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Mathematical modeling of proximal femur geometry and bone mineral density

Proksimal femur geometrisinin kemik mineral ölçümü bağlamında matematiksel modellenmesi

Mesut Taştan,[1] Özgür Çelik,[2] Gerhard-Wilhelm Weber,[3] Bülent Karasözen,[4] Feza Korkusuz[5]

[1]Department of Mathematics, University of Texas, Arlington, USA; Middle East Technical University, [2]Faculty of Education, [3]Institute of Applied Mathematics, Department of Physical Education and Sports, [4]Institute of Applied Mathematics and Department of Mathematics, [5]Department of Physical Education and Sports and Institute of Applied Mathematics, Ankara

Objectives: Bone mineral density measured by dual energy X-ray absorptiometry is a major determinant of proximal femoral fractures. In former studies, researchers considered the hip axis and femoral neck length as predictors of fracture risk and the width of the femoral neck was not considered. In this study, various functional relationships between density, length, and width were assessed using analytical models and numerical tests.

Materials and methods: Fifty-eight healthy sedentary university students (age range 18 to 25 years) participated in the study. Bone mineral density was measured by dual energy X-ray absorptiometry in five rotation positions, namely external 30°, external 15°, neutral 0°, internal 15°, and internal 30°. The length and width of the femoral neck was measured in each position. Three mathematical models were developed and assessed. Least squares parameter estimation was used and errors of these models were assessed.

Results: Linear mathematical models demonstrated the importance of the neck width measurements in assessing fracture risk.

Conclusion: Our results suggest that femoral neck width is important and should be regarded as a risk factor when appropriate formula is used.

Key words: Bone density; densitometry, X-ray/methods; femur neck; hip fractures/physiopathology; models, theoretical; osteoporosis; risk factors.

Amaç: Kemik mineral yoğunluğu, çift enerjili X-ışını soğurma cihazı ile ölçüldüğünde kalça kemiği kırığının temel belirleyicilerinden biridir. Önceki çalışmalarda, araştırmacılar kalça ekseni ve uyluk kemiği boynunun uzunluğunu kırılma riskinin habercileri olarak görmüşlerdir; uyluk kemiği boynunun genişliği dikkate alınmamıştır. Bu çalışmada, analitik model ve sayısal testler kullanılarak, yoğunluk, uzunluk ve genişlik arasındaki çeşitli işlevsel ilişkiler değerlendirildi.

Gereç ve yöntem: Çalışmaya, yaşları 18-25 arasında değişen, sağlıklı 58 üniversite öğrencisi katıldı. Kemik mineral yoğunluğu, 30° dış, 15° dış, doğal 0°, iç 15° ve iç 30° dönme pozisyonlarında çift enerjili X-ışınları kullanılarak ölçüldü. Her pozisyonda uyluk kemiği boyun uzunluğu ve genişliği ölçüldü. Üç matematiksel model geliştirildi ve değerlendirildi. Asgari kare parametre tahmini kullanıldı ve üç matematiksel modelin hataları değerlendirildi.

Bulgular: Doğrusal matematiksel modeller, kırık riskinin değerlendirilmesinde uyluk kemiği boyun genişliğinin önemini ölçümlerle göstermiştir.

Sonuç: Bulgularımız, uygun formül kullanıldığında, femur boynu genişliğinin önemli olduğunu ve kırık için bir risk faktörü sayılması gerektiğini göstermektedir.

Anahtar sözcükler: Kemik yoğunluğu; dansitometri, X-ışını/yöntem; femur boynu; kalça kırığı/fizyopatoloji; teorik model; osteoporoz; risk faktörü.

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- *Correspondence: Dr. Gerhard-Wilhelm Weber. Institute of Applied Mathematics, Middle East Technical University, 06531 Ankara. Tel: 0312 - 210 56 52 Fax: 0312 - 210 29 85 e-mail: gweber@metu.edu.tr*

Osteoporosis-related hip fractures, characterized by compromised bone strength, affect millions of people with considerable morbidity and mortality, and have major impacts on health care resources.[1] To allow the targeting of preventive care, there is an increasing interest in predicting fracture risk.[2]

Several researchers[3-5] have proved that, with age and gender, bone mineral density (BMD) measurement is one of the most reliable methods to evaluate the risk for osteoporosis-related hip fractures. Bone mineral density of the proximal femur can be defined as the rate of radiation beam attenuated by the three-dimensional bone structure that is evaluated through a two-dimensional projected image; the so called *a real bone density*.[6] It is well-stated that the attenuation of radiation beam is dependent on physical density, bone size, and position at measurement.[6,7] The importance of hip geometry (Fig. 1) has been well defined in previous studies.[8-11] Geometrical variations in the femoral neck between races have been assumed to predict osteoporosis-related hip fractures.[12] Hip axis length (HAL) and femoral neck length (FNL) are defined as the distance along the femoral neck axis between the lateral margin of the base of the greater trochanter to the inner pelvic rim and the length to the apex of the femur head, respectively. Some studies[12-14] demonstrated a relation between HAL/FNL and risk for fracture while others[15,16] failed to do so. These two may represent only one dimension of hip geometry and it is assumed that the neck dimension may add additional value to predict fracture risk. Although the neck dimension has been measured in several studies,[8,13-15,17-20] to our knowledge, these proximal femur geometry measures have not been modeled mathematically.

This study aims to incorporate the femoral neck width into the modeling and to analyze proximal femur geometry from BMD measurements by dual energy X-ray absorptiometry (DXA).

MATERIALS AND METHODS

Participants

Participants of this study were 58 healthy sedentary university students with an age range of 18 to 25 years; 35 were females and 23 were males. Physical characteristics of participants are tabulated in Table I. The experimental protocol was approved by the local ethics committee. All participants signed a consent form after being fully informed on the study's purpose, methods, and possible side effects.

Experimental design

A comparative research design was utilized based primarily on the BMD values of the proximal femur at five different positions: external 30°, external 15°, neutral 0°, internal 15°, and internal 30° rotation (Table II). In this cross-sectional descriptive study, BMD and geometric variables including proximal FNL and neck width (NW) of bilateral hip were compared in both sexes. Bone mineral density of the proximal femur was measured with a Lunar DPX bone densitometer. During scans, the right and left lower extremities of the subjects were positioned with a specially designed rotation positioning device. Abduction between the legs during BMD measurements was 15°. Total femoral BMD values were used for the study.

A dual femur analysis software program was used to determine BMD of the proximal femur.

Body height and weight were measured with an anthropometer and beam-balance scale (Seca, Vogel and Haike; Hamburg, Germany). Body mass index (BMI) was also calculated.

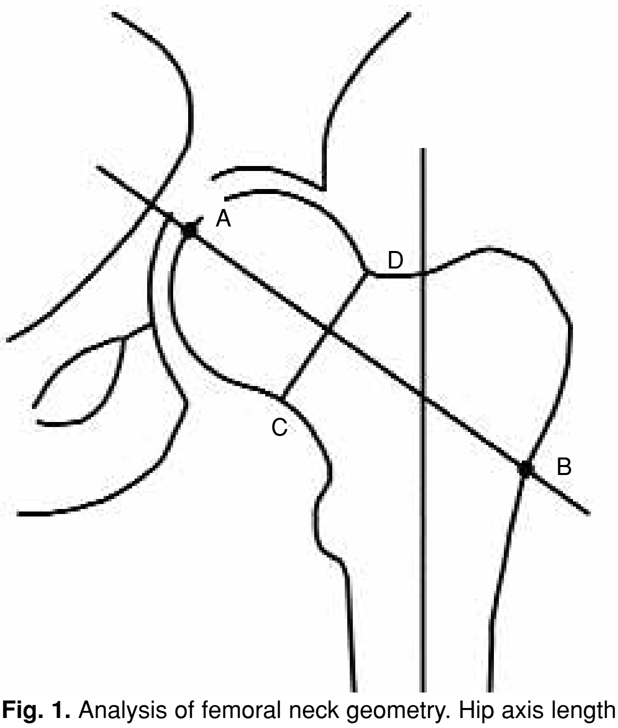

Fig. 1. Analysis of femoral neck geometry. Hip axis length was measured as the distance from A to B and femoral neck width as the distance from C to D, which was set at the narrowest point of the femoral neck.[37]

TABLE I

Physical characteristics of the subjects

	Mean	SD
Age (years)	21.7	1.6
Height (cm)	1.7	0.1
Weight (kg)	62.6	13.4
Body mass index (kg/cm²)	21.5	3.2

Measurement of the length and width of the femur neck

Femoral neck length was measured as the linear distance from the base of the trochanter to the apex of the femoral head by aligning the ruler manually during the analysis procedure by the software provided with the device. Femoral neck width was measured as the shortest distance to the femoral neck perpendicular to the femoral neck axis (Fig. 1).

Development of the mathematical model

A dependence of BMD, A and FNL, x_1 was previously defined.[13,18] Since the easiest functional relationship is of a linear affine model, a two-parametric approach was initially preferred:

$$A = \beta_0 x_1 + \beta_1 \qquad \textit{(Linear model)}$$

However, the goodness-of-fit resulting from numerical calculations (see Table III later on), i.e., the high residuals (errors) of approximation, shows that this linear approach is not useful for the three-dimensional interpretation of BMD. Those calculations were called *least squares approximation*. Thus, instead of a linear model, one-term polynomial models (quadratic, cubic ones, etc.), root models and their reciprocal terms are proposed here. The models with two variables x_1 and x_2 in the form of $\beta_0 x_1^{\beta_1} x_2^{-\beta_2}$ represent an area-like interpretation for bone length and width.

Since powers of variables can give closer clues for understanding the mathematical structure, three different models were successively compared. Firstly, in the case of one variable, x_1, the following model was taken into account.

$$A = \beta_0 x_1^{\beta_1} \qquad \textit{(Model 1)}$$

However, based on knowledge and familiarity with the measurement data drawn from Anatolian (Turkish) people, the fracture risk is dependent not only on the hip length but also on other geometric variables like width x_2. Thus, secondly, we compared the numerical results of Model 1 with the one developed below:

$$A = \beta_0 \frac{x_1}{x_2^{\beta_2}} \qquad \textit{(Model 2)}$$

Finally, combining these two, a three-parameterized model was obtained in the form.

$$(P):\ A = \beta_0 \frac{x_1^{\beta_1}}{x_2^{\beta_2}} \qquad \textit{(Model 3)}$$

How least squares approximation works will be explained by this model. Both the practical importance and the beauty of the conjecture *(P)* is based on its simplicity. However, this model together with the associated inverse problem represents a *nonlinear regression* problem; therefore, from the viewpoint of numerical optimization,[21,22] it belongs to a much harder problem class than linear regression does. (For that nonlinear class, special algorithms such as the Gauss-Newton and Levenberg-Marquardt procedures are provided.[22]) However, as an expression of the inner harmony of *(P)* that it is a "natural" one according to the underlying very natural motivation, it turns out that it can, by a change of scale, be equivalently represented as a *linear regression problem* $(R)_{lin}$. For this transformation, we apply natural logarithm log to both sides of *(P)*:

$$log(A) = log(\beta_0) + \beta_1\, log(x_1) - \beta_2\, log(x_2)$$

The following denotations help for an easier representation:

$$y := log\ (A),\ \tilde{\beta}_0 := log\ \beta_0,\ \tilde{\beta}_1 = \beta_1,\ \tilde{\beta}_2 = -\beta_2,\ \tilde{x}_1 := log\ (x_1),\ \tilde{x}_2 := log\ (x_2)$$

After these substitutions, one arrives at the *linear* regression problem:

$$(R)_{lin}:\ y = \tilde{\beta}_0 + \tilde{\beta}_1 \tilde{x}_1 + \tilde{\beta}_2 \tilde{x}_2$$

Now, the problem is in a canonical form, well-investigated in numerical mathematics,[23,24] statistical learning[25] and inverse problems theory.[26] Let $N = 58$,

$$X := \begin{pmatrix} 1 & \tilde{x}_1^{(1)} & \tilde{x}_2^{(1)} \\ 1 & \tilde{x}_1^{(2)} & \tilde{x}_2^{(1)} \\ \vdots & \vdots & \vdots \\ 1 & \tilde{x}_1^{(N)} & \tilde{x}_2^{(N)} \end{pmatrix} \quad and\ y := \begin{pmatrix} y_1 \\ y_2 \\ \vdots \\ y_N \end{pmatrix} \qquad (1)$$

These modeling preparations and notations give rise to the following linear system of equations which shall be resolved in a "best possible" way (specified below):

$$(\Lambda) \quad X\beta = y \qquad (2)$$

Concerning the other models, the linearization and solution approach described in the following can also be stated by some easy modifications. The linear system *(Λ)* is overdetermined because in the matrix *X* there are more equations than unknowns and there need not be an exact (unique) solution in the usual sense. Thus, we apply linear least squares data-fitting method to *(Λ)*: By a best choice of the vector β we look for the minimal distance $\|X\beta - y\|_2$ between both vectors $X\beta$ and y. Here, $\|.\|_2$ stands for ("natural") Euclidean distance, and we denote

$$\beta = \begin{pmatrix} \tilde{\beta}_0 \\ \tilde{\beta}_1 \\ \tilde{\beta}_2 \end{pmatrix}$$

This (minimal in norm) $X\beta - y$ is also called *residuum* while we call $\|X\beta - y\|_2$ the *norm of the residuum*. We minimize its squared value:

$$\|X\beta - y\|_2^{\,2} = \sum_{i=1}^{N} (\tilde{\beta}_0 + \tilde{\beta}_1 \tilde{x}_1^{(i)} + \tilde{\beta}_2 \tilde{x}_2^{(i)} + \tilde{y}_i)^2$$

The global minimizer, called least squares estimator for

$$\beta = \begin{pmatrix} \tilde{\beta}_0 \\ \tilde{\beta}_1 \\ \tilde{\beta}_2 \end{pmatrix} \quad \text{is } \beta = (X^T X)^{-1} Xy.$$

In general, $(X^T X)^{-1}$ *exists, i.e.,* $(X^T X)^{-1}$ is a regular matrix. In case of nonregularity, ill-conditioning of *(Λ)* where the problem becomes unstable, singular-value decomposition and (e.g., Tikhonov) regularization of the linear system serve for a stabilization and approximate problem solution in a best sense.[26]

Having found β, the solution is obtained by means of the inverse transformation:

$$\begin{pmatrix} \beta_0 \\ \beta_1 \\ \beta_2 \end{pmatrix} = \begin{pmatrix} \exp(\tilde{\beta}_0) \\ \tilde{\beta}_1 \\ -\tilde{\beta}_2 \end{pmatrix}$$

RESULTS

The mean BMD values for each position are presented in Table II.

Comparison of the residuals computed showed that Model 1 was associated with a stronger improvement than the Linear Model (Table III). Both models revealed dependencies on one single variable, namely x_1. In Model 2, the residuum decreased compared with the Linear Model, but slightly increased compared with Model 1. Furthermore, by the average exponents of 0.0967 and 0.1262, respectively, x_2 became respected and accounted. Although these powers were not very large, they guaranteed a good modeling of the relation between A, x_1 and x_2, as well. The combined model, Model 3, with its three parameters brought a small, but not very strong improvement.

For this reason, in respect of the residuum, we would slightly prefer Model 3. Moreover, in Model 3 having one more parameter, the rank-deficiency of the matrix X was reduced. However, Model 2 with a smaller number of parameters seemed to be more attractive with respect to simplicity, less complexity, and, less numerical instability expected. Moreover, when changing from Model 2 to Model 3, the values of β_1 became less than 1 and the values of β_2 sometimes even became negative. This could also be interpreted as the "masking" effect of bone width x_2. In Model 2, this role was much clearly represented compared to Model 3 (Table III).

When analyzing the residual norms, i.e., the measured difference between model and data results, we excluded the Linear Model. Simple Model 1 and final Model 3 had very comparable (near) per subject errors (Fig. 2).

However, in terms of norms of residuals, Model 2 was not much worse than Models 1 and 3 on one hand, and, on the other, it had the big advantage that, by the fixed exponent β_1=1 and up to the degree of freedom given by β_0, the role and necessity of the bone width x_2 was respected and by β_2 quantified. For this reason, it was concluded that Model 2 was the most favorable, Model 1 was welcomed for its simplicity and usefulness, and that Model 3 could be reserved until a more refined explanation would be brought parametrically.

DISCUSSION

The work of Mourtada et al.[27] was a milestone in the measurement of structural geometry *in vivo*

TABLE II

Descriptive values of bone mineral density (BMD) measures and geometry of subjects at five different proximal femoral rotations (n=58)

Position		BMD (gr /cm²)	FNL (cm)	FNW (cm)
External	30° right	1.07±0.17	9.17±0.81	3.05±0.33
	30° left	1.06±0.18	9.11±0.82	3.05±0.34
	15° right	1.07±0.16	9.26±0.78	3.05±0.32
	15° left	1.06±0.17	9.22±0.82	3.05±0.34
Neutral	0° right	1.07±0.17	9.29±0.82	3.05±0.33
	0° left	1.06±0.17	9.21±0.80	3.05±0.35
Internal	30° right	1.09±0.17	9.31±0.80	3.05±0.33
	30° left	1.08±0.17	9.26±0.81	3.05±0.34
	30° right	1.01±0.17	9.32±0.81	3.05±0.52
	30° left	1.01±0.17	9.28±0.82	3.05±0.59

FNL: Femoral neck length; FNW: Femoral neck width.

and analytic calculation of mechanical stress for the investigation of individual differences in hip strength. Using data from DXA, the authors developed a structural geometry of the femur from the proximal shaft through the femoral neck. To estimate stresses on the lateral and medial bone surfaces, the geometric properties are used in a two-dimensional model of the proximal femur. The technique of employing DXA scanners for deriving bone geometry (used also by us in this study) has the advantage that it uses a simple screening to obtain bone properties relevant to strength. However, a disadvantage exists in the intrinsical two-dimensionality of the image plane. Furthermore, as the authors conclude, DXA scanners are neither designed nor

TABLE III

Comparison of the results between the models used

	Right leg						Left leg					
Intercept/Angle	30° int	15° int	0°	15° ext	30° ext	Avg	30° int	15° int	0°	15° ext	30° ext	Avg
Linear model												
β_0	0.0654	0.0897	0.0873	0.094	0.0944	0.08616	0.0818	0.0848	0.0837	0.0882	0.0888	0.08546
β_1	0.5035	0.2519	0.2611	0.1978	0.2043	0.28372	0.3464	0.2973	0.2847	0.2484	0.2512	0.2856
ResNorm	1.5077	1.3091	1.3495	1.1169	1.3995	1.33654	1.4595	1.385	1.3491	1.3049	1.489	1.3975
Model 1												
β_0	0.0818	0.0848	0.0837	0.0882	0.0888	0.08546	0.2175	0.1979	0.1886	0.1811	0.1796	0.1929
β_1	0.3464	0.2973	0.2847	0.2484	0.2512	0.2856	0.7254	0.7591	0.7713	0.7917	0.7986	0.7692
ResNorm	1.4595	1.385	1.3491	1.3049	1.489	1.3975	1.2097	1.175	1.2446	1.1756	1.3208	1.2251
Model 2												
β_0	0.1374	0.1295	0.1224	0.129	0.1267	0.129	0.1219	0.1348	0.142	0.1356	0.1305	0.133
β_1	0.1322	0.1005	0.0608	0.107	0.0829	0.0967	0.028	0.1361	0.1996	0.1554	0.112	0.1262
ResNorm	1.2599	1.0827	1.1533	0.9727	1.1797	1.1297	1.2412	1.1871	1.2383	1.1786	1.3309	1.2352
Model 3												
β_0	0.3098	0.1823	0.1854	0.152	0.1569	0.1973	0.235	0.205	0.1557	0.1706	0.1879	0.1908
β_1	0.5633	0.7707	0.7463	0.8944	0.86	0.7669	0.649	0.7264	0.94	0.8477	0.7543	0.7835
β_2	-0.0107	-0.0366	-0.0884	0.0434	-0.0037	-0.019	-0.0824	-0.0337	0.1628	0.0579	-0.0474	0.0115
ResNorm	1.2036	1.0732	1.1396	0.9708	1.1758	1.1126	1.2036	1.1747	1.2377	1.1747	1.3203	1.2222

ResNorm: Residual norm.

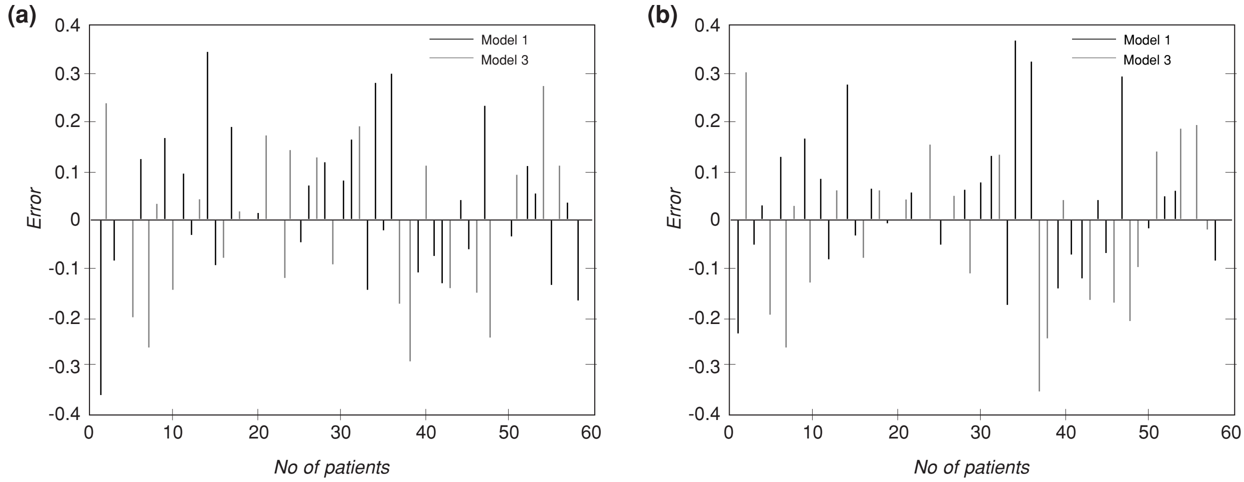

Fig. 2. Errors for **(a)** the left and **(b)** the right leg under an angle of 15°.

optimized for structural measurements, and DXA image resolution is suboptimal since the measured point size is relatively large. We remark that, in DXA technology, a profile of pixel values is obtained by extracting all pixel values along an orthogonal line drawn on the image traversing the bone. For new approaches to X-ray tomography, computed tomography and discrete tomography have been described.[28-30] The above-mentioned work[27] will be referred to in subsequent discussions where the importance of its analytical care becomes evident in the introduction of further physical parameters and dimensions. Since the latter criteria can be compared with the ones of the present study, which additionally presents less analytical complexity by only basing on neck bone length and width, we are in favor of our approach on the grounds of practicability.

Cheng et al.[31] assessed DXA technology using 64 right proximal femora from 36 male and 28 female cadavers. They measured the anteversion angle θ, which is known to influence femoral BXM records by DXA, was measured on computed tomography images. DXA measurements were made in the neutral position (i.e., at 0± anteversion, femoral neck axis parallel to the table) and in the simulated anteverted position (i.e., femoral shaft axis parallel to the table, greater and lesser trochanters in contact with the table, and femoral neck free). The femoral neck BMD turned out to increase with growing anteversion, but with a smaller magnitude than it was reported before; trochanteric BMD was less affected by anteversion in the anteverted position.[31] The authors concluded that careful repositioning of the foot and leg was essential in monitoring changes in BMD longitudinally. In the present study, we also prepared a careful experimental design with five angular constellations, and an averaging was done over all the corresponding results.

There was one more achievement in the above-mentioned study.[31] Besides the neck axis length the neck width was also taken into account separately. However, by the t-test used, the authors stated that the width did not significantly influence BMD. In our study, however, we quantified (by β_2) the effect of the width on BMD and, furthermore, we studied the length x_1 and the width x_2 jointly in their functional interplay. Unlike Mourtada et al.[27] who obtained the following (so-called "simple") mathematical model for BMD,

$$A = (\rho D \frac{\pi}{4}) / \cos^2 \theta$$

where ρ is the volumetric BMD and D is the femoral neck diameter, our model just depends on length x_1 and width x_2 and it allows rational (broken) or parabolic-hyperbolic combinations between both parameters, refined by up to three parameters β_k.

Nakamura et al.[18] presented a comparison between Eastern and Western people, namely, female Japanese and white Americans, by applying t-test on the values of the so-called *fall index*. Their results showed that Japanese, despite their lower femoral bone mass, had a lower risk for structural failure in the femoral neck, attributable mainly to a shorter neck length, but also to the neck angle θ. The authors referred to the *section of minimum CSMI* (cross-sectional moment of inertia), which somewhat corresponds to the bone width of our present study. CSMI is a measure of distribution of mineral within the neck and, herewith, it denotes rigidity under a bending moment exposed; it correlates with bone mineral content as well. A detailed analytical introduction of CSMI was presented by Mourtada et al.[27]

This bending moment is the product of a fall force, *minimum cross section of the neck d* (in contrast to full neck length considered in our study) and –cos (neck angle). The fall index (FI) was defined as the yield strength of bone in compression divided by the compressive stress on the femoral neck. Furthermore, the authors statistically studied the dependence of FI on bone mineral content, CSMI, d and θ in all the female participants from Japan and the USA. They concluded that the geometric properties (CSMI, θ, and also the neck length) were significant, determining the stresses generated by a fall. Our present study can be regarded as a deepening of this recommendation made by Nakamura et al.[18] We, however, are emphasizing the neck width explicitly. The aforementioned paper concluded with a linear regression analysis for FI depending on those factors, for both groups of females separately. Hereby, also some linear dependence between FI and the cross-sectional area,[27] related with neck width, was discovered.[18] Among further insights, the authors concluded that increases in bone mass produced a greater mechanical advantage in Japanese women compared to their American counterparts. In contrast, we placed particular emphasis on BMD (related with bone mineral content)[18] as a criterion for fracture risk and allowed nonlinear joint dependencies on neck length and width. Having acknowledged that the hip size is related with fracture risk, Faulkner et al.[32] established a sound analysis of how the hip fracture risk depended on the axis length. Unlike our young participants of a similar age, they studied 198 women covering a wide age range.[32] An automated analysis procedure was defined using software tools provided by a manufacturer of DXA. By a cross-sectional study, no relationship was found between the axis length and age in a normative group of 471 volunteers. After identifying and plotting an automatic hip axis length against that of manually measured, they found a linear dependence. A similar proportionality was found by correlating lunar HAL with hologic HAL.

It has been shown that each standard deviation increase in the HAL corresponds to a 2.3-fold increase for fracture when corrected for age, height, weight, and femoral bone density.[32] In our study, the average HAL was 10.5 cm, with a standard deviation of 0.62. Based on this result, the relative risk for hip fracture obtained from an HAL measurement in women can be determined by the following formula,

$$RR = 2.3^{\frac{x_1 - 10.5}{0.62}}$$

where RR represents the relative hip fracture risk compared with the mean value for HAL, and x_1 represents the measured HAL value. Based on this *exponential* function, the authors conclude that an x_1 value of 11.0 corresponds to a doubling of fracture risk compared to a woman with an average HAL, and an x_2 value of 11.6 increases this risk by about four times.

In our study, we referred to BMD as a factor to which the hip fracture risk is related and sought a functional dependence of BMD in the form of $\beta_0 x_1^{\beta_1}$, which is in between the linear model and the above exponential one, concerning possible growth behavior. The additional role of the width x_2 was taken into account and its masking effect was discussed. As noted by Faulkner et al.[32] x_1 has sensitivity with respect to positional variations and it represents a purely geometric measurement. In view of the proposed exponential relation, slight measurement errors could lead to significant changes in the risk. Here, our nonexponential model seems to be more stable. In addition, using a richer experimental design with five radiation angles and taking the average, the effect of specific measurements, errors, and outliers could be more widely ruled out.

A limitation of the current study was that all measurements were made in young and healthy adults. Therefore, interpretation of the results for osteoporotic patients should be made in a cautious manner.

CONCLUSION

Our results suggest that femoral neck width be incorporated into the understanding of bone mineral density. Our Model 1 would serve very well when only the length is taken into account. In our extended approach, the combined Model 3 seems to be the best, and slightly better than Model 2, which actually has the advantages of greater simplicity and less complexity in underlining and quantifying the importance of bone width.

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