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Effects of age and sex on the strength and cortical thickness of the femoral neck ☆

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ABSTRACT

A group of 48 men (22 aged 65–75 years, 26 aged 80–90 years) and 59 women (32 aged 65–75 years, 27 aged 80–90 years) were enrolled in the Age, Gene/Environment Susceptibility-Reykjavik study and imaged with *in vivo* volumetric Quantitative Computed Tomography (QCT) to investigate the effects of age and sex on femoral neck structure and strength. Femoral neck cross-sectional moment of inertia for bending directions near those of standing and walking (I_{AP}), bending strength (M_y), and axial compressive strength (F_y) were computed at the location of minimum cross-sectional area (minCSA). Local cortical thickness was computed in the inferior femoral neck based on density profiles extending through the cortex of the minCSA femoral neck section. Multivariate models accounting for height, weight, and age group (younger or older) showed that men had a 46% higher M_y and a 23% higher F_y than women, while women had a 13% thicker inferior cortex than men. Cortical thickness in the inferoposterior region of the femoral neck was significantly related to bending and axial strength after adjusting for overall volumetric bone mineral density. Both minCSA and I_{AP} were higher in the older, gender-pooled age group, but F_y and M_y did not differ between the two age groups. The results suggest that age-related expansion of the femoral neck primarily occurs in the superior and inferior directions and helps maintain homeostasis of femoral neck stiffness and strength. The higher bending strength of the male femoral neck may partly explain why elderly men have a lower risk of hip fracture than elderly women.

Introduction

Approximately half of all osteoporotic hip fractures occur at the femoral neck [1]. The structure of the femoral neck, including its size and geometry, partly determines its physical strength and whether a neck fracture will occur under mechanical loads of sufficient magnitude. To better understand the differential effects of age and sex on the structure of the proximal femur in an aging population, our research group has previously employed quantitative computed tomography (QCT) to analyze the volumetric bone mineral density (vBMD), cortical thickness, bending strength, and compressive strength of the femoral neck and shaft in women [2] and in men and women enrolled in the Age, Gene/Environment Susceptibility-Reykjavik (AGES-REYKJAVIK) study [3]. These previous results revealed important sex-based differences in femoral neck structure and suggested that the increase in cross-sectional area of the femoral neck that occurs with age may have the effect of maintaining homeostasis of femoral neck stiffness as trabecular bone is lost.

The structure of the femoral neck is known to change with age [3–8]. Current understanding of bone functional adaptation suggests that age-related changes in the density and cross-sectional area of the femoral neck are in fact closely related. A loss of trabecular bone with age causes femoral neck stiffness to decrease, leading to

Abbreviations: QCT, quantitative computed tomography; vBMD, volumetric bone mineral density (mg/cm^3); RFOV, reconstruction field of view (cm); CSA, cross-sectional area (mm^2); minCSA, minimum cross-sectional area (mm^2); BMC, bone mineral content (mg); I_{AP}, second area moment of inertia about the anterior–posterior axis (mm^4); I_{IS}, second area moment of inertia about the inferior–superior axis (mm^4); $\rho_{HA,L}$, liquid K_2HPO_4 concentration (mg/cm^3); $\rho_{HA,S}$, solid calcium hydroxyapatite concentration (g/cm^3); ρ, apparent density (g/cm^3); E, Young's modulus (MPa); M_y, yield moment (N m); $M_{y,avg}$, average yield moment over 360 different bending directions (N m); $M_{y,max}$, maximum yield moment over 360 different bending directions (N m); $M_{y,min}$, minimum yield moment over 360 different bending directions (N m); F_y, compressive yield force (N); $t_1 - t_4$, cortical thickness in sectors 1 through 4 (mm).

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elevated strains at the periosteal surface during habitual activities such as walking. Bone cells respond to these increased strains by adding new bone tissue at the periosteal surface, maintaining homeostasis of femoral neck stiffness. The result is an ongoing increase in femoral neck size with declining trabecular vBMD. It is unproven whether periosteal expansion occurs equally around the perimeter of the femoral neck or if bone is added in such a way that strains are reduced for a limited number of loading directions. We hypothesize that bone is primarily added at the superior and inferior femoral neck, where stimulating strains are expected to be highest during habitual activities like standing and walking.

Femoral neck structure also differs between men and women. Elderly male femoral necks have a larger cross-sectional area than those in elderly women, and these disparities increase with age [3,7]. Body mass and height account for a large part of these sex-based differences, but male bones appear to be larger and stronger for a given body mass or muscle size [9,10]. Measurements of cortical thickness made using digitized histological samples have also suggested differences between the femoral necks of males and females. In a study of 9 male and 10 female femoral necks, the cortex in the inferior region of the femoral neck was slightly thicker in females than in males, while the cortex in the superior region of the femoral neck was slightly thicker in males than in females [11]. These differences were not statistically significant, most likely because of the small sample size. If the spatial distribution of cortical thickness around the perimeter of the femoral neck does in fact differ between males and females, this fact may have important implications in understanding the different effects of falling direction on femoral neck strength in men and women.

To provide a more detailed understanding of the effects of age and sex on femoral neck size, cortical thickness, bending strength, and axial compressive strength in the elderly population, in the current study we used *in vivo* QCT imaging of the hip in a sample of men and women enrolled in the AGES-REYKJAVIK study. We sought to determine the magnitude of age and sex-based differences in explicit estimates of femoral neck strength, as opposed to surrogates for bone strength such as BMD or section modulus. The effects of different loading directions on femoral neck bending strength were included in the analysis, and we also examined the effects of age-related periosteal expansion on the bending resistance of the femoral neck in different planes of bending.

Material and methods

Subjects

A subset of 107 men and women enrolled in the AGES-REYKJAVIK study, an ongoing population-based study of Icelandic men and women [3], were included in the current study. Informed consent was obtained from all participants in the study, which was approved (VSN 00-063) by the National Bioethics Committee in Iceland, the Institutional Review Board of the Intramural Research Program of the National Institute on Aging, and the Committee on Human Research at the University of California, San Francisco. Subjects were randomly selected from the overall AGES-REYKJAVIK cohort to fall within two decadal age groups at the youngest and oldest margins: 65–75 years old and 80–90 years old. The younger group was composed of 26 men and 32 women and the older group composed of 22 men and 27 women. Subjects were selected to exclude those who were currently using medications known to affect bone mineral status, including estrogen replacement therapy, tibolonum, antiepileptics, systemic glucocorticoids and agents for the treatment of osteoporosis (raloxifen, calcitonin or bisphosphonates). No subjects had a history of hip fracture. Subject characteristics are listed in Table 1.

Table 1
Age, height, and weight of subjects included in the study.

	Females (n = 59)	Males (n = 48)	65–75 years old (n = 58, 32 females)	80–90 years old (n = 49, 27 females)
Age (years)	76 ± 7	77 ± 6	71 ± 3	83 ± 2
Height (cm)	162 ± 6	175 ± 7	170 ± 9	165 ± 8
Weight (kg)	71 ± 11	80 ± 15	79 ± 15	70 ± 11

Imaging

Images of both hips of each subject were obtained on a 4-detector CT system (Sensation, Siemens Medical Systems, Erlangen, Germany). A region extending from a point 1 cm superior to the acetabulum to 3–5 mm distal to the lesser trochanter was imaged using a scanning field of view of 50 cm, 120 kVp, 140 mAs, 1-mm slice thickness, pitch = 1. A solid calcium hydroxyapatite QCT calibration phantom (Image Analysis, Inc., Columbia, KY, USA) was scanned along with each subject and appeared in each image slice. A standard resolution image (0.98-mm in-plane voxel size, 1-mm slice thickness) was reconstructed using the standard kernel with a 50-cm reconstruction field of view (RFOV), and a magnified image (0.39-mm in-plane voxel size, 1-mm slice thickness) centered on the left hip was reconstructed using the standard kernel with a 20-cm RFOV (Fig. 1).

Image analysis

The neck axis of the left femur in each standard-resolution image was defined in the axial and coronal planes using AVS5 image processing software (AVS, Waltham, MA, USA), and the image was then digitally rotated and resliced to obtain cross-sectional slices of the left femoral neck with 0.98-mm isometric voxels [12]. The corresponding magnified image was reformatted using the same set of rotations calculated for the standard resolution image, producing a set of femoral neck cross-sectional slices with 0.39-mm isometric voxels. The proximal femur in both images was segmented from the surrounding tissue using a threshold-driven region growing algorithm. Density and structure measurements were then made using both the standard resolution image and the magnified image.

The cross-sectional area (CSA) of each section was computed by summing the area of all voxels contained within the periosteal margin, and the section of minimum cross-sectional area (minCSA) was isolated for analysis. Voxels containing a large proportion of fatty marrow have negative equivalent hydroxyapatite concentration, and these voxels were excluded from further analyses. The mean vBMD of each minCSA slice was computed by summing the bone mineral content (BMC, equivalent hydroxyapatite concentration multiplied by voxel volume) of each voxel with a positive hydroxyapatite concentration and then dividing by the total volume of those voxels. The vBMD measurement therefore included both trabecular and cortical bone. The cross-sectional moment of inertia about the anterior–posterior axis (I_{AP}) and the cross-sectional moment of inertia about the inferior–superior axis (I_{IS}) were also computed using these voxels [13].

To compute the equivalent compressive strength and bending strength of the minCSA section, first each voxel's hydroxyapatite concentration was used to compute the equivalent Young's modulus (material stiffness) using a series of conversions:

$$\rho_{HA,L} = \left(\rho_{HA,S} + 7.32\right) / 1.15\,\mathrm{mg/cm^3}, \tag{1}$$

$$\rho = 0.0012\left(\rho_{HA,L}\right) + 0.17\ \mathrm{g/cm^3}, \tag{2}$$

$$E = 2043^{2.5}\mathrm{MPa\ for}\ \rho \le 1.2\,\mathrm{g/cm^3}, \tag{3}$$