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Assessment of Age-related Adaptive Changes in Relative Transverse Dimensions of the Tibia and Fibula: A Preliminary Study towards a Different Approach for Age Prediction in Adults

Fábio Rodrigues de Souza[1], **Leandro Procópio Alves**[2,3], **Antonio Balbin Villaverde**[2,3*] **and Egberto Munin**[2,3]

[1]*University Center of the Great Dourados Region (UNIGRAN), Rua Balbina de Matos, Jardim University, Dourados, Brazil*

[2]*Center for Biomedical Engineering, University Anhembi Morumbi (UAM)/ Laureate International Universities, Sao Jose dos Campos, Brazil*

[3]*Center for Innovation, Technology and Education (CITE), Dr Altino Bondensan Road, Sao Jose dos Campos, Brazil*

[*]**Corresponding author:** Antonio Balbin Villaverde, Center for Innovation, Technology and Education (CITE), Dr Altino Bondensan Road, Sao Jose dos Campos, Brazil, Brazil, Tel: +551239451359; E-mail: abvillaverde@gmail.com

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Abstract

Objectives: The study of transverse dimensions of long bones of the limbs provides valuable information of the human aging process and is of importance in forensic and anthropological sciences. The aim of the present study was to introduce a method to assess age-related adaptive changes in transverse dimensions of lower-limb bones employing a combined osteometric analysis as a different approach for age prediction in adults.

Material and methods: Twenty-four individuals (13 females and 11 males) aged from 22 to 65 years old were enrolled in the study. The mediolateral diameter of the tibia and fibula of the right leg at the one-third distal site was determined by conventional radiographs. An X-ray system model GE XR6000 (GE Hualun Medical Systems Co Ltd., Beijing, China) was used to obtain the radiographic images. Changes in bone dimensions were evaluated by regression and correlation analysis. The StatMate 2.0® software (GraphPad Software Inc., La Jolla, CA, USA) was used for the statistical analysis, with a significance level of 5% ($p<0.05$). Cohen's d effect of size parameter was employed to estimate the effect of size on the statistical analysis.

Results: The plot of age as function of the ratio between tibial and fibular dimensions for the entire studied population showed a linear fit slope of (-24.1) year, $p=0.0059$, and $r=0.55$, indicating a linear relation of age with the tibia/fibula ratio of mediolateral diameters, regardless of the height or sex of the subject. Distribution analysis of the absolute values of the residuals (actual age-predicted age) gives a median of 7.9 years, with 6.1-10.6 years confidence interval at 95%.

Conclusion: The transverse fibular dimension serves as a normalization factor to compensate for different subjects height and sex when evaluating tibial morphometry. The preliminary data indicate that this method could be an alternative tool for predicting adult age in forensic matters.

Keywords: Osteometrics; Radiology; Forensic science; Aging; Long bones; Age prediction

Introduction

Cross-sectional dimension and length analysis of human bones has long attracted the interest of scientists and continues to be a topic of interest. The relationship of bone dimensions with aging [1-6] and subject height [7-9] as well as sex dimorphism of bone geometry [9,10-13] are the main streamlines of bone anthropometric and forensic studies. Different techniques are employed to determine such relationships: radiographic x-rays [14-16], CT, QCT, and pQCT images [3,4,11,16-19], osteometric determination of bone length, and foot dimensions assessment [20]. Two recent reviews were published on the methods and implications of age determination from the forensic point of view [21,22].

Most of the works found in the literature that evaluate the long bone of the lower limb study the tibia and femur [3,4,7,10,11,13], and little data are available for the tibia and fibula [8]. Furthermore, almost all the studies that evaluated several bones of the upper and lower limbs analyzed each one individually. No work has been reported in the literature combining geometric information of two long bones to evaluate the general pattern of long bone adaptation with age due to endosteal resorption and periosteal apposition of bone tissue.

The objective of this study was to introduce a method to assess age-related changes in lower-limb bone geometry in healthy adult subjects using a combined osteometric analysis, i.e. the ratio between the tibial and fibular mediolateral dimensions. Specifically, we investigated if a combined bone analysis could lead to a different approach for age prediction. To accomplish this goal, we used radiographic images of the tibia and the fibula in a group of adults of varying ages and both sexes.

Material and Methods

The local universities ethics review board approved the present research work. The protocol was registered on the "Plataforma Brasil" under protocol CAAE46294115.6.0000.5159. The research was conducted at the radiologic sector of the medical care unit of Dourados City (Mato Grosso do Sul, Brazil). Radiograph images taken from people assisted at the radiologic sector with suspected legs trauma were analyzed. If the trauma was not subsequently confirmed and the individuals fulfilled the inclusion criteria of the study, they were invited to participate. After accepting the invitation and signing the informed consent form, they were enrolled in the study.

Twenty-four volunteers with ages ranged from 22 to 65 years old (38 ± 12), height from 1.52 m to 1.85 m (1.67 ± 0.11), and weight from 49 kg to 124 kg (74 ± 17), participated in the present research. The sampled population was divided into two study groups according to sex, with 13 females and 11 males. All volunteers had similar socio-economic background. In view of the multi-racial spectrum of the local population, the male group comprised seven whites and four black-white mixed ancestries, and the female group contained nine whites and four black-white mixed ancestries, corresponding to the actual racial distribution of the local population.

Inclusion criteria: males and females with ages from 20 to 65 years old, white and black-white mixed ancestries. Exclusion criteria: males and females younger than 20 years or older than 65 years, history of previous tibial or fibular fracture, osteopenia or osteoporosis symptoms.

Height of the 24 individuals was assessed in erect position, barefoot, and adjusting the measuring rod until touching the upper part of the head [8]. The mediolateral diameter of the tibia and fibula of the right leg at the one-third distal site was determined by conventional radiographies. A stationary X-ray system model GE XR6000 (GE Hualun Medical Systems Co Ltd., Beijing, China) was used to obtain the radiographic images, with the following operating parameters: 100 mA, 55 KeV, and 0.06 mAs. The X-ray tube was positioned 1 m from the radiographic film. The supine position was adopted for taking the images of the right leg for all individuals. Therefore, the measured diameters correspond to the bone mediolateral dimension.

We used the public domain ImageJ software (National Institutes of Health, USA) for mediolateral bone diameter measurements, specifically the "plot profile" tool of the software. The normality of the data was tested using the Kolmogorov-Smirnov normality test. A parametric two-tailed unpaired 't' test was applied to analyze the difference between male and female data. Tibial and fibular mediolateral diameters as a function of height and age were submitted to regression and correlation analysis. The StatMate 2.0® software (GraphPad Software Inc., La Jolla, CA, USA) was used for the statistical analysis, with a significance level of 5% ($p<0.05$). To calculate the effect of size on the statistical analysis, we adopted Cohen's 'd' effect of size parameter [23,24]. According to Sawilowsky's classification values of the parameter 'd', between 1.20 and 2.0 and higher than 2.0, correspond to a very large and huge effect of size, respectively [24].

Study scheme

The study was conducted through the following research steps:

- Comparison between the mean heights of men and women.
- Determination of the dependence of the mediolateral diameter of the tibia and fibula with height for men and women.
- Analysis of the dependence of the mediolateral diameter of the tibia with age for men and women.
- Analysis of the dependence of the mediolateral diameter of the fibula with age for men and women.
- Verifying if the ratio between the mediolateral diameters of tibia and fibula presents a linear dependence with age for all volunteers, regardless of height and sex. Thus, allowing obtaining a new approach for adult age prediction.

Results

A comparison of the mean height between male and female groups shows that the mean height for males is 10.6% greater than for females (1.77 ± 0.071 m *vs.* 1.60 ± 0.070 m, p=0.0001, Cohen's d=2.41). A Cohen's d parameter higher than 2.0 indicates that the data presents a huge effect of size.

Figure 1 displays the mediolateral diameters of the tibia (1A) and fibula (1B) as a function of the height for males and females. Although mean heights for males and females are different, it is observed from Figure 1 that there is a linear relation between the tibia and fibula mediolateral diameters and height when both sexes are considered together (tibial diameter *vs.* height–slope=20.5 ± 3.2 mm/m, r=0.80, p=0.0001; fibular diameter *vs.* height–slope=6.62 ± 2.2 mm/m, r=0.53, p=0.0076).

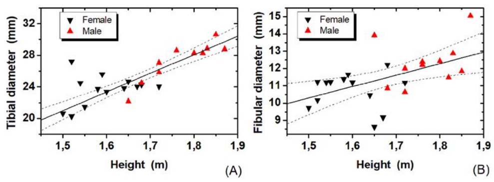

Figure 1: Mediolateral diameters of the tibia (A) and the fibula (B) as a function of the height for males and females. Solid lines represent the linear fit. Dashed lines represent the 95% confidence interval.

Figure 2A shows the measured mediolateral tibial diameter *vs.* age and the linear fit for males and females. The obtained straight-line slopes are -0.0965 mm/year for males (p=0.0761) and 0.0201 mm/year for females (p=0.720). The high data dispersion observed for males and females (p>0.05) does not allow asserting if there is a linear dependence of the tibial diameter on age for both groups. Figure 2B displays the statistical analysis of the mediolateral tibial diameter for both groups using a box plot diagram. The mean mediolateral tibial diameter for males is 15.6% larger than for females (27.4 ± 2.4 mm *vs.* 23.7 ± 1.9 mm, p=0.0003, Cohen's d=1.75), indicating a statistically significant difference in the tibial diameters between the groups (very large effect of size).

The measured mediolateral diameters of the fibula *vs.* age and a linear fit for each group are shown in Figure 3A. The obtained straight-line slope is 0.0389 mm/year for males (p=0.193) and 0.0520 mm/year for females (p=0.0625). Similarly to the tibia, it is not possible to assert that there is a linear dependence of the mediolateral fibular diameter on age for both groups. It is observed from Figure 3B that the mean mediolateral fibular diameter for males is 15% larger than for females (12.3 ± 1.3 mm *vs.* 10.7 ± 1.0 mm, p=0.0025, Cohen's d=1.38), again indicating a statistically significant difference between male and female groups (very large effect of size).

The comparison of data shown in Figures 1A, 1B, 2B, and 3B infers that the difference in tibial and fibular diameters observed for different sexes can be attributed mostly to height differences between groups.

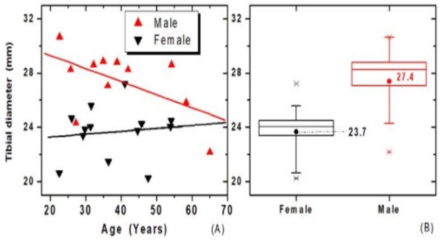

Figure 2: Mediolateral diameters of tibia *vs.* age for male and female groups, including a linear fit for both groups (A). Statistical distribution represented by box plots (B). Numbers in the box are mean values (mm). Statistical difference between female and male groups: p=0.0003, d=1.75.

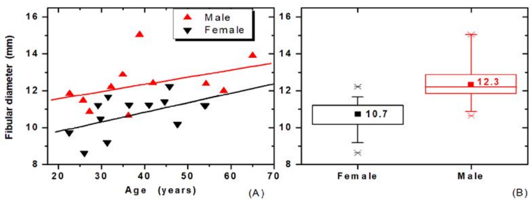

Figure 3: Mediolateral diameters of fibula *vs.* age for male and female groups, including linear fit for both groups (A). Statistical distribution represented by box plots (B). Numbers in the box are mean values (mm). Statistical difference between female and male groups: p=0.0025, d=1.38.

Tibial and fibular mediolateral diameters do not show a linear dependence on age (Figures 2A and 3B). This may be due to the fact that the varied data among subjects (different height, sex, and physiological variability) mask the dependence on age. To avoid such a drawback, we propose to normalize the tibial diameter, dividing it by the fibular diameter of the same subject and leg.

Based on other related published studies [6-9,25,26] we analyzed the data using a linear correlation model. Figure 4 shows the scatterplot of age *vs.* tibial/fibular diameters ratio (Ti/Fi) for the 24 subjects and the regression line.

The linear fit of the data gives a slope of 24.1 year, with a value of p=0.0059 and r=0.55, indicating that the slope is statistically different from zero; therefore, the age shows a linear correlation with the Ti/Fi ratio, whatever the height or sex of the subject.

The dependence on age with Ti/Fi can be expressed as follows:

Age(year)=56.0-24.1 [(Ti/Fi)-1.5]

The residuals ε are defined as:

ε=actual age-predicted age

The absolute values of ε show a normal distribution (p>0.10, Kolmogorov-Smirnov normality test) with a median of 7.9 years and 6.1-10.6 years confidence interval at 95%.

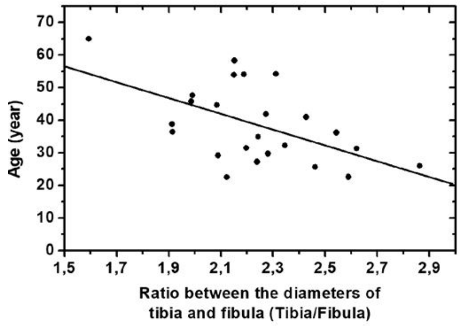

Figure 4: Dependence on age with the ratio of the mediolateral cortical diameter of the tibia to the mediolateral cortical diameter of the fibula. Solid line is the linear fit to the 24 data points.

The obtained results are summarized in Table 1 for easier comparison.

		Slope	Correlation coefficient 'r'	p-value
Tibial mediolateral diameter *vs.* age	Male	-0.0965 (mm/year)	-0.555	0.076
	Female	0.0201 (mm/year)	0.11	0.72
Fibular mediolateral diameter *vs.* age	Male	0.0389 (mm/year)	0.425	0.193
	Female	0.052 (mm/year)	0.53	0.063
Age *vs.* Tibial/Fibular diameters	Both genders	-24.1 (year)	-0.545	0.0059

Table 1: Regression and correlation analysis for the experimental data.

Discussion

Usual approaches to examine skeletal aging effects through the geometry of long bones of the upper and lower limbs employ dimensions of a single bone. For instance, McNeil et al. compared the bone geometry of tibia and fibula of the leg in three different stages of age; they assessed the cortical, medullary and total cross-sectional areas of both bones [27]. Bone dimension strongly depends on the subject's height, and applications require correction for such a bias. Some studies use the subject's height as a normalization factor for the cross-sectional geometric parameters [28]. However, when dealing with cadaveric or skeletal remains, which are a common situation in forensic analysis and physical anthropology, the height may not be directly available as a normalizing factor. Therefore, the major contribution of the present work is the introduction of a method for osteometric evaluation, in which the mediolateral diameter of the fibula was used as a parameter to compensate for different subjects' height. This can be seen by analyzing Figures 2-4. Figures 2 and 3 show evident differences between the studied groups with respect to the tibial and fibular mediolateral diameters. At first glance, such differences seem to be sex-related, but we showed that convenience sampling of males and females resulted in strong bias due to different height distributions between the studied groups. Remarkably, dividing the tibial mediolateral dimension by that of the fibula removed the bias due to different heights, and a dependence on age emerged strongly.

Our data show that the mediolateral diameter of the fibula can, ultimately, be used as an alternative normalization factor when evaluating other bones such as the tibia. Our finding seems to indicate that when dividing two anatomic dimensions, both proportional to the height, the height will cancel out.

The age changes of the mediolateral cortical diameters measured in the present work agree with previously published works [28,29]. Increasing diameters with age, as shown by the positive slopes of the straight lines fitted to our experimental data in Figures 2A and 3A, agree with the principle of sub-periosteal bone apposition [30,31]. An exception to the rule is the observed age change of the tibial diameter for males shown in Figure 3A, for which the straight-line slope is negative (-0.0965 mm/year). We may attribute such occurrence to the large scattering of our experimental data, since in this case the obtained slope is not statistically different from zero (p=0.0761). Despite the cortical "expansion" of both the tibia and fibula, the age shows a negative slope (-24.1 year, p= 0.0059) when plotted against the ratio of the tibial to the fibular mediolateral diameters (Figure 4), indicating that, for the evaluated bone site, the fibular expansion exceeds the tibial expansion. It has been asserted that site-specific differences in mechanical stress may modulate the degree of sub-periosteal expansion of bones [32].

The precision in the age prediction of 7.9 years obtained in the present work agrees with those reported in the literature, based upon the recent review published by Villa et al. [21] in which the precision for many of the known different methods stays around 10 years.

The aim of this preliminary work was to show that it is possible to observe a linear dependence on age with the ratio between tibial and fibular mediolateral diameters even when a large span of age, sex, and race is included in the study. Although the sample size is restricted because of the selection process, the statistical analysis shows a very large effect of size. Further improvement of the predictive age accuracy is expected to be achieved by increasing the research population and limiting the study to some specific groups of individuals such as: reduced age interval, sex, race, and nationality. These further refinements will possibly allow this method to be applied in forensic matters.

Furthermore, the present work is limited by the inaccuracies and limitations inherent to one-dimensional radiographic breadths. Therefore, better results are expected by using higher-quality imaging techniques, like computed tomography.

Conclusion

This work employed an osteometric approach to extract age-related changes in the mediolateral dimension of the tibia and the fibula, aiming to obtain a new method for adult age prediction. It was observed that bias in mediolateral tibia dimension that arises from different subject's height can be compensated by using the mediolateral dimension from the fibula as a normalization factor. A linear relation of age with the ratio of the mediolateral diameters of the tibia and fibula was found. This method seems promising for predicting adult age in anthropometric and forensic matters. This work employed an osteometric approach to extract age-related changes in the mediolateral dimension of the tibia and the fibula, aiming to obtain a new method for adult age prediction. It was observed that bias in mediolateral tibia dimension that arises from different subject's height can be compensated by using the mediolateral dimension from the fibula as a normalization factor. A linear relation of age with the ratio of the mediolateral diameters of the tibia and fibula was found. This method seems promising for predicting adult age in anthropometric and forensic matters.

Conflict of Interest

The authors declare that they have no conflict of interest.

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Ethical Approval

The local universities ethics review board approved the present research work, which was registered in the "Plataforma Brasil" under protocol CAAE46294115.6.0000.5159.

Informed Consent

Informed consent was obtained from all individual participants included in the study.

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