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Gender differences in a reference database of age-related femoral neck geometric parameters for Chinese population and their association with femoral neck fractures

Yi Shen [a,b,c,d], Meng-Lu Tang [a,b,c,e], Xian-Ping Wu [a,b,c], Ling-Qing Yuan [a,b,c], Ru-Chun Dai [a,b,c], Hong Zhang [a,b,c], Zhi-Feng Sheng [a,b,c], Yi-Qun Peng [a,b,c], Xiang-Hang Luo [a,b,c], Xi-Yu Wu [a,b,c,*], Er-Yuan Liao [a,b,c]

[a] *National Clinical Research Center for Metabolic Diseases, The Second Xiangya Hospital, Central South University, No.139 Middle Renmin Road, Changsha, Hunan 410011, PR China*
[b] *Institute of Endocrinology and Metabolism, The Second Xiangya Hospital, Central South University, No.139 Middle Renmin Road, Changsha, Hunan 410011, PR China*
[c] *Department of Endocrinology and Metabolism, The Second Xiangya Hospital, Central South University, No.139 Middle Renmin Road, Changsha, Hunan 410011, PR China*
[d] *Department of Orthopedics, The Second Xiangya Hospital, Central South University, No.139 Middle Renmin Road, Changsha, Hunan 410011, PR China*
[e] *Heze Hospital of Traditional Chinese Medicine, Shandong Province, No.1036 Danyang Road, Heze, Shandong 274000, PR China*

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ABSTRACT

Femoral neck geometric parameters (FNGPs) are closely related to the strength of the femoral neck and the risk of fragility fractures. No reference database is available for FNGPs for Chinese population, and gender-related differences in FNGPs as well as their association with the risk of femoral neck fractures are unknown. This investigation aimed to set up reference databases for FNGPs, understand gender-related differences in FNGPs, and examine the association between FNGPs and the risk of osteoporotic fractures of the femoral neck. This study included 5268 females and 2156 males (aged 15–91 years) from Chinese population. A total of 384 patients (282 females and 102 males) had sustained femoral neck fractures; 384 age- and sex-matched individuals without any fractures served as controls. Femoral neck DXA images were used to measure bone mineral density (BMD) and eight FNGPs. Our results showed that the age-related trends of FNGPs were fitted with the best goodness-of-fit by applying the cubic regression model. The trends shown by FNGPs were significantly different between male and female subjects, and the fitting curves were significantly higher in male subjects. After adjustments were made for age, height, weight, and body mass index, Cox regression analysis showed that changes in all FNGPs were related to increased hazard ratios (HRs) of femoral neck fractures. After further adjustment was made for BMD of the femoral neck, the HRs related to a cortical thickness (CT) decrease and buckling ratio (BR) increase in females went up by 3.35-folds (95% CI: 2.75–4.07) and 1.86-folds (95% CI: 1.33–2.60), respectively. In males, the HRs related to the decrease in CT and cross-sectional area (CSA) increased by 3.21-folds (95% CI: 2.32–4.45) and 1.88-folds (95% CI: 1.03–3.44), respectively. In conclusions, the reference databases of FNGPs established in this study will assist in the evaluation and prediction of femoral neck fracture risk in the clinic. The decrease in CT and increase in BR of the femoral neck were independent risk factors for osteoporotic fractures of the femoral neck in females from mainland China, while a decrease in CT and CSA were risk factors in male.

1. Introduction

Although they account for less than 20% of all fractures, femoral neck fractures are some of the most serious osteoporotic fractures and are responsible for high medical costs and associated with high mortality [1, 2]. They have become an important cause of increased morbidity and mortality among the elderly [3–6]. Fragility fractures of the femoral neck occur because of decreased bone strength, which depends on geometric parameters and bone quality. In the clinic, dual energy X-ray absorptiometry (DXA) has been extensively applied to measure bone mineral density (BMD), evaluate bone strength, and predict the risk of fragility fractures. However, BMD only represents 50–70% of bone strength [7,8]. In fact, the geometric properties, remodeling state, and microstructure of bone contribute substantially to bone strength [8,9]. Prediction of hip fracture risk was significantly improved when proximal femur geometric parameters were combined with BMD [10,11]. Femoral neck geometric parameters (FNGPs) were found to be key factors affecting bone strength and highly heritable [12–16], which dominated the fragility fracture of femoral neck. Epidemiologic studies showed that the morbidity of fragility fracture differed by race and

* Corresponding author at: Institute of Endocrinology and Metabolism, The Second Xiangya Hospital, Central South University, No. 139 Middle Renmin Road, Changsha, Hunan 410011, PR China.
E-mail address: wuxiyu640@sohu.com (X.-Y. Wu).

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region [2,17–20]. Hip fracture morbidity was lower in Canadians than in Americans and Germans [18]. In China, the morbidity of hip fracture was considerably lower in Beijing than in Hong Kong and Taiwan [17,20]. In America, the hip fracture morbidity of was higher in white than in black [19,21], because of differences in FNGPs, which are an important factor affecting fragility fractures of the femoral neck.

Although the hip fracture morbidity of white patients in developed countries (like Canada and America) has decreased [3,22–24], it has sharply increased in the Beijing area because of an increase in urbanization and the aging population [17,25]. China has a large population of elderly residents, and the large number of patients with osteoporotic fractures imposes a heavy public health burden. Investigations on FNGPs in Chinese populations and the association between FNGPs and fragility fractures of the femoral neck are important to improve the prediction of femoral neck fracture risk. Although some geometric parameters of the femoral neck and hip have been studied in populations from Shanghai in the east of China and Xian in the north west of China [26,27], the surveyed groups and focus of these studies differ from those of the present study. Here, research subjects from mainland China with no previous history of bone metabolism-related disease were investigated for 8 age-related FNGPs, including outer diameter (OD), cross-sectional area (CSA), cortical thickness (CT), endocortical diameter (ED), buckling ratio (BR), section modulus (SM), cross-sectional moment of inertia (CSMI), and compressive strength index (CSI), on the basis of our previously established BMD reference database [28,29]. Additionally, the optimal fitting curves of FNGPs as a function of age and gender differences in FNGPs were studied, and the association of FNGPs with the risk of femoral neck osteoporotic fractures was examined.

2. Materials and methods

2.1. Study subjects

A total of 7413 health subjects (5268 females, 2156 males; aged 15–91 years), were randomly selected from 1996 to 2014. These volunteers, all residents of Changsha and surrounding areas, were recruited by public health organizations providing health care for local residents. All subjects were screened using a detailed questionnaire, history, and physical examination. Subjects were excluded from the study if they had conditions affecting bone metabolism, such as diseases of kidney, liver, parathyroid, thyroid, diabetes mellitus, oligomenorrhea or menopause before age 40, hyperprolactinemia, oopherectomy, rheumatoid arthritis, ankylosing spondylitis, malabsorption syndromes, malignant tumors, hematologic diseases, or previous pathological fractures. Also excluded were subjects who had been receiving glucocorticoids, estrogens, thyroid hormone, fluoride, biphosphonate, calcitonin, thiazide diuretics, barbiturates, antiseizure medications, vitamin D or calcium-containing drugs. All participants were of Han ethnicity.

In addition, 384 patients (282 females, 102 males; aged 39–93 years) with femoral neck fracture, were patients came to the department of orthopedic in our hospital for treatment. After interrogation and X-ray photograph they were diagnosed as osteoporotic fractures of the femoral neck. These patients were not affected by any impact force, but had sustained a femoral neck fracture caused by a low trauma that a fall from standing height or lower than the standing position, who were recruited as the case group. Case group and control group on a 1:1 basis for gender and age matched, 384 subjects of control group (282 female, male 102; aged 39–93 years) is chosen randomly from the healthy subjects, these subjects were excluded from the disease and drug factors affecting bone metabolism, and never had any fracture. This study was approved by the ethics committee of Second Xiangya Hospital affiliated to Central South University, and each participant signed an informed consent form.

2.2. BMD and FNGPs measurement

BMD and geometric parameters were measured using a DXA fan-beam bone densitometer (Hologic Delphi A; Hologic, Bedford, MA, USA) at the proximal femur, including the femoral neck and total hip. If the patient has fracture or artificial joint replacement surgery on the left hip, measured the right hip. If bilateral hip fractures on the patient, abandon the hip measurement and the subjects were excluded. The in vivo precision deviations between two repeated BMD measurements at the proximal femur in 33 subjects were determined by the root-mean-square CV method and were 1.17% for the femoral neck, and 0.88% for the total hip. The control spine phantom scan performed each day had a longterm (>17 years) CV of <0.48%.

FNGPs of all subjects were calculated using the DXA derived femoral neck BMD and projective bone area. The calculation equations regarding the FNGPs from the papers have been reported earlier [15,27,30–32]. We measured eight FNGPs in total, which are OD, CSA, CT, ED, BR, SM, CSMI, and CSI. OD is the femoral neck outer diameter at the middle point of femoral neck axis length, CSA is an indicator of bone axial strength, CT is an estimate of mean cortical thickness, ED is the endocortical diameter of the femoral neck, BR is an index of bone structural instability, SM is an index of bone bending strength indicating the bending resistance of a tube, CSMI is a measure index of bone stiffness, and CSI is a composite index of resist the pressure of the main shaft of the femoral neck (CSI = BMD × OD/body weight) [32].

2.3. Statistical analysis

All calculations were performed using SPSS V17.0 for Windows software (SPSS Inc., Chicago, IL, USA). Reference population were stratified by 5-year age groups, descriptive statistics were used to characterize the distribution of femoral neck geometric parameters. All parameters were expressed as the mean ± standard deviation (SD). Femoral neck geometric parameters change with age were evaluated, and the best-fitting models were determined with the largest R^2 from a comparison of the various regression models, including linear, logarithmic, inverse, quadratic, cubic, compound, power, growth, exponential, S, and logistic equations. The fitting curves of two kinds of gender geometric parameters were compared by paired t test. The one-way ANOVA was used to compare the differences of height, weight, BMI, BMD and geometric parameters between the fracture groups and the control groups. Cox proportional hazard regression models were used to analysis the association between different factors and femoral neck fractures risk. The BMD and femoral neck geometric parameters respectively were descending stratified by tertiles [16]. We used multivariate analysis to calculate hazard ratio (HR) with their corresponding 95% confidence intervals (CI).

3. Results

3.1. Age-related FNGPs

Table 1 shows the average values and standard deviations of FNGPs in each group. For female subjects, the average CSA, CT, SM, and CSMI reached the peak values at the age of 30–39 years, after which they decreased with age. The CSI reached the maximum at 25–29 years and then gradually decreased after 30 years. The ED and BR of the femoral neck remained low before the age of 40 years and then increased gradually. The maximum values were observed in the group aged ≥80 years. For male subjects, the CSA, CT, SM, and CSI of the femoral neck remained high in young subjects and then gradually decreased with age. However, the changes in ED and BR showed the opposite tendency, the values increased with age, and the maximum values were observed in the group aged ≥80 years.

Fig. 1 shows the variations in FNGPs with age, for which the curves were fitted with the best goodness-of-fit model and 95% confidence intervals (CIs). The variations in FNGPs with age for female subjects were