = -0.007 * X + 1.66, p > 0.05$; Quadrant IA. Women: $Y = -0.024 * X + 3.76, p < 0.001$ vs

Men: $Y = -0.0003 * X + 2.25, p > 0.05$; Quadrant IP. Women: $Y = -0.035 * X + 5.86, p < 0.001$ vs Men: $Y = -0.006 * X + 3.96, p > 0.05$; Quadrant SP. Women: $Y = -0.022 * X + 2.18, p < 0.001$ vs Men: $Y = -0.011 * X + 1.61, p < 0.05$. *Ct.Th* cortical thickness

location within the FN. Tb.vBMD appeared to be negatively associated with age in women; however, no relationship was observed in men. CSA, one of the main determinants

of bone strength being closely related to resistance to compression, was lower in women than in men before and after adjustment.

Table 3 Simple main effect tests for variables of sub-regional cortical and trabecular bone

Variables	Age group-specific sex difference		
	Middle (55–64 years)	Elder (65–74 years)	Elder-Elder (≥75 years)
Quadrant IA Ct.Th (mm)	0.68	0.13	0.002
Quadrant IP Ct.Th (mm)	0.062	0.023	0.001
Ave. Ct.Th (mm)	0.92	<0.001	0.001
Tb.vBMD (mg/cm ³)			
Quadrant SA	0.027	0.22	<0.001
Quadrant IA	0.54	0.10	<0.001
Quadrant IP	0.008	<0.001	<0.001
Quadrant SP	0.68	0.001	<0.001
It.vBMD (mg/cm ³)			
Quadrant SA	0.82	0.001	<0.001
Quadrant IA	0.025	0.89	0.002
Quadrant IP	<0.001	0.48	0.035
Quadrant SP	0.22	<0.001	<0.001

Cortical bone is a key to the structural stability of the proximal femur [12]. This bone shell makes up most of the skeletal mass, can withstand much greater load than the trabecular bone, and initially deforms prior to failure. Our study indicated no difference in Ct.Th of Quadrants IA and IP between sexes in the 55–64 years age group, whereas differences were significant in the advanced elderly group. The inferior quadrant is highly loaded during walking; thus, the BMD is preserved or increased in this region. This may partially explain the results. However, women had significantly thinner Ct.Th than men did in the superior quadrant (27.4 and 15.1% thinner in SA and SP, respectively). A recent study, using the same image analysis software, demonstrated that healthy female controls had 15% thinner mean Ct.Th than male controls; however, in Quadrant IA, no significant difference was noted [8]. The sex-related differences we found are similar to those reported by Johannesdottir et al. [8], except for the IP area. Johannesdottir et al. also illustrated that compared to Ct.Th in the inferior region, that in the superior region of the FN was a stronger predictor for hip fracture in both

sexes. Furthermore, Ct.Th in Quadrant SA was considered the best determinant of fracture risk in healthy controls [8]. Other studies have also reported thinner cortex as a risk factor for hip fractures [13, 14]. Our data indicated that thinner Ct.Th in the superior region of the FN in women could provide additional information for identifying those at risk for hip fractures, which is consistent with previous studies [8, 15]. However, this remains inconclusive and needs confirmation in a case-control study with a similar cohort. Another study, focusing on Mainland Chinese, showed that the difference in Ct.Th between sexes failed to reach statistical significance in both young and elderly groups [16]. In this study, the estimated average Ct.Th was measured by DXA and seemed to confound the effect of no sex-related differences on the inferior quadrant.

There is a long-standing interest in hip fractures increasing with age. Numerous studies reported proximal femur bone loss and fractures with age [7, 14, 15, 17–20]. However, little is known about the sub-regional cortical bone age-related change in the Chinese population. Figure 2 shows that Ct.Th of the superior FN was significantly associated with age in both sexes. However, Ct.Th of the inferior region in men showed no relationship with age, whereas reduced Ct.Th was associated with age in women. In a cross-sectional study, Poole et al. showed that age is the principal determinant of Ct.Th in women and has significantly different effects within the anatomic quadrants [17]. They also compared young women with elderly subjects and found relative preservation of Quadrant IA; however, Ct.Th and BMD were strikingly reduced in Quadrant SA. Furthermore, a longitudinal study illustrated that elderly women lose Ct.Th more rapidly than elderly men, and in both sexes, the relative losses were significantly greater in all variables in the superior region than in the mechanically loaded inferior region [14]. Our data demonstrated that Ct.Th might have a negative association with age in all four quadrants of the FN in Chinese elderly women. The explanation for this sex-related difference remains unclear.

Noticeably, our finding that men did not have reduced Ct.vBMD associated with increasing age, except in Quadrant SP, is not consistent with previous studies. Riggs et al. showed that Ct.vBMD decreased over adult life more in women than in men [21]. Some studies, including cross-sectional studies and longitudinal studies, confirmed this observation [14, 17]. The relationship of increasing age with lower Tb.vBMD found in our study is similar to those reported by Riggs et al. Moreover, our results showed that women appeared to have lower Tb.vBMD with increasing age, whereas men apparently showed no relationship of age and trabecular bone (Table 1).

The Mindways BIT module was used to direct automatic mid-FN cross-sectional placement where the approximate ratio of the maximum to minimum diameters (max/min ratio)

equaled to 1.4 (Femoral Neck Eccentricity = 1.4 or EPS = 1.4 region) in most studies [8, 12, 14, 17, 22]. The region intended for measurement in Poole et al.'s study tends to be centered closely to the neck/trochanter junction region; thus, only the first six images (six most proximal images of the neck) of the 11 images when generating sector averages were used in the analysis. The EPS = 1.4 region, however, might not be as useful in Asian populations because of genetically based anatomical difference in the shape of the proximal femur between Asians and Caucasians [22, 23]. Therefore, we used min-CSA FN placement to measure the mid-femoral structure. The first six slices were used in the BIT analysis because the last two or three images in the group of 11 images might include a portion of the greater trochanter.

Little is known about the distribution of cortical and trabecular bone of the FN in the Asian population, especially in a Chinese cohort, and hip fracture incidence rates vary considerably between races [23]. Compared to the incidence rates described in Scandinavian regions and North America, the incidence in the Chinese population is relatively lower [23–25]. Thus, the outcomes of this investigation may contribute to the understanding of different hip fracture incidence rates worldwide. Further studies comparing potentially significant ethnically based structural differences between Chinese and Caucasians are warranted.

Our study has several limitations. First, we performed a cross-sectional study which is indeed a weaker study design than a longitudinal study or randomized controlled trial (RCT) and the causality in a cross-sectional study limits the ability reflecting differences in the relationship with age in the bone geometry. Second, as some previous studies discussed [8, 12], the limitation of the methodology could result in inaccurate measurement of the cortical shell in vivo by the BIT software, especially in the thin superior region. Third, we used a single threshold for all CT images to estimate cortical thickness. Although there is no single Ct.Th and with the considerable heterogeneity in Ct.Th, a single threshold to separate cortical and trabecular bone as one transition to another is necessary.

In summary, the superior femoral neck geometry between males and females was significantly different, even after adjustment for body size and age, and the sub-regional cortical and trabecular bone negatively age-related changes in women indicated that women apparently have a more vulnerable geometrical outcome with age for fractures than men.

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Compliance with ethical standards

Conflicts of interest Ling Wang, Xiaoguang Cheng, Yongbin Su, Li Xu, Kai Li, Chenxin Zhang, Yong Zhang, Yangyang Duanmu, Xinbao Wu, and Manyi Wang declare that they have no conflict of interest. Keenan Brown is a stockholder of Mindways Software Inc.

Ethical approval All procedures performed that involved human participants were in accordance with the ethical standards of the institutional and/or national research committee and are approved by the Institutional Review Board.

Informed consent Informed consent was obtained from all individual participants included in the study.

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