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The differences of femoral neck geometric parameters: effects of age, gender and race

F. Zhang,

Laboratory of Molecular and Statistical Genetics, College of Life Sciences, Hunan Normal University, Changsha, Hunan 410081, People's Republic of China

L.-J. Tan,

Laboratory of Molecular and Statistical Genetics, College of Life Sciences, Hunan Normal University, Changsha, Hunan 410081, People's Republic of China

S.-F. Lei, and

Laboratory of Molecular and Statistical Genetics, College of Life Sciences, Hunan Normal University, Changsha, Hunan 410081, People's Republic of China. Departments of Orthopedic Surgery and Basic Medical Sciences, University of Missouri-Kansas City, 2411 Holmes St., Room M3-C03, Kansas City, MO 64108-2792, USA

H.-W. Deng

Laboratory of Molecular and Statistical Genetics, College of Life Sciences, Hunan Normal University, Changsha, Hunan 410081, People's Republic of China. Center of Systematic Biomedical Research, Shanghai University of Science and Technology, Shanghai, China. Departments of Orthopedic Surgery and Basic Medical Sciences, University of Missouri-Kansas City, 2411 Holmes St., Room M3-C03, Kansas City, MO 64108-2792, USA

H.-W. Deng: dengh@umkc.edu

Abstract

Summary—This study aims at investigating the effects of age, sex, and ethnicity on five femoral neck geometric parameters (FNGPs): femoral neck periosteal diameter, cross-sectional area, cortical thickness, sectional modulus, and buckling ratio and found that the three factors would influence the FNGPs.

Introduction—Bone geometry is one of the most important predictors of bone strength and osteoporotic fractures. This study aims at investigating the effects of age, sex, and ethnicity on five femoral neck geometric parameters (FNGPs): femoral neck periosteal diameter (W), cross-sectional area (CSA), cortical thickness (CT), sectional modulus (Z), and buckling ratio (BR).

Methods—In the studied 861 Caucasian subjects and 3,021 Chinese individuals, CSA, CT, and Z displayed trends of decrease with age, but W and BR showed increasing trends with age in both Chinese and Caucasian females and males ($p < 0.05$). W , CSA, CT, and Z were significantly higher ($p \leq 0.001$) in Caucasians than in Chinese and higher in males than in females except for BR between Chinese males and Chinese females.

Conclusion—In conclusion, the differences of FNGPs according to gender and ethnicity provide important implications in the different prevalence of osteoporotic fracture among different gender and ethnic groups.

Correspondence to: H.-W. Deng, dengh@umkc.edu.

Fang Zhang and Li-Jun Tan contributed equally to this study.

Conflicts of interest None.

Keywords

Age; Femoral neck geometric parameters; Race; Sex

Introduction

Osteoporosis is a systematic bone disease characterized by low bone strength, leading to increasing susceptibility to bone fracture. Hip fracture is the most serious osteoporotic fracture (OF). Bone mineral density (BMD) is widely used in estimating bone strength and predicting OF [1–4]. Other bone structural phenotypes, such as femoral neck geometric parameters (FNGPs), may also be important determinants of bone strength [5]. Patients with hip fracture had lower cross-sectional area (CSA), sectional modulus (Z), cortical thickness (CT), and higher buckling ratio (BR) than health controls [6].

The prevalence of hip fracture is different in groups classified by gender or ethnicity [7–10]. Most of studies reported higher rates of hip fracture in women than in men [11–13]. And comparing race, numerous previous studies have constantly reported that the age-adjusted annual rates of hip fracture were lower in Asians than Caucasians [12–15]. The different bone strength may be the leading factor responsible for the differences in prevalence of hip fracture in groups according to gender or ethnicity. However, currently, it is largely unknown if there are differences of bone parameters of hip in such groups, which may result in differences of bone strength.

Materials and methods

Subjects

A. The Chinese sample—The study on Chinese samples was approved by the necessary Institutional Review Board in China. The subjects were collected in Changsha, Xi'an, and Shanghai. A total of 3,021 unrelated subjects aged 19–80 years, who belong to the Chinese Han ethnic group, were recruited. After the subjects signed the informed consent document, a questionnaire was given to obtain the subject's information on age, sex, medical history, family history, female history, physical activity, alcohol use, dietary habits, and smoking history under direction of clinician. We adopted the exclusion criteria detailed elsewhere [16] to screen and recruit “healthy” subjects. To be specific, individuals with history of diseases or therapies, such as rheumatoid arthritis or collagen disease, chronic renal disease, recent major gastrointestinal disease (within the past year), such as peptic ulcer, malabsorption, or treatment with anticonvulsant therapy for 6 months duration, which might probably influence bone mass, structure, or metabolism, have been excluded from our study.

B. The Caucasian sample—The study on Caucasian samples was approved by the Creighton University Institutional Review Board. Signed informed consent documents were obtained from all study participants before they entered the study. People with chronic diseases and conditions that might potentially affect bone mass, structure, or metabolism were excluded as detailed before [16]. The sample contains a total of 861 unrelated Caucasian subjects aged from 19 to 80 years which were selected from our previous data including 4,498 individuals from 451 pedigrees. All the Caucasian subjects were of European origin. The basic characteristics of both the Chinese and Caucasian subjects were listed in Table 1.

Individuals without genetic relationships are considered unrelated and selected for the present study. For example, if an individual was selected, his/her children, cousins, siblings, parents, parents' siblings, and parents' siblings' children were not chosen, but the person

who married the one in the pedigree was selected. In this way, 861 individuals have been picked out for our study. In order to keep the similar age range in both Caucasian and Chinese, all the 861 samples are aged between 19 and 80.

Measurements

The areal BMD (g/cm^2) and bone size (cm^2) at the femoral neck (FN) of all the subjects were measured by Hologic 2000+ or 4500 DXA scanners (Hologic, Bedford, MA, USA). All scanners are calibrated daily, and long-term precision is monitored with external phantoms. The coefficient of variations (CVs) of FN BMD and bone size measurement obtained on Hologic 2000+ were 1.87% and 1.94% [17–19] in our USA center and 0.8% and 1.18% in our Chinese center. Similar CVs were obtained on Hologic 4500 scanner [19]. Data obtained from different machines are transformed to a compatible measurement by an algorithm as in our previous studies [20]. What is more, technicians maintain scan-by-scan surveillance for quality control in both America and China [21], and each of them was trained and got an International Society for Clinical Densitometry certification. Therefore, BMD and bone size measurements by different scanners and technicians in our center are highly compatible with one another and are well within the precision limits [19].

The FNGPs were estimated using the FN BMD and bone size following the methods detailed well earlier [22–24]. The five estimated FNGPs are: (1) W , femoral neck periosteal diameter; (2) CSA , the area with mineralized bone tissue, excluded bone marrow space; (3) Z , an index of bending resistance; (4) CT , cortical thickness; and (5) BR , an index of bone geometric instability [14]. FNGPs were computed as follows: $CSA = \frac{BMD \times W}{\rho_m}$, where ρ_m is the effective density of fully mineralized bone tissue, which is assumed to be $1.05 \text{ g}/\text{cm}^3$ [25,26], and W , the femoral neck periosteal diameter, can be estimated by dividing the bone size by the width of the region of interest (in Hologic DXA systems, the width of the femoral neck region is standardized at 1.5 cm) [24]. $CT = \frac{W - ED}{2}$, where ED is the estimated

endosteal diameter. $ED = 2 \sqrt{\left(\frac{W}{2}\right)^2 - f_c \frac{CSA}{\pi}}$, where f_c is the assumed proportion of cortical mass in the femoral neck, taken as 0.6. $Z = \frac{CSMI}{W/2}$, where $CSMI$ is the cross-sectional moment inertia. $CSMI = \frac{\pi}{4} \left[\left(\frac{W}{2}\right)^4 - p_t \left(\frac{ED}{2}\right)^4 \right]$, p_t is the trabecular porosity, which is calculated by the following formula:

$$p_t = 1 - \left[\frac{(1 - f_c) \times CSA}{\pi \times \left(\frac{ED}{2}\right)^2} \right] \quad BR = \frac{W/2}{CT}$$

Statistics analysis

The data were normally distributed. Independent-samples t tests were used to analyze the effects of race (Chinese vs. Caucasians) and sex (women vs. men) on each FNGP. Each FNGP except for BR was adjusted for age, height, and weight. The trends to change with age for each FNGP were estimated by linear regression methods, designating age as the independent variable and the FNGPs as the dependent variables, adjusted for weight and height. R squares for each covariate and overall R squares showing the proportion of FNGP variation explained by age, height, and weight and all three factors through regression analysis are listed in Table 2.

The level of statistical significance was originally set at $p = 0.05$. However, the problem of multiple tests has arisen owing to 20 times of t tests and regression. Therefore, we have adopted the most conservative method addressing the multiple test problem—Bonferroni. As

a result, the cutoff of significance was set at $p = 0.05/20 = 0.0025$. The SPSS software was used to perform all the statistical analyses.

Results

As shown in Table 3, compared to Caucasian, Chinese had significantly smaller W ($p < 0.001$ in both males and females), smaller CSA ($p < 0.001$ in both males and females), lower Z ($p < 0.001$ in both males and females), thinner CT ($p = 0.001$ in males; $p < 0.001$ in females), and lower BR ($p \leq 0.001$ in both males and females). In the same ethnic group, the males have significantly higher ($p \leq 0.0025$) values of FNGPs than females with an exception for BR in Chinese.

Figure 1 intuitively showed the distribution of FNGPs against age in both ethnic groups. CSA, CT, and Z decreases with age in both males and females (Fig. 1b–d), while W and BR showed increasing trends with age (Fig. 1a, e). In the same gender group (Fig. 2), all the studied FNGPs were significantly associated with age ($p \leq 0.001$) in both Caucasian and Chinese except for Z in Caucasian females, which was significant at 0.05 level but not significant at the strictest level 0.0025, with increasing trends for W and BR (Fig. 2a, e) and with decrease trends for CSA, Z , and CT (Fig. 2b–d).

Discussion

The present results represented our first efforts to investigate the differences of FNGPs in the studied groups stratified by gender and ethnicity, and the change of FNGPs against age and all the three factors have been shown to influence values of the parameters.

Compared with Caucasians, Chinese had smaller cross-sectional areas, periosteal diameter, sectional modulus, and thinner cortex, implying that the mechanical strength and resistance to bending and torsional stresses is smaller in Chinese than in Caucasian. Predicted only by the results of smaller and weaker FNs, hip fracture rates would be inferred to be higher in Chinese than in Caucasian. However, in fact, numerous studies showed that hip fracture rates were lower in Asians than Caucasians [11–13,15,27]. The seeming controversy between smaller and weaker FN but lower fracture rate of hip shows that except for bone geometric parameters, other risk factors such as hip axis length, femoral neck axis length [8,28], or ratio of leg length to trunk length [8,27] may explain less fractures occurring in Asians.

Our study also found a significant effect of age on FNGPs. CSA, CT, and Z decreased, while BR and W increased with aging. Thinning cortices and narrowing CSA with aging contribute to smaller mechanical strength and lower bending stresses along the cortical surfaces of bone. Thinning cortices may result from more endocortical bone resorption than periosteal bone apposition with aging [10]. Decline in sectional modulus, which best define resistance to bending and torsional stresses, and increment in BR which defined resistance to bending and hip bone geometric stability, revealed that bone becomes weaker and more inclined to fracture with aging.

The femoral neck structure was deteriorated with age as shown in our study and previous studies [9,29–31]. The deterioration as well as the gradual drop in mechanical strength would be partly compensated by expansion of the neck through widening the outer diameter (W). Nevertheless, these compensatory mechanisms could only be partly effective, and bone strength finally deteriorates, as indicated by falling section modulus [32] and other FNGPs such as cross-sectional area, cortical thickness, and buckling ratio.

The deterioration may partly be caused by estrogen deficiency [33–37]. Estrogen deficiency produces increased osteoclast formation and recruitment to bone surfaces, combined with the increased osteoblast apoptosis [38–40], which results in enlarged resorption area, perforated trabecular plate and loose trabecular connectivity in cancellous bone, and subendocortical cavitation in cortical bone [41,42], therefore degrading bone quality. Besides sex hormones, loss of muscle mass with aging, the principal cause of involutional osteoporosis [10,43], abnormalities in the vitamin D-endocrine and growth hormone-insulin-like growth factor-I regulatory systems [44] are other important causes of bone loss giving rise to deterioration of FN structure.

The structure changes increased fracture risk in both races. However, racial difference in the speed of the changes of the FNGPs has also been seen in our study, indicating that bone quality of Chinese individuals deteriorated at a comparatively faster speed. The similar trend has been reported by studies on BMD before: the age-related decline in femoral neck aBMD seems to be faster in Asians than in Caucasians [45,46]. Perhaps this phenomenon can be ascribed to earlier menopause in Chinese than in Caucasians, giving rising to better maintenance of estrogen in Caucasians which is the significantly important hormone in determining bone quality. But the true mechanism deserves more researches in the future. The speed of age-related changes in the FNGPs also differs by genders, implying faster speed of deterioration of bone structure in females. The earlier onset age of puberty and the great drop in estrogen after menopause in females may explained the lower values (with an exception for BR between Chinese males and females) and faster age-related deterioration of the FNGPs in females than in males [47,48]. And the different values and age-related changes of the FNGPs between females and males partly explained the higher hip fracture incidence observed in females [25,29,32].

Our study has some limitations. Firstly, different fat distribution around the hip could affect the DXA measurements of the proximal femur and thus the FNGPs. Secondly, the FNGPs were not three-dimensional data since they were calculated using two-dimensional DXA data assuming that the femoral neck is a circular structure and the cortical shell has an even thickness in the entire rim. Two-dimensional data are subject to errors in modeling three dimensions. However, this method is more readily available to researchers and less costly than three-dimensional techniques (e.g., quantitative computed tomography). Thirdly, the number of Chinese, especially males, aged between 40 and 50, is limited, making the age frequency of the two ethnic cohorts, to some extent, differ.

In conclusion, our study firstly reported that there were differences in FNGPs between two main ethnic groups (Caucasians vs. Chinese), and between two genders (males vs. females). Furthermore, the deterioration of bone structure is associated with age. The differences of FNGPs according to gender and ethnicity may partly explain the different prevalence of osteoporotic fracture among different gender and ethnic groups.

Acknowledgments

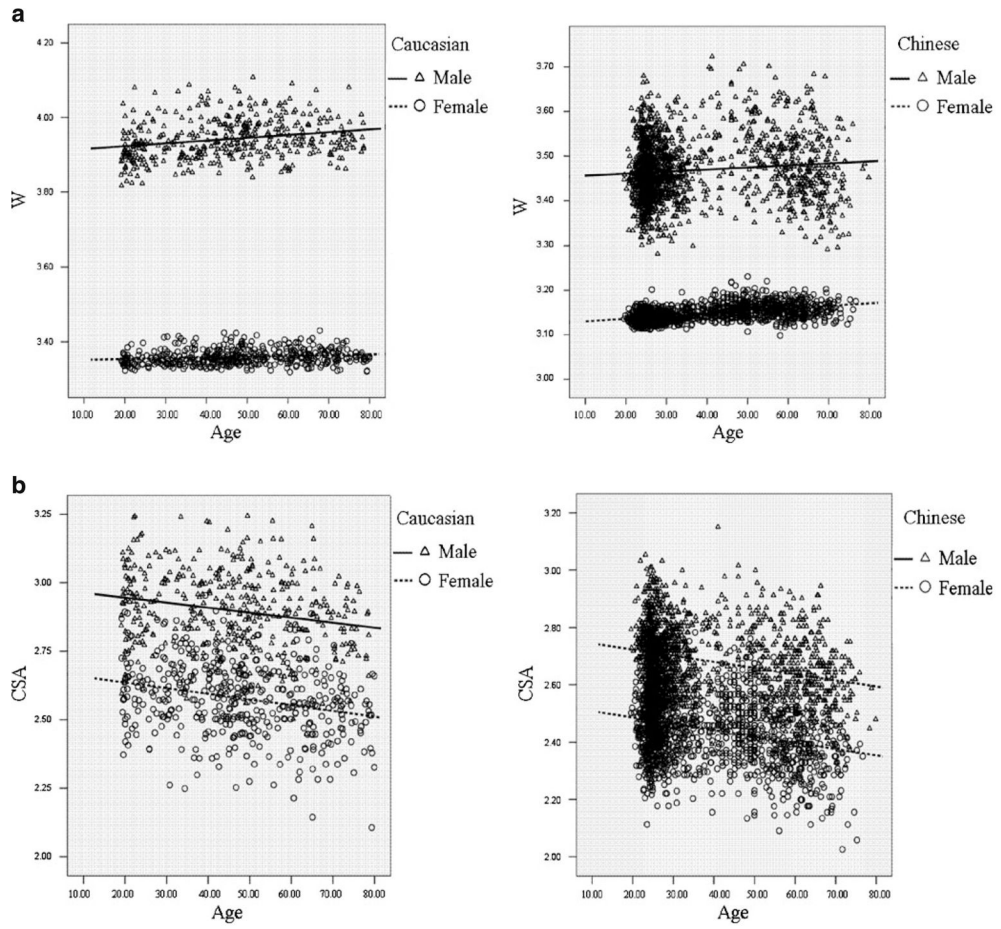
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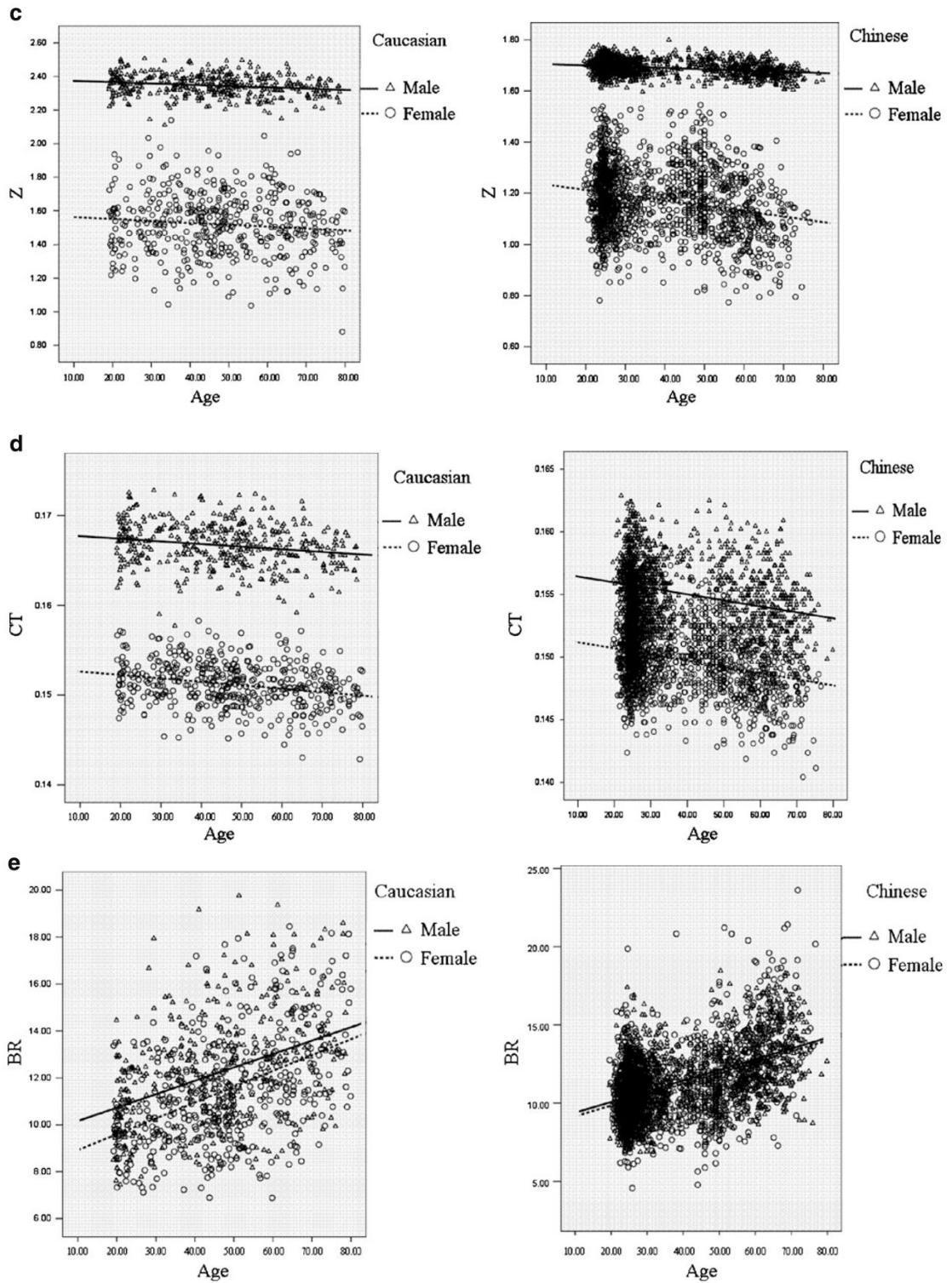
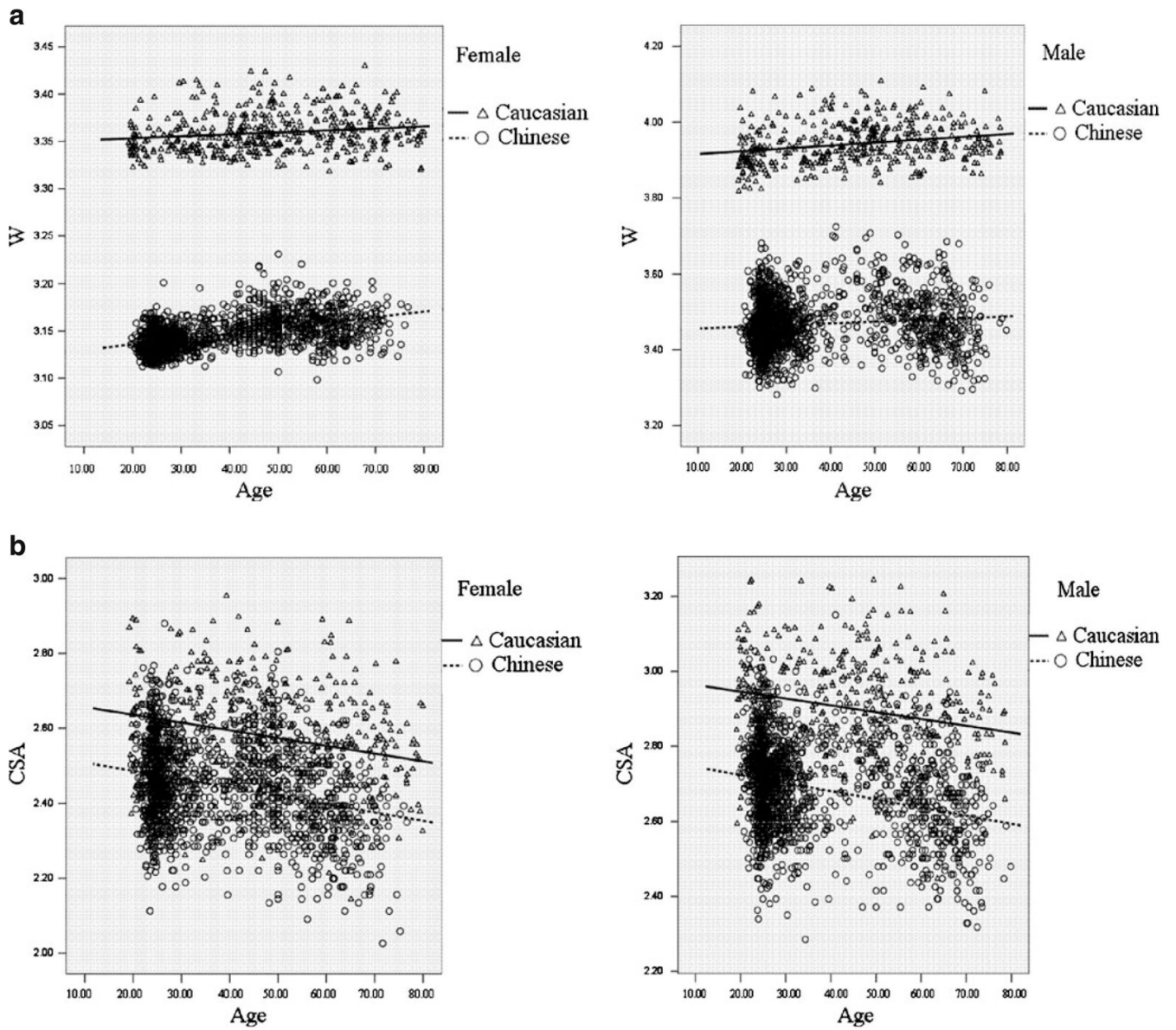


Fig. 1. The distributions of FNGPs against age in both Caucasian and Chinese (black lines for males; broken lines for females). **a** Males vs. females, in Caucasian: $p < 0.001$, slope = 0.00076 vs. $p = 0.001$, slope = 0.00021; in Chinese: $p < 0.001$, slope = 0.00045 vs. $p <$

0.001, slope = 0.00057. **b** Males vs. females, in Caucasian: $p < 0.001$, slope = -0.0018 vs. $p < 0.001$, slope = -0.0021 in Chinese: $p < 0.001$, slope = -0.0021 vs. $p < 0.001$, slope = -0.0022 . **c** Males vs. females: in Caucasian: $p < 0.001$, slope = -0.00077 vs. $p = 0.04$, slope = -0.0011 in Chinese: $p < 0.001$, slope = -0.00051 vs. $p < 0.001$, slope = -0.0021 . **d** Males vs. females: in Caucasian: $p < 0.001$, slope = -0.000029 vs. $p < 0.001$, slope = -0.000039 in Chinese: $p < 0.001$, slope = -0.000048 vs. $p < 0.001$, slope = -0.000049 . **e** Males vs. females: in Caucasian: $p < 0.001$, slope = 0.057 vs. $p < 0.001$, slope = 0.067 in Chinese: $p < 0.001$, slope = 0.068 vs. $p < 0.001$, slope = 0.069



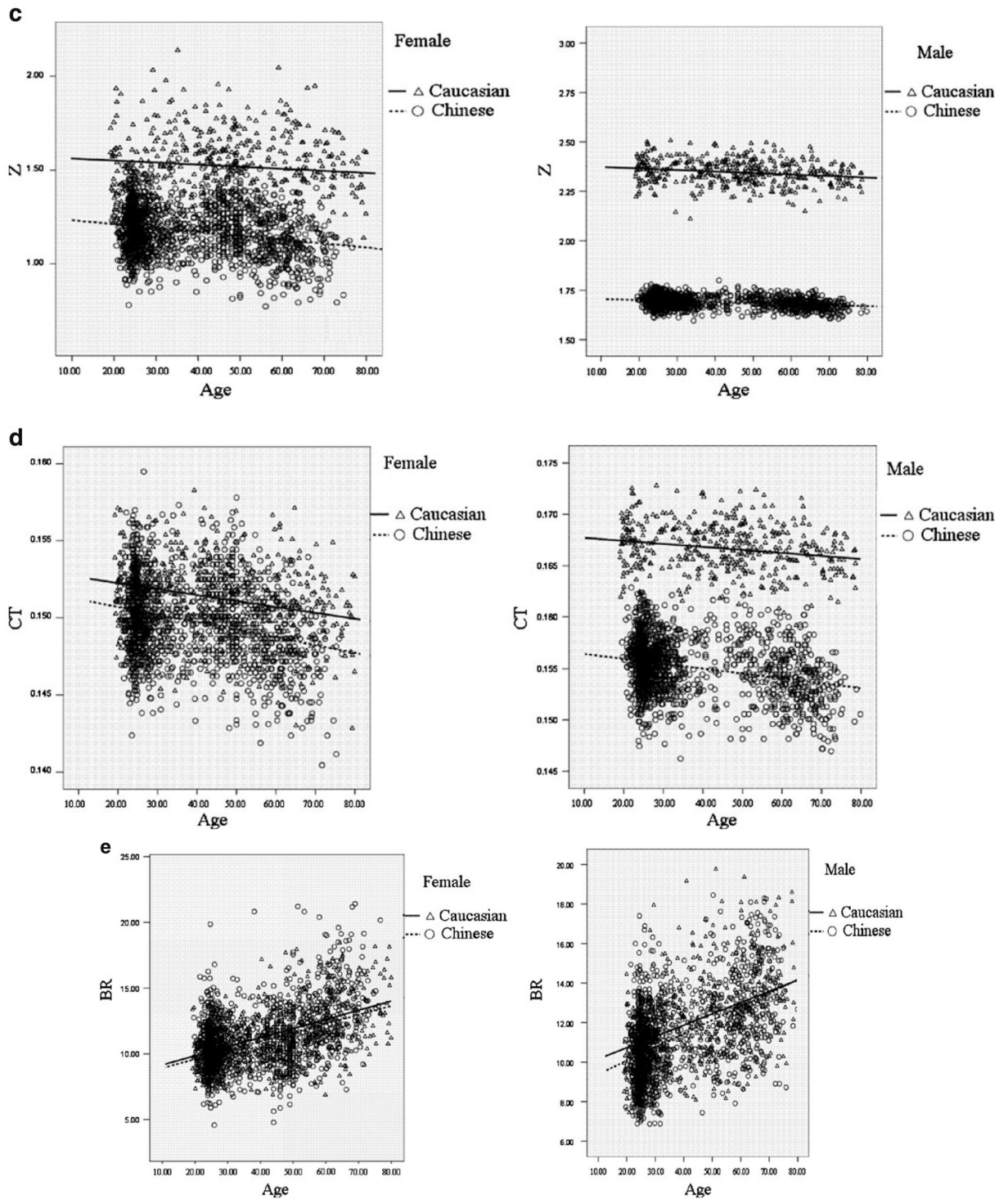


Fig. 2. The distributions of FNGPs against age in both gender group (*black lines* for Caucasian; *broken lines* for Chinese). **a** Caucasian vs. Chinese: in females: $p = 0.001$, slope = 0.00021 vs. $p < 0.001$, slope = 0.0057 in males: $p < 0.001$, slope = 0.0076 vs. $p < 0.001$, slope = 0.00045. **b** Caucasian vs. Chinese: in females: $p < 0.001$, slope = 0.0021 vs. $p < 0.001$, slope = -0.0022 in males: $p < 0.001$, slope = -0.0018 vs. $p < 0.001$, slope = -0.0021 . **c** Caucasian

vs. Chinese: in females: $p = 0.04$, slope = -0.0011 vs. $p < 0.001$, slope = -0.0021 in males: $p < 0.001$, slope = -0.00077 vs. $p < 0.001$, slope = -0.00051 . **d** Caucasian vs. Chinese: in females: $p < 0.001$, slope = -0.000039 vs. $p < 0.001$, slope = -0.000049 in males: $p < 0.001$, slope = -0.000029 vs. $p < 0.001$, slope = -0.000048 . **e** Caucasian vs. Chinese: in females: $p < 0.001$, slope = 0.067 vs. $p < 0.001$, slope = 0.069 in males: $p < 0.001$, slope = 0.057 vs. $p < 0.001$, slope = 0.068

Table 1

Basic characteristics of the studied samples

	Caucasians		Chinese	
	Male (n = 417)	Female (n = 445)	Male (n = 1544)	Female (n = 1477)
Age (years)	45.49 (16.63)	47.74 (16.38)	36.61 (16.08)	38.37 (14.90)
Height (m)	1.78 (0.07)	1.64 (0.06)	1.69 (0.06)	1.57 (0.07)
Weight (kg)	88.98 (14.70)	72.55 (16.73)	64.45 (9.60)	54.25 (8.37)
FN BMD (g/cm ²)	0.87 (0.15)	0.79 (0.14)	0.81 (0.12)	0.78 (0.14)
Bone size (cm ²)	5.92 (0.53)	5.04 (0.39)	5.20 (0.46)	4.72 (0.45)

The data were expressed as Mean (SD)

Table 2*R* squares for adjusted covariates and overall *R* squares

Covariates FNGPs	Height	Weight	Age	Overall <i>R</i> squares
W	0.15	0.10	0.04	0.41
CSA	0.10	0.10	0.06	0.52
Z	0.13	0.08	0.03	0.54
CT	0.03	0.10	0.12	0.37

BR has not been adjusted

Table 3
Comparisons of femoral neck geometric parameters in studied groups classified by gender and ethnicity

	Males		Females		p values					
	Chinese (n = 416)		Caucasians (n = 1544)		Chinese (n = 1477)		Caucasians vs. Chinese		Females vs. males	
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Males	Females	Caucasians	Chinese		
W	3.79 (0.19)	3.45 (0.15)	3.43 (0.17)	3.19 (0.17)	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
CSA	3.27 (0.36)	2.73 (0.28)	2.64 (0.37)	2.28 (0.26)	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Z	2.28 (0.32)	1.67 (0.25)	1.57 (0.33)	1.20 (0.23)	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
CT	0.17 (0.02)	0.16 (0.01)	0.15 (0.02)	0.15 (0.01)	<0.001	0.001	0.001	<0.001	<0.001	<0.001
BR	12.19 (2.42)	11.13 (2.21)	11.55 (2.61)	11.13 (2.33)	<0.001	0.002	<0.001	<0.001	<0.001	0.21

The data were expressed as Mean (SD); independent-samples *t* tests were used to analyze the effect of race (Chinese vs. Caucasians) and sex (women vs. men)

W femoral neck periosteal diameter, CSA femoral cross-sectional area, Z section modulus, CT cortical thickness, BR buckling ratio