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Associations between leisure physical activity participation and cortical bone mass and geometry at the radius and tibia in a Canadian cohort of postmenopausal women

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Conflicts of Interest

All authors have no conflicts of interest.

Abstract

Few studies have examined the effects of leisure physical activity (PA) participation on bone mass and geometry in postmenopausal women using pQCT. The purpose of this study was to determine associations between leisure PA participation and bone mass and geometry at the radius and tibia in a Canadian cohort of healthy postmenopausal women (n=234, mean age 62 years). Leisure PA participation was assessed using the Minnesota Leisure Time Physical Activity Questionnaire and by generating a total activity score (TAS, mean=105, range=0-840). Bone mass and geometry at the distal and midshaft sites of the non-dominant radius and tibia were measured using peripheral quantitative computed tomography (pQCT). Associations between TAS and bone mass and geometry variables were determined using linear regression models adjusted for clinically relevant confounding variables. TAS was positively and significantly associated with total content, total area, cortical content and cortical area at the midshaft sites of the radius and tibia ($p<0.05$ for all associations). TAS was also positively and significantly associated with bone bending and torsional strength parameters at the midshaft radius and tibia ($p<0.05$ for all associations). No associations were observed between TAS and trabecular bone parameters. Leisure PA participation is positively associated with cortical bone mass and geometry as well as bending and torsional strength at weight-bearing and non weight-bearing bone sites and may have the potential to modify bone strength and influence bone fragility in postmenopausal women.

Keywords: bone geometry, pQCT, physical activity, leisure, postmenopausal women

Introduction

In Canada, 1 in 6 women over the age of 50 years has osteoporosis (OP) [1] and OP is the alleged cause of over 24 000 hip fractures each year, a figure that is expected to double by 2040 [2]. While there are many pharmacologic agents available for the prevention of osteoporosis, widespread and long term use of these agents is limited due to side-effects [3, 4], costs [5] and poor long term compliance [6]. Therefore, it is essential that non-pharmacologic strategies to prevent osteoporosis continue to be evaluated.

Physical activity is an important lifestyle factor that has the potential to modify bone strength in postmenopausal women through its effects on bone mineral density (BMD) and bone geometry (size and shape parameters of bone). In fact, recent studies using peripheral quantitative computed tomography (pQCT) demonstrate that participation in physical activity can benefit both trabecular and cortical components of bone in this population [7-11]. Cross-sectional studies report greater cortical area and bending strength at weight bearing bone sites (tibia, femur) among active postmenopausal women compared to those who are inactive [9-11]. Further, prospective investigations report slower rates of cortical and trabecular BMD loss at weight-bearing bone sites among postmenopausal women participating in activities such as recreational volleyball and Tai Chi Chuan [7, 8].

While there is some evidence to suggest that physical activity can positively influence bone geometry in postmenopausal women, few studies have examined the influence of physical activity participation that is community based and accessible to populations of women that

cannot or prefer not to participate in institutionally based activity programs. Further, studies to date are predominantly in Asian and European women, thus current findings cannot be generalized to North American women who may have differences in diet and lifestyle factors known to affect bone. To address the limitations of the current literature, we conducted a cross-sectional study in a cohort of healthy Canadian postmenopausal women to determine associations between leisure physical activity participation and bone mass and geometry at the radius and tibia.

Materials and Methods

Subject Selection

We contacted 243 healthy, ambulatory, postmenopausal women currently participating in a randomized double-blind placebo-controlled study entitled The Effects of Organic Nitrates on Osteoporosis (Nitrate and Bone Study; NCT00252421, ISRCTN 94484747); a 2-year, phase 3 clinical trial designed to examine the effects of nitroglycerin ointment on bone mineral density (BMD), bone turnover markers, and bone geometry in healthy postmenopausal women. From this parent study, a total of 234 women consented to participate in a physical activity questionnaire and were enrolled in our ancillary study.

Women recruited from the parent study met the following inclusion criteria: 49 years of age or older, at least 1 year postmenopausal, BMD at the lumbar spine (L1-L4) between 0 and 2.0

standard deviations below the mean for young adults (T-score) and at the total hip above a T-score of 0. These T-score ranges reflected specific eligibility criteria necessary for the drug trial. Women were excluded if they had a prior history of hip, wrist or spine fracture, active metabolic bone disease, used androgen, estrogen, progesterone, calcitonin, fluorides, raloxifene, tamoxifen or etidronate within 6 months of study entry, were treated with corticosteroids (prednisone equivalent of 5 mg/day for ≥ 12 months) within 3 months of study entry, reported use of a bisphosphonate within 3 years of study entry or were currently taking nitrates or had a hypersensitivity to nitrates. Women were also excluded if they had severe or chronically disabling conditions, a life expectancy of < 5 years, a self-reported history of migraine headaches, myocardial infarction, angina, valvular or congenital heart disease, a systolic blood pressure of ≤ 100 mmHg, a diastolic blood pressure ≥ 110 mmHg, or an abnormal 12-lead electrocardiogram (ECG) at study entry. All women provided written informed consent in accordance with the research ethics boards at the affiliated University of Toronto hospitals and in compliance with the Declaration of Helsinki.

Demographics

At entry into the parent study, each woman completed an interviewer-administered baseline questionnaire to collect general demographics and medical history including; age, race, education and type of employment, current use of medications, alcohol and caffeine intake at study entry, past and current tobacco use, total dietary and supplemental calcium intake, total dietary and supplemental vitamin D intake, age at menarche, age at menopause and family history of fractures.

Physical activity assessment

A single interviewer assessed each woman's physical activity participation over the past year using the Minnesota Leisure-Time Physical Activity Questionnaire (LTPA) [12]. The questionnaire was administered anywhere between baseline entry into the parent study and onward up to 2 years of study participation, because subjects were at different points in their individual progression of the parent study when we decided to do the sub-analysis. Women were asked to report on their participation in the 63 different sports, recreational, yard, and household activities included in the LTPA, as well as on any additional activities not listed. Women were also asked to provide details on the seasonality, frequency and duration of participation in each activity. Activities were assigned intensity codes in metabolic equivalents (MET) using the updated Compendium of Physical Activities [13]. Each woman's current level of physical activity was then determined by calculating a total activity score (TAS). This score considers the frequency, aerobic intensity, duration and loading components (weight bearing or non-weight bearing) of each activity and has previously been described in detail elsewhere [14]. We modified the original TAS equation for the present study to include all leisure physical activities reported by a subject and not just the three most frequently reported.

Anthropometric measurements

Standing height was measured to the nearest 0.1 cm using a wall-mounted harpenden stadiometer (Holtain Ltd, Crymych UK). Body weight was assessed using a digital column scale (Seca

Model 707, Hamburg, Germany) and was recorded to the nearest 0.1 kg. Tibial length was defined as the distance from the distal edge of the medial malleolus to the tibial plateau. Radial length was defined as the distance from the radial styloid process to the radial head. Both tibial and radial lengths were measured using anthropometric tape to the nearest 0.1 cm.

Bone mass and geometry measurements

Bone mass and geometry at the radius and tibia were measured using pQCT (Norland/Stratec XCT 2000; Stratec Medizintechnik GmbH, Pforzheim, Germany) at baseline entry into the parent study. All scans were executed by one technician and a quality assurance measurement was performed prior to all scanning sessions.

Measurements were made at the distal and midshaft sites of the radius and tibia on the non-dominant side. A 30 mm planar scout view over the joint line was used to locate a standard anatomical reference (distal endplate of the radius or tibia) from which the distal and midshaft sites were measured proximally. Single tomographic scans (2 mm in thickness, voxel size 0.2mm) were obtained at the 4% (4% of the radius length proximal to the distal end plate of the radius) and 20% sites of the forearm. At the lower leg, scans were obtained at 4% (4% of the tibial length proximal to the distal end plate of the tibia) and 38% sites. At the distal (4%) sites of the radius and tibia we measured bone mass and geometry parameters including: total content (mg/mm), total density (mg/cm³), trabecular content (mg/mm), trabecular density (mg/cm³), total area (mm²) and trabecular area (mm²). At the midshaft sites (20% and 38%) of the radius and tibia we measured bone mass and geometry parameters as well as bone strength parameters.

Bone mass and geometry parameters included: total content (mg/mm), total density (mg/cm³), total area (mm²), cortical content (mg/mm), cortical density (mg/cm³) and cortical area (mm²). Bone strength parameters included: axial area moment of inertia (with respect to both the x and y axes) (mm⁴), polar moment of inertia (mm⁴), axial strength-strain index (with respect to the x and y axes) (SSIx or SSly) (mm³) and polar strength-strain index (SSIp) (mm³). Briefly, axial area moments of inertia and axial SSIs provide estimates of the bone's resistance to bending in the x and y planes, while the polar indices provide estimates of the bone's resistance to torsion. Detailed definitions of moments of inertia and SSIs have been described elsewhere in detail [15]. In vivo precision in our laboratory for these bone mass and geometry parameters ranges from 1 to 3% CV for both radial and tibial sites.

All scans were analyzed using the manufacturer's software package Stratec Version 5.50. Contour mode 2, which uses an edge detection algorithm and default threshold of 280 mg/cm³, was used to define the outer contour of the bone (periosteal boundary). Peel mode 1 was used to separate cortical and trabecular bone and defined trabecular area as equivalent to 45% of total bone area. For all analyses except the determination of SSIs, a threshold value of 710 mg/cm³ was used to define cortical bone. A default threshold of 480 mg/cm³ was used in the calculation of SSIs.

Statistical Analysis

Ordinary least-squares regression models were used to determine associations between TAS and bone mass and geometry outcome variables at the radius and tibia. Separate regression

analyses were completed for each outcome variable. Analyses were performed unadjusted and adjusted for clinically relevant confounding variables including age and weight. We also adjusted for radius and tibial length to account for the effect of body size on bone outcomes. The level of significance was set at $p < 0.05$. All analyses were performed using STATA Special Edition software Version 10.0.

Results

Subject characteristics

Subject characteristics are outlined in Table 1. The majority of women were Caucasian (93%), the mean age was 62 years, the mean BMI was less than 30 kg/m^2 and the average number of years since menopause was greater than 10 years. Nearly all women were non-smokers, consumed less than 7 alcoholic beverages per week and less than 3 caffeinated beverages per day.

Physical activity

Most women were physically active, the majority (61%) averaging more than 6 hours of physical activity per week or approximately 1 hour of physical activity per day. This amount of activity is typical of Canadian women over the age of 45, of whom 40-50% are reported to be moderately active on most days of the week [16]. Approximately 1/3 of the women (28%) participated in

physical activity between between 3 to 6 hours per week and a small portion (11%) participated in less than 3 hours of physical activity per week. Mean TAS was 105 (98) with the lowest TAS being 0 and the highest being 840 (Table 1).

Associations between TAS, bone mass, bone geometry and bone strength parameters

Linear regression models adjusted for age, weight and limb length showing the associations between TAS and bone mass and geometry parameters are presented in Table 3a for the radius and Table 4a for the tibia. Linear regression models adjusted for age, weight and limb length showing associations between TAS and bone strength parameters are presented in Table 3b for the radius and 4b for the tibia.

Discussion

Stress from gravitational loading and muscle pull on bone during physical activity, causes bone to primarily experience bending and torsional forces, which place the greatest amount of stress on the bone's outer surface. As the outer surface is comprised of cortical bone, we would expect to see favorable geometrical adaptations in the cortical compartment among individuals participating in greater amounts of physical activity as a logical response mechanism to preserve mechanical competence. Further, we would expect to see concurrent adaptations in the bone's resistance to bending and torsion as cortical indices affect the way in which these strength parameters are derived. These expectations are consistent with findings from this study, which

demonstrated significant positive associations between TAS and cortical bone components as well as bone strength (bending and torsion) parameters.

We observed significant positive associations between TAS and bone mass and geometry parameters at the midshaft radius and tibia sites, where we primarily assessed changes in the cortical bone compartment. For every 1 SD increase in TAS (equivalent to 2 hours of moderately paced walking performed daily), we observed marginal (between 0.02% and 0.21%) but significant increases in total content, total area, cortical content and cortical area. Negative associations between TAS and total and cortical density were also observed, however these associations did not reach statistical significance. Given the mechanism by which mechanical loading induces adaptations in bone (ie. causing bending and twisting and thus increasing stresses on the outer surface of bone), it is not surprising that we observed significant positive associations between TAS and cortical measures. The positive associations observed between TAS and cortical area reflect a logical compensatory response of bone to the stresses induced by participation in physical activity, because a larger cross-sectional area can bear larger bending and torsional loads [17]. The trend of TAS to be negatively associated with cortical density corresponds with this expansion in cortical area, based on the way in which density is derived. The positive associations observed between TAS and total bone area and content likely also reflect these cortical adaptations.

Although, in this particular study the associations we found between TAS and bone mass and geometry parameters at the midshaft radius and tibia sites were marginal and thus their clinical significance questionable, there are several observational studies that do support the notion that

the cortical compartment adapts to physical activity participation. For example, a cross-sectional study by Uusi-Rasi et al. [10], examining bone geometry at the tibia in a comparable population, observed superior tibial midshaft geometry in women who were more physically active. Cortical area and bone strength were greater among active women compared to those who were sedentary. Further, another cross-sectional study by the same group [11], also reported greater cortical area and cortical bone mineral content among postmenopausal recreational gymnasts versus sedentary referents.

The only significant association we observed at a distal bone site was between TAS and total bone content at the radius (0.03% increase in total bone content for every 1 SD increase in TAS). This was likely a reflection of an increase in cortical bone content, given that we did not observe any associations between TAS and measures of trabecular bone. However, it should be reiterated that the association we observed was very modest. At the distal tibial site, we did not observe any significant associations between TAS and bone mass and geometry parameters. This finding is consistent with a number of other studies that have failed to observe improvements in trabecular bone in response to exercise training [18-20]. One explanation for the lack of observed effects on trabecular bone may simply be the mechanism behind which exercise exerts its effects on bone. As aforementioned, stress from gravitational loading and muscle pull on bone during exercise causes a bone to primarily experience bending and torsional forces which place the greatest amount of stress on the bone's outer surface. In turn it is primarily the cortical compartment that is forced to adapt to these forces. Another explanation may be related to the more sensitive response of trabecular bone to hormonal changes, such as the decline in estrogen characteristic of menopause [21]. Perhaps, the adaptation of trabecular

bone to mechanical loading may be masked by the more rapid loss of trabecular bone compared to cortical bone that occurs in the postmenopausal skeleton. Alternatively, our relatively small sample size may have simply obscured significance for cancellous bone.

We observed significant positive associations between TAS and bone strength parameters at both the radius and tibia midshaft sites. For every 1 standard deviation (SD) increase in TAS, we observed increases in axial area moments of inertia as well as polar moments of inertia at both the midshaft radius (between 0.3% and 0.7%) and tibia (between 2.5% and 6.3%). Moment of inertia is a measure of the distribution of material around the centre (neutral axis) of a cross-section [22], and this distribution reflects the capacity of the cross-section to resist bending (axial area moments of inertia) and torsional (polar moment of inertia) forces. A larger moment of inertia indicates that the cross-section is better able to resist bending or torsional forces. Therefore, in a bone cross-section at the midshaft site, the axial area moment of inertia and polar moment of inertia parameters are dependent on how the cortical area is distributed around the neutral axis of the bone's cross section. In this study, we observed significant positive associations between TAS and moments of inertia at both the radius and tibia midshaft sites, suggesting that women who are participating in greater amounts of leisure physical activity have a more mechanically competent cortical structure at both weight-bearing and non weight-bearing sites. Similar findings were also reported in a cross-sectional study by Uusi-Rasi et al. [10] examining the influence of habitual physical activity participation and calcium intake on bone at the radius in Finnish postmenopausal women.

While we found relatively strong positive associations between TAS and moments of inertia at the midshaft sites of both the radius and tibia, we did not observe comparable strength in the associations reported between TAS and SSIs. For every 1 standard deviation (SD) increase in TAS, we observed marginal but significant increases in axial and polar SSIs at both the midshaft radius (between 0.04% and 0.08%) and tibia (between 0.2% and 0.4%). SSI is derived by the product of section modulus (polar moment of inertia/maximum radial distance of a bone cross-section) and cortical BMD normalized to the maximal physiological cortical BMD of human bones [23]. SSI attempts to account for an estimate of the bone's apparent elastic modulus, representative of the bone's material properties. This is enabled by the fact that volumetric BMD of cortical bone in the narrow physiological range is known to have an approximately linear relationship with elastic modulus [17]. The smaller associations we observed between TAS and SSIs at the midshaft sites of the radius and tibia are likely due to the fact that we observed negative (non-significant) associations between leisure physical activity participation and cortical BMD at these sites. However, it should be noted that overall, the positive associations we observed between TAS and SSIs were still in keeping with the trend for favorable adaptations in bone strength.

A recent study by Shedd et al. [9] also reported on the association between TAS and bone mass and geometry variables in healthy postmenopausal women. Associations were reported on at the distal tibia (4%) and midshaft femur (33%). Consistent with our findings, the study by Shedd et al. found no associations between TAS and bone mass and geometry variables at the distal weight-bearing site (tibia) but found positive associations between TAS and cortical bone components (cortical area $\beta=0.16$, $p=0.01$; cortical thickness $\beta=0.15$, $p=0.03$) at the weight-

bearing bone shaft (femur). In contrast to our findings, Shedd et al. did not report any associations between TAS and estimates of bone strength. This may be partially explained by the fact that subjects in the study by Shedd et al. were younger. Women lose bone more rapidly around and for a few years after menopause [24], which may have masked some of the effects of physical activity on bone geometry that we were able to observe in the older cohort. Our study population was also more active, participating in twice as much activity per week as the cohort in the study by Shedd et al. Lorentzon et al. [25] have suggested that a threshold of 4 hours of physical activity per week is required to induce a positive bone response (an increase in bone mass). The majority of subjects in our sample were well above that threshold, which may have accounted for the additional modifications in bone geometry that we observed. Finally, the mechanical stress experienced by the femur during physical activity is likely different than the stress experienced by the tibia and may have also contributed to the differences in findings between our study and the study by Shedd et al.

Our study had several limitations. While we reported positive associations between TAS and a number of different bone variables at both weight-bearing and non weight-bearing sites, we were unable to infer causal effects of exercise on bone due to the cross-sectional nature of our study design. We also determined physical activity information by self-report via questionnaire, which may have introduced recall bias. Self-report of physical activity is subject to a variety of factors, most notably over reporting of time and intensity [26], which may have affected our ability to observe true associations between leisure physical activity participation and bone variables. Further, the formula we used to calculate the TAS with has not been validated. There is currently no standardized method for quantifying the loading component of weight-bearing

physical activity in observational settings [9]. Given that the TAS considers both the frequency and duration of an activity, as well as a weight-bearing component, the use of TAS seemed like the most appropriate measurement tool for our study. The TAS does not specifically account for loading at the radius, however, in many of the activities where the radius is loaded, the tibia is loaded as well which would have minimized this issue. However, that this may have impeded our ability to observe appropriate associations at the radial site. Finally, while we aimed to provide data representative of North American women, it should be noted that our sample was quite healthy, had a narrow range of BMD values and was more physically active compared to activity levels reported for postmenopausal women in the United States [27].

In summary, the positive associations we observed between leisure physical activity participation and cortical bone mass and geometry measures as well as bone strength parameters at the radius and tibia, suggest an important lifestyle factor which may have the potential to modify bone strength and influence bone fragility in postmenopausal women. Our findings provide an important framework for future research which will further the development and implementation of physical activity guidelines for the prevention of OP and OP related fractures in postmenopausal women.

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Table 1. Subject demographics.

Variable (n=234)	Mean $\pm$ SD (Range) or Frequency (%)
Caucasian	217 (92.7%)
Age, years	62 $\pm$ 7 (48-82)
Weight, kg	70.9 $\pm$ 13.2 (45.4-116.8)
Height, cm	162.0 $\pm$ 6.2 (140.0-184.9)
BMI, kg/m ²	27.0 $\pm$ 4.9 (16.7-46.2)
Age of menarche, years	13 $\pm$ 1 (9-17)
Age of menopause, years	50 $\pm$ 6 (27-58)
Years since menopause	12 $\pm$ 8 (1-35)
Daily total calcium intake, mg	1558 $\pm$ 353 (725-2800)
Daily supplemental vitamin D intake, IU	763 $\pm$ 247 (400-1600)
Caffeine consumption ^a	62 (26.5%)
Alcohol consumption ^b	35 (15.0%)
Current smoker ^c	3 (1.3%)
Family history of fractures ^d	32 (13.7%)
Total activity score	105 $\pm$ 98 (0-840)

^a>3 caffeinated beverages per day^b>7 alcoholic beverages per week^cAt least 1 cigarette per day^dAt least 1 immediate family member with a previous fracture

Table 2. Mean bone geometry values for variables at the radius and tibia.

Variable	Mean (SD)	Mean (SD)
Distal	Radius (4%) (n=234)	Tibia (4%) (n=234)
Total content (mg/mm)	92.8 (15.1)	279.0 (32.7)
Total density (mg/cm ³)	319.2 (56.1)	271.9 (34.3)
Total area (mm ²)	295.6 (53.2)	1035.6 (133.1)
Trabecular content (mg/mm)	22.0 (6.5)	100.6 (15.8)
Trabecular density (mg/cm ³)	166.2 (38.0)	217.0 (30.9)
Trabecular area (mm ²)	133.0 (23.9)	466.0 (59.9)
Midshaft	Radius (20%) (n=233)	Tibia (38%) (n=234)
Total content (mg/mm)	88.1 (10.5)	323.3 (37.5)
Total density (mg/cm ³)	833.6 (108.9)	845.0 (90.2)
Total area (mm ²)	107.1 (16.7)	387.7 (66.7)
Cortical content (mg/mm)	81.6 (10.7)	303.3 (35.3)
Cortical density (mg/cm ³)	1230.7 (33.8)	1175.2 (29.1)
Cortical area (mm ²)	66.3 (8.0)	258.0 (29.2)
Axial area moment of inertia x-axis (mm ⁴)	562.1 (142.7)	12158.6 (3069.9)
Axial area moment of inertia y-axis (mm ⁴)	948.7 (264.6)	8766.2 (2209.0)
Polar moment of inertia (mm ⁴)	1510.4 (383.8)	20982.4 (4704.9)
Axial strength-strain index x-axis (mm ³)	109.9 (20.5)	890.4 (156.3)
Axial strength-strain index y-axis (mm ³)	133.4 (27.2)	726.0 (135.1)
Polar strength-strain index (mm ³)	205.7 (38.9)	1397.3 (225.3)

Table 3a. Linear regression models examining the associations between TAS and bone mass and geometry parameters at the distal and midshaft radius.*

Variable	β -coefficient	95% CI	p value
Distal radius (4%) (n=234)			
Total content (mg/mm)	0.0287	0.0087-0.0487	0.005
Total density (mg/cm ³)	0.0178	-0.0581-0.0938	0.644
Total area (mm ²)	0.0653	-0.0054-0.1360	0.070
Trabecular content (mg/mm)	0.0076	-0.0013-0.0164	0.092
Trabecular density (mg/cm ³)	0.0132	-0.0384-0.0647	0.615
Trabecular area (mm ²)	0.0294	-0.0024-0.0612	0.070
Midshaft radius (20%) (n=233)			
Total content (mg/mm)	0.0263	0.0134-0.0391	0.000
Total density (mg/cm ³)	-0.0492	-0.1875-0.0892	0.484
Total area (mm ²)	0.0354	0.0142-0.0567	0.001
Cortical content (mg/mm)	0.0219	0.0090-0.0349	0.001
Cortical density (mg/cm ³)	-0.0112	-0.0536-0.0313	0.605
Cortical area (mm ²)	0.0184	0.0087-0.0282	0.000

*adjusted for age, weight and radius length

Table 3b. Linear regression models examining the associations between TAS and bone strength parameters at the midshaft radius.*

Variable	β -coefficient	95% CI	p value
Midshaft radius (20%) (n=233)			
Axial area moment of inertia x-axis (mm ⁴)	0.2530	0.0733-0.4328	0.006
Axial area moment of inertia y-axis (mm ⁴)	0.6832	0.3380-1.0283	0.000
Polar moment of inertia (mm ⁴)	0.8335	0.3469-1.3200	0.001
Axial strength-strain index x-axis (mm ³)	0.0413	0.0157-0.0668	0.002
Axial strength-strain index y-axis (mm ³)	0.0744	0.0388-0.1099	0.000
Polar strength-strain index (mm ³)	0.0899	0.0409-0.1389	0.000

*adjusted for age, weight and radius length

Table 4a. Linear regression models examining the associations between TAS and bone mass and geometry parameters at the distal and midshaft tibia.*

Variable	β -coefficient	95% CI	p value
Distal tibia (4%) (n=234)			
Total content (mg/mm)	0.0271	-0.0148-0.0690	0.204
Total density (mg/cm ³)	-0.0136	-0.0597-0.0326	0.563
Total area (mm ²)	0.1318	-0.0326-0.2963	0.115
Trabecular content (mg/mm)	0.0087	-0.0119-0.0294	0.405
Trabecular density (mg/cm ³)	-0.0121	-0.0539-0.0296	0.567
Trabecular area (mm ²)	0.0593	-0.0147-0.1333	0.115
Midshaft tibia (38%) (n=234)			
Total content (mg/mm)	0.0818	0.0385-0.1252	0.000
Total density (mg/cm ³)	0.0315	-0.0844-0.1475	0.593
Total area (mm ²)	0.0849	0.0072-0.1625	0.032
Cortical content (mg/mm)	0.0716	0.0305-0.1126	0.001
Cortical density (mg/cm ³)	-0.0172	-0.0564-0.0219	0.386
Cortical area (mm ²)	0.0656	0.0323-0.0988	0.000

*adjusted for age, weight and tibia length

Table 4b. Linear regression models examining the associations between TAS and bone strength parameters at the midshaft tibia.*

Variable	β -coefficient	95% CI	p value
Midshaft tibia (38%) (n=234)			
Axial area moment of inertia x-axis (mm ⁴)	3.9025	0.2762-7.5287	0.035
Axial area moment of inertia y-axis (mm ⁴)	2.5495	-0.0030-5.1020	0.050
Polar moment of inertia (mm ⁴)	6.3034	0.9833-11.6236	0.020
Axial strength-strain index x-axis (mm ³)	0.2139	0.0326-0.3952	0.021
Axial strength-strain index y-axis (mm ³)	0.1707	0.0127-0.3287	0.034
Polar strength-strain index (mm ³)	0.3810	0.1240-0.6379	0.004

*adjusted for age, weight and tibia length