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Computed Tomography-based Study of Age- and Sex-related Variation in Morphology of the Femur

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SUMMARY

Background. The femur has a complex shape with marked individual differences. The aim of our study was to investigate the anatomy of the femur in normal subjects using computed tomography imaging with the aim of building a digital database of human femoral anatomy

Material and methods. We studied age- and sex-related variation in the shape of the femur in 169 normal subjects (80 men and 89 women) using Computed Tomography. Subjects were divided into three age groups (Group I: < 35 years; Group II: 36 - 55 years; Group III: > 56 years). Measurements were taken of transverse sections at 25%, 50% and 75% of femoral length.

Results. The bony surface at the transverse section at 50% of the length of the femur was greater in the older men (p=0.007). There were differences in the medullary canal surface area of the femur at the section at 50% of its length in both women and men (p=0.02).

Conclusion. Our study provides a detailed characterization of the anatomical features of the femur of normal subjects, and can be helpful in modelling prosthetic implants or internal fixation devices in relation to the age and sex of the patients.

Key words: femur, morphology, age, bone, osteoporosis, anatomy, morphology

BACKGROUND

The shape and architecture of a bone is largely genetically determined, although mechanical factors, diet, hormones and the central nervous system can modify both shape and architecture [1,2].

Bone mass decreases with age. With decreases in bone mass, the strength of the bone is reduced, and the risk of fracture increases. On the other hand, from the fourth decade of life onwards, there is also a decline in physical activity and muscular strength, accompanied by a reduction in muscle mass, which by itself contributes to the reduction in bone mass by decreasing the cyclical compression and tension stresses acting on the bone [3]. In the fifth decade of life, bone density begins to fall, especially in the cancellous bone of women. After the age of 40, the index of bone formation is constant but resorption increases, and, starting at this age, men lose from 0.5% to 0.75% of their bone mass per year. Women lose between 1.5% and 2% annually, and, during menopause, they may experience temporary losses of 3% per year 4. In men, loss of bone density with age seems to result from the drop in bone formation, whereas in post-menopausal women it results from an increase in bone resorption.

The femur has a complex shape with marked individual differences, for instance, in the rotation of the shaft, angulation of the neck, and head diameter [5]. There is evidence of time-dependent variation in the relationship between proximal and distal ends 6-8. The mammalian diaphyseal cortical bone shows marked plasticity, dependent on habitual levels and patterns of loading on the lower limbs from body mass, proportions, and locomotion [9,10]. The femoral neck width increases with age in men and women, and the femoral neck bone density decreases in women [11]. There is a close relationship between bone mineral density and proximal femur fracture, and as regards the relationship between the various portions of the femur, the neck-shaft angle is the best predictor of fractures of the proximal femur [12,13].

In elderly men and women, fractures at any location are a risk factor for subsequent fractures [14, 15,16]. The risk of a hip fracture at the age of 90 years is 33% in North America women [17]. A man aged 65-74 years with a hip fracture has an 8-fold increased risk of further fractures at another site compared with a 4-fold increased risk among women of the same age [18]. Rates of falling may play a role in the difference in fracture rates, but bones in males may be intrinsically stronger or may suffer less structural degradation with age than those of women [19].

We studied the anatomy of the femur of normal subjects using Computed Tomography (CT) imaging with the aim of building a digital database of human femoral anatomy, and investigating possible age-related differences in morphology of the femur in men and women.

METHODS

The experiments were undertaken with each subject having understood their nature and having provided their written consent, with the approval of the appropriate local ethics committee, and in compliance with national legislation and the Code of Ethical Principles for Medical Research Involving Human Subjects of the World Medical Association (Declaration of Helsinki)

Eligibility criteria

All subjects enrolled in the study were healthy Caucasians. None had a history of early or late onset of puberty, or any disease likely to affect growth or bone mineral accretion. Subjects were included in the study if they had no disorders of the musculoskeletal system, no dysplastic or dysmorphic hips (centre to edge <20°) 20, no previous musculo-skeletal operations, no history of trauma of the lower limbs, or musculo-skeletal infections or tumours. Patients were excluded from the study if they had inflammatory joint disease, prior lower limb surgery, or frank osteoporosis managed with drugs.

Patients' demographics

The study was performed on the right femurs of 169 people (80 men and 89 women). Our study population was divided into three age groups:

- Group I: up to 35 years (31 women; 24 men)
- Group II: from 36 to 55 years (30 women; 22 men)
- Group III: over 56 years (28 women; 34 men).

The following data were collected in each subject: sex, age (years), body weight (kg), height (cm), body mass index (BMI) (Kg/cm^2), length of the femur (cm), and relationship between bone length and height of subject (femoral length/height) (Table 1).

Imaging

All subjects received a CT scan (Siemens® Somaton Plus 4, Erlangen, Germany). For each individual, data were obtained covering the entire length of the femur, including the hip and knee joints, with 10 mm thick cuts. A rotation time of one second was used, with rotation parameters of 140 kV and 94 mA. A window was used with a centre of 300 Hounsfield Units (HU) and amplitude of 1400 HU.

Tab. 1. Anthropometrics of the subjects

	Women						Men					
	< 35 years		36 - 55 years		> 56 years		< 35 years		36 - 55 years		> 56 years	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Age	21.1	4. 7	46.2	6.0	66.9	7. 1	21.3	4.3	48.9	5.9	65,8	7,1
Weight (Kg)	56.2	7.9	60.9	8.4	64.9	12.1	71.6	8.6	78.5	14.4	75,4	13,1
Height (cm)	164.1	5.3	158.0	6.8	157.1	5.3	176.9	5.5	171.3	5.4	170,4	7,2
BMI	21	2	24	3	26	5	22	2	26	4	26	3
Femur length (cm)	42.1	1.8	40.5	1.7	40.2	1.6	45.1	1.7	43.7	1.8	43,4	2,2
Femur length/Height	0.25	0.01	0.25	0.01	0.25	0.01	0.25	0.01	0.25	0.01	0,25	0,01

The right femur was measured in the supine position in all subjects. The initial image was used to measure the length of the femur from the most proximal point of the greater trochanter to the most distal point of the lateral condyle.

The transverse sections were taken at 25%, 50% and 75% of the total length of the femur (Figure 1). On a high resolution computer screen, an orthopaedic trainee used an electronic tool to delineate the margins of the medullary canal and the surface of the bone. The researcher had been specially trained in these radiographic measurement techniques, and reached an intra-observer variation of less than 2% in all measurements used in the present study. For every section, the following variables were measured using commercially available software on three separate occasions, and the mathematical average was used for the purposes of subsequent analyses:

1. Total bone surface area, inclusive of the surface area of the medullary canal and of the surface area of the cortex;
2. Medullary canal surface area;

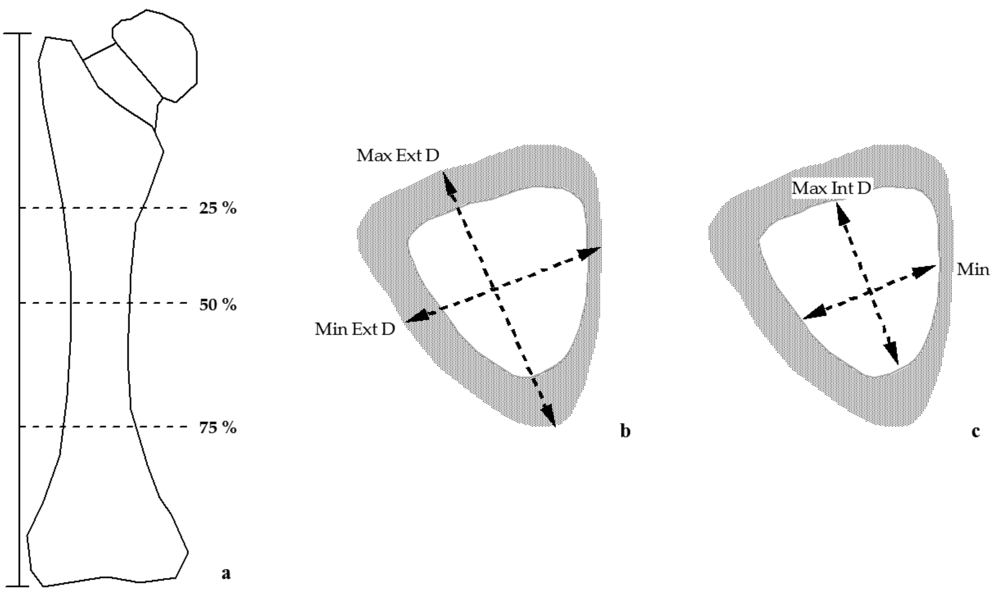

Fig. 1. a – Transverse sections at 25%, 50% and 75% of the femoral length, b – maximal and minimal external diameters, c. maximal and minimal medullary canal diameters

3. Cortical surface area;
4. Cortical thickness (calculated as maximum external diameter – maximum internal diameter);
5. Circularity of the medullary canal (minimum internal diameter / maximum internal diameter).

Statistics

The variables of height and length of femur fitted a straight line on linear regression (p=0.001, R= 0.885). Therefore, all variables were normalized in relation to femur length and expressed as percentages. Normality was verified by Kolmogorov-Smirnov's test using Lilliefors's correction. To compare the two sexes, Student's t test was used for independent samples if the variable followed normal distribution. Otherwise, the Mann-Whitney U test was applied. To compare age groups, one-criterion ANOVAs were used, followed by Tukey's multiple comparison test if the variable under study followed normal distribution, and Kruskal-Wallis followed by Mann-Whitney's U test and Bonferroni's adjustment if it did not.

All the statistical analyses were performed using SPSS 9.0 for Windows (SPSS Inc. Chicago, IL, USA).

RESULTS

Height, body weight and femur length showed statistically significant associations (p=0.001) with all the study variables, except for the circularity of the medullary canal in the three sections and the thickness of the cortex at 75% of the length of the femur.

In both men and women, the bone surface and the medullary canal surface at 25% of the length of the bone were greater in the older age groups than in the youngest one (p=0.001). The bony surface at 50% of the bone length was greater in the older men (p=0.007) (Table 2 and 3).

The medullary canal surface area of the bone at 50% of its length was significantly greater in the oldest age group (subjects over 56 years) in both men and women when compared with the other two age groups (p=0.02). We found no differences in the cortical surface area between the different groups.

We also found differences in the medullary canal surface area of the bone at 50% of its length in both men and women (p=0.02). These differences were greater in the oldest age group (subjects over 56 years). We found no differences in the cortical surface area between the different groups.

Tab. 2. Morphology of femur of men in different age groups (Normalized value) (*** p<0.001; ** p<0.01; * p<0.05)

	< 35 years		36 - 55 years		> 56 years		
	Mean	SD	Mean	SD	Mean	SD	p
Bone Surface Area (%)							
25%	15.09	1.66	16.58	1.68	17.57	1.60	***
50%	14.42	1.35	15.03	1.31	15.62	1.45	**
75%	20.64	2.37	21.52	2.60	21.35	2.78	
Medullary Cavit y Surface Area (%)							
25%	3.94	1.03	5.36	1.49	6.02	1.49	***
50%	3.39	0.64	3.73	0.75	4.15	1.28	*
75%	12.00	2.55	13.29	2.24	13.05	2.77	
Cortical Surface Area (%)							
25%	11.15	1.28	11.22	1.49	11.55	1.11	
50%	11.30	1.15	11.31	1.20	11.47	0.88	
75%	8.64	0.82	8.23	0.87	8.30	0.89	
Cortical Thickness (%)							
25%	3.23	0.50	3.19	0.76	3.24	0.89	
50%	3.60	0.34	3.47	0.52	3.55	0.61	
75%	1.64	0.29	1.51	0.17	1.54	0.27	
Circularity of the Medullary Cavity (%)							
25%	1.75	0.30	1.88	0.27	1.97	0.35	*
50%	1.91	0.23	1.99	0.18	2.06	0.32	
75%	1.68	0.14	1.76	0.22	1.76	0.15	

Tab. 3. Morphology of femur of women in different age groups (Normalized value) (*** p<0.001; ** p<0.01; * p<0.05)

	< 35 years		36 - 55 years		> 56 years		
	Mean	SD	Mean	SD	Mean	SD	p
Total Bone Surface Area (%)							
25%	12.93	1.42	14.00	1.74	14.45	1.14	***
50%	12.11	1.31	12.64	1.46	12.50	1.34	
75%	18.26	2.72	17.76	2.55	18.32	2.52	
Medullary Cavity Surface Area (%)							
25%	3.92	0.99	4.43	0.99	5.39	1.79	***
50%	3.40	0.76	3.17	0.81	4.05	1.61	*
75%	11.24	2.32	10.36	2.07	11.62	2.56	
Cortical Surface Area (%)							
25%	9.01	0.99	9.58	1.38	9.07	1.57	
50%	8.70	0.86	9.47	1.24	8.89	1.53	
75%	7.02	0.74	7.40	1.33	6.70	1.29	
Cortical Thickness (%)							
25%	2.63	0.44	2.82	0.65	2.79	0.73	
50%	3.28	0.38	3.49	0.55	3.02	0.83	*
75%	1.45	0.25	1.66	0.40	1.55	0.48	
Circularity of the Medullar y Cavity (%)							
25%	1.84	0.19	1.99	0.46	1.99	0.30	
50%	1.90	0.19	2.15	0.38	2.16	0.42	**
75%	1.87	0.17	1.88	0.20	1.88	0.17	

In the youngest group (up to 35 years), the values for total bone surface area, cortical surface area and cortical thickness were greater in men than women in all sections (p=0.001). The circularity of the medullary canal at 75% of bone length was greater in women (p=0.001).

In the group aged 36 to 55 years, the values for the total bone, medullary and cortical surface area in all sections were greater in men than in women (p=0.001). The circularity of the medullary canal at 75% of the length was greater in women (p=0.044).

In the oldest group (over 56 years), the values for the total bone surface area and cortical surface area were greater in the men than in the women in all sections (p=0.001). Cortical thickness was greater in men than women at 50% of the length of the bone (p= 0.008). The circularity of the medullary canal at 75% of the bone length was greater in women (p=0.01).

DISCUSSION

We investigated age- and sex-related variation in the shape of the femur of healthy male and female subjects. Height, body weight and femur length showed statistically significant associations with all the study variables except for the circularity of the medullary canal in the three sections and the thickness of the cortex at 75% of the length of the femur. The area of the medullary canal surface was significantly greater in the older age groups. In all groups, the values for the total bone surface area, cortical surface area and cortical thickness were greater in men than women in all sections. In all groups, the circularity of the medullary canal at 75% of the bone length was greater in women. Regardless of age, women had smaller bones, less cortical bone area and higher circularity of the medullary canal at 75% of the bone length than men.

CT allows for evaluation of the anatomical features of the femur of subjects with no musculo-skeletal disease. Rubin et al. [21] analysed ex vivo the accuracy of bone measurements of 32 femora, comparing the dimensions obtained from radiographs and CT scans with the true anatomical dimensions. CT was much more precise, and the greatest errors in CT measurements occurred when the bone thickness was less than 1-1.5 mm 21-23, as in the proximal and distal ends of the femur.

One of the strengths of this study includes the use of a single radiologist (JP) with a special interest in CT scanning of musculoskeletal conditions, and of a single specially trained medically qualified measurer. Moreover, we are not aware of any study to present the morphological features of the femur bone in the Spanish population. Results from the present study were obtained from a homogeneous group of healthy Caucasian subjects using CT. CT provides a non-invasive and relatively low health risk approach for assessing compartmental bone geometry, even though new MRI techniques have been recently developed 24.

We are fully aware of the limitations of our study. The most obvious is its cross-sectional design, which precludes generalization on the temporality of the changes described in our study. As a consequence, the findings may not translate completely to longitudinal studies. Although our population was ethnically and geographically selected, a further challenge to interpretation of our data can arise from the fact that we did not collect data on diet and exercise, which can affect changes in bone mass, area, and density. Moreover, no information on hormonal status, e.g., menopause, age of sexual maturity, or activity levels, was available for our subjects.

In our study, the femur measured one quarter of the body height in all the groups of both sexes. We found differences between men and women in the dimensions of the femur. At every age, women had smaller bones, a smaller cortical area and medullary canal in all age groups 25. African-Americans have larger bones than white subjects, although the cortical thickness is very similar in both sexes and races 26. However, heterogeneity in bone mineral density exists among African heritage populations, and is not necessarily higher than the average in all African populations [27].

At 75% of the length of the femur, the bone surface, the medullary canal surface, and the circularity of the medullary canal were greater in older men and women. Our results are in agreement with those of Stein et al. [25], who also observed that older people have bones with greater external dimensions than young people, but that the cortical area is greater in younger individuals. However, not all studies indicate that the diaphyses are wider in older people [17]. Bone size increases with periosteal apposition [4], which is greater in men than in women, and this compensates for bone loss at the endosteal surface, which is also greater in men than in women [26]. The net bone loss is therefore lower in men than women. This mechanism of internal resorption and external apposition maintains the mechanical properties of the bones.

The proximal femur expands with age in both sexes, the rate being faster in women than in men over 65 years of age. This is sometimes accompanied by thinning of the cortices, given the more rapid expansion of the endosteal vs. periosteal envelope 19. Part of the effect of aging on bone density could be due to expansion of the bony envelope without loss of bone mineral content [19].

Variations in geometry of the bone section account for differences in the mechanical behaviour of the femur. We found sex-related differences in the bone and cortical surfaces in the different age groups. Long bones gain structural rigidity as their diameter expands without unchanged mineral content [19]. Bone size is greater in young men than in women, but the load the bones have to bear is greater, even though the stress is similar in both sexes [26]. The increased bone sections reduce bone mineral density, due to increasing area/volume, and maintain the bending strength [19]. Bone stiffness correlated with the area of the section and had less relation to the density of the section even though the mechanical properties of cortical bone tissue depend on its mineral content [28,29].

CONCLUSIONS

1. Our study provides a detailed characterization of the anatomical features of the femur of normal subjects over a relatively large age span, with precise data on the anatomical features of the femur, which may be instrumental in improving the quality of anatomically shaped orthopaedic implants in relation to the age and sex of the patients.
2. Additional research is required to improve our understanding of the association demonstrated in this study.

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