Site and Sex Effects on Tibia Structure in Distance Runners and Untrained People

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ABSTRACT

FELDMAN, S., R. F. CAPOZZA, P. A. MORTARINO, P. S. REINA, J. L. FERRETTI, J. RITTWEGER, and G. R. COINTRY. Site and Sex Effects on Tibia Structure in Distance Runners and Untrained People. *Med. Sci. Sports Exerc.*, Vol. 44, No. 8, pp. 1580–1588, 2012. **Purpose**: The purpose was to study the relationship between mechanical environment and bone structure by comparing the tibia in people with different physical activities. **Materials and Methods**: Indicators of bone mass (bone mineral content), bone material "quality" (cortical volumetric mineral density (vBMD)), and diaphyseal design (endocortical and periosteal perimeters (EcPm and PoPm, respectively), cortical thickness (CtTh), circularity, and bending and torsion cross-sectional moments of inertia (CSMIs)) were determined in serial peripheral quantitative computed tomography scans taken at 5% steps of the tibia in 40 voluntary men and women age 25–40 yr who were either physically inactive or experienced distance runners (n = 10–12 per group). **Results**: Bone mass and design indicators were higher in runner than in nonrunner men, with a variable effect size along the tibia. In the distal tibia, runners had enhanced bone mineral content and CtTh (resistance to compression), but EcPm, PoPm, circularity, and CSMI were unaffected. In the midshaft, CSMIs (resistance to bending/torsion) were enhanced in runners, whereas bone mass was unaffected. In the proximal third, effects were observed for CtTh, EcPm, and PoPm. In female runners, these benefits were restricted to CSMIs only. Cortical vBMD, naturally lower in men than in women, was reduced in runners of either sex. **Discussion**: Results are coherent with previous findings in physically inactive people and with Frost's mechanostat theory. The observed group differences in cortical vBMD could reflect an increase in intracortical porosity (enhanced remodeling for damage repair), eventually compensated biomechanically by CSMI improvements. The sex specificity of exercise effects may suggest the interference by the endocrine environment. Results confirm that the mechanical environment is a strong determinant of regional tibia structure and suggest that the endocrine environment may reduce the effects of physical interventions on bone health in fertile women. **Key Words:** EXERCISE AND BONE, OSTEOPENIA, OSTEOPOROSIS BONE BIOMECHANICS, BONE STRUCTURE, BONE STRENGTH

Beyond the morphogenetic determination of the bones' primary shape by the so-called *anlagen*, the structural characteristics of every bone are determined by mechanical usage and the endocrine–metabolic environment of the skeleton (17,20). Of the various theories to explain the bone's adaptation to mechanical usage, Frost's mechanostat (17) is still the most popular one. That theory proposes that the mechanical strains (e.g., body weight bearing, regional muscle contractions) would orient the structural adaptation of bones, whereas the endocrine–metabolic environment would modulate that directional regulation by a systemic modulation of the threshold that governs the bone modeling or remodeling mechanisms to maintain the mineral equilibrium of the organism.

In a recent study (7), during which serial scans were taken by peripheral quantitative computed tomography (pQCT) in the tibiae of healthy, physically inactive men and women age 20–40 yr, we found that the tibia follows a pattern along its length that is bearing great similarity between subjects.

More specifically and regardless of the sex or other individual traits, the minimal total bone mass along with the maximal circularity and minimal values of cross-sectional moments of inertia (CSMIs, indicators of the rigidity in bending and torsion) were found at 14% of the tibia's length (from its distal end). This suggested that the mechanical competence of this bone site is mainly adapted to compression. Moving along the tibia more proximally, there were increases in cortical mass, thickness, diameters, and bending

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TABLE 1. Means ± SD of age, weight, and height of the studied groups and running performance of the trained groups.

	Physically Inactive Men	Physically Inactive Women	Runner Men	Runner Women
Age (yr)	31.9 ± 3.1	30.9 ± 3.2	33.9 ± 3.2	31.3 ± 3.9
Weight (kg)	79.7 ± 10.7	56.1 ± 2.5	78.6 ± 4.4	54.5 ± 4.3
Height (cm)	176.1 ± 3.2	164.0 ± 1.8	174.7 ± 2.9	160.5 ± 5.0
Minimum/maximum running distance per session (km)			10/15	10/15
Minimum/maximum number of sessions per week			3/5	3/5
Minimum/maximum kilometers run per week			40/60	40/60
Average velocity ($km \cdot h^{-1}$)			11.9 ± 0.5	10.6 ± 0.7
Years in running training			12.2 ± 2.9	13.3 ± 2.8

and torsion CSMIs that, in combination with the more complicated cross-sectional design of the diaphysis, suggested a progressive adaptation of the bone to additional stresses caused by bending and/or torsion. Moving further up to the knee, there was a further increase in total bone mass and diameters, whereas the cortical thickness decreased and the cross-sectional design turned more or less oval, suggesting that competence to bear compressive loads from either of the two femur condyles (called biaxial loading from hereon) is the governing pattern in the shape of the proximal tibia. In general terms, bone features were analogous in men and women, although the latter showed smaller values of all indicators of mass and structural rigidity and greater values of the volumetric mineral density of cortical bone (cortical vBMD).

In agreement with the general concepts outlined above, we were interested to see how far the mechanical environment could affect the tibia's principle layout as described in our previous article. To this purpose, we have organized a study to compare the principle descriptors of the tibia design in people who engage in long-distance running with those who are physically inactive.

The aim was to gain further insight into how physical exercise affects bone. More specifically, we hypothesized that the runners would have generally elevated bone strength indicators in their tibiae.

MATERIALS AND METHODS

Study Participants

The 10 men and 12 women who had been previously studied (7), age 25–40 yr, all healthy and physically inactive (untrained individuals who were involved in regular habitual activity and whose recreational activities did not include any sport practice or training at all, at least during the last 10 yr) as revealed by a simple anamnesis, were recruited to match 10 male and 10 female endurance runners for age and height. Both the male and female runners were self-selected teams of friends living in the city of Rosario, who have been performing regular running in a group (average = 40–60 $km \cdot wk^{-1}$, separate groups for men and women) since school and for a minimum of 8 yr (Table 1). However, they have never competed in official running events. None of the participants had a history of fractures or diseases, smoking or drinking, or treatments affecting the skeleton, and none of the women had a history of menstrual disorders. Age, weight, and height of all the studied groups and the average distance run per week by the two trained groups are given in Table 1. No significant differences in any of the indicated parameters were found between runner and nonrunner men or women.

Informed consent was obtained from each individual before inclusion in the study. The study had been approved by the hospital's ethics committee (application number 83, Comité de Ética del Hospital Provincial del Centenario, Rosario, Argentina).

pQCT Measurements

Following the same procedure as stated in the previous study in physically inactive people (7), an XCT-2000 scanner (Stratec, Pforzheim, Germany) was used to scan the whole right tibia of each individual. According to the manufacturer, the expected radiation dose involved a total body equivalent dose of 0.9 μSv per scan, and the cumulative dose for the whole study therefore was in the order of 20 μSv. The x-ray beam generated by the XCT-2000 scanner has a thickness of 2.5 mm, and the pixel edge size was set to 0.5 mm. Cross-sectional images were obtained at regular intervals equivalent to 5% of the tibia's length. We have numbered the scans from S5 (5% site, next to the tibiotalar joint) to S95 (95% site, next to the knee joint). For technical reasons, the scan at S50 could not be obtained in any case. Thus, a total of 18 scans were obtained for the entire bone (Fig. 1). All analyses were done with the software provided with the XCT-2000 scanner in its version 5.50. In particular, the following parameters were applied for all

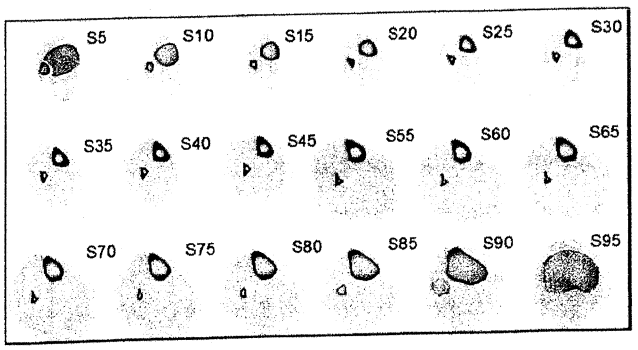

FIGURE 1—pQCT scans of the studied bone sites, taken at every 5% of the tibia length throughout the bone and numbered from S5 (close to the heel) to S95 (close to the knee). Technical details are given in the text.

sectional images: "contmode 2" (automatic, centripetal peeling of nonbone tissue to define the periosteal boundary of the bone, on the basis of a selected 398.5-mg·cm^{-3} limiting threshold value of x-ray attenuation by the tissue) and "cortmode 1" (automatic peeling of every voxel of the bone image showing an attenuation value below a selected 700.0-mg·cm^{-3} threshold to define the "cortical" bone area).

The following indicators were obtained from each scan, as far as allowed by the corresponding bone structure (15,31).

Bone "mass" indicators

- Mineral content of cortical bone (cortical BMC): amount of mineral present in the defined cortical bone area of the tibia cross section, in milligrams per millimeter of slice thickness.
- Mineral content of total bone (total BMC): total amount of mineral (cortical + trabecular) contained in the whole tibia cross section, in milligrams per millimeter of slice thickness.

Mineral content and volumetric density (vBMD) of trabecular bone were not specifically analyzed.

The tomographic discrimination between "cortical" and "trabecular" bone depends obviously on the selected attenuation thresholds (15). It must be considered at this point that the separation of trabecular and cortical portions is inherently difficult with a resolution of only 0.5 mm. In consequence, trabecular BMC as determined by the standard thresholding or concentrical peeling procedures cannot be assessed accurately as required for the proposed analyses. Furthermore, the structural stiffness and strength of the trabecular network 1) increase proportionally to the cube and the square, respectively, of its apparent (archimedean) density (8), which is highly variable between sites; 2) depend largely on the trabecular connectivity and directionality (which cannot be determined by pQCT); and 3) cannot be analyzed separately in the combined cortical–trabecular structure (1). These limitations do not impede the application of trabecular bone measurements to comparative diagnostic purposes (12), but they preclude the application of any trabecular mass or density determination in the structural analysis approached in this study. For the purpose of this study, therefore, we decided to analyze the trabecular bone mass (trabecular BMC) only as a fraction within the total BMC determinations but not on its own.

Diaphyseal design indicators

- Total bone area: "overall" area delimited by the periosteal perimeter, including pores and the central medullar cavity.
- Cortical bone area: area of the defined cortical bone region of the tibial cross section, in square millimeters.
- Periosteal perimeter: external perimeter of the tibia cross section, assessed automatically as "Peri-C" as the circumference length, in millimeters, of the bone cross section, idealized as a "ring" model, just for technical and comparative (i.e., not descriptive) purposes.
- Endocortical perimeter: internal perimeter of the cortical area, assessed automatically as "Endo-C" following a similar procedure to that applied to calculate Peri-C, in millimeters.
- Cortical thickness: average thickness of the bone cortex assuming the same ring model as defined for Peri-C and Endo-C determinations, calculated as the difference between the (homogeneous) radiuses of the corresponding circumferences.
- Circularity: calculated as the ratio between the perimeter of the circularized area (Peri-C) and the actual perimeter of the total bone area.
- Cross-sectional moment of inertia (CSMI, also callod second moment of inertia) of the cortical bone: integrated sums of products of the area of every pixel in the defined cortical image by their squared perpendicular distance to the neutral bone axes passing through the center of mass of the bone image, namely, the longitudinal axis (polar or torsion CSMI (pCSMI)), the lateral–medial axis (anterior–posterior bending CSMI (xCSMI)), and the anterior–posterior axis (lateral bending CSMI (yCSMI)), in millimeters raised to the fourth power. These measures capture the architectural efficiency of the cross-sectional design of the cortical shell to resist torsion and bending in the frontal and sagittal planes, respectively (28). Analysis of CSMI data was restricted to the diaphyseal parts where cortical bone structures dominate (from S15 to S85) because their thinness and degree of porosity in the other regions would lead to measurement errors as well as to erroneous interpretations, given the directional adaptation of the trabecular networks to support compressive forces restrained upon the joints. To test the differences between runner and nonrunner women in more depth, some of the CSMI data were processed following two different procedures:
  a. the xCSMI values were recalculated after rotating the axis system on the image until achieving a maximal (y) value, as the perpendicular axis to (y) passing through the center of gravity ($xCSMI_{max}$). This procedure reduced substantially the xCSMI variance resulting from the unavoidable differences in leg positioning during the measurements.
  b. All the yCSMI, pCSMI, and $xCSMI_{max}$ values were expressed as the percentage of the value obtained at S40 in every individual (%CSMIs). This procedure reduced very much every size-related intergroup difference in all the CSMIs.
- Buckling ratio: this variable was computed as the ratio between the bone's cortical thickness and periosteal diameter as defined above. It indicates a high risk of diaphyseal buckling; this may be a possibility when the cortex is rather thin.

Bone material "quality" indicator

- Cortical vBMD = cortical BMC/cortical area, in milligrams per cubic millimeter: it expresses the amount of mineral per unit of cortical bone volume including the pores (apparent volumetric density) and is known to vary linearly with the intrinsic stiffness (elastic modulus) of cortical bone tissue (10). This indicator was mathematically adjusted for the "partial volume effect" according to Rittweger et al. (32), assuming that the bone mass "dispersed" by the partial volume effect is "conserved" in the surrounding tissue and that the size of the dispersion zone is a function of the bone circumference and pixel size. A mathematical formalism then achieves the necessary adjustment. This correction allowed determination of cortical vBMD data in every image with a cortical thickness larger than twice the pixel edge length (in practical terms, from S10 to S90).

Statistical Analyses

Eighteen serial values of every variable studied per each individual studied were available for analysis. Statistical analyses were performed with the factorial ANOVA program included in the STATISTICA (StatSoft, Tulsa, OK) software. The dependent variable was always the value of the assessed indicator, and the independent variables or "factors" were a variable factor, the "bone site," and a fixed factor, the "runner/nonrunner" condition. This approach assesses whether the site-related differences between runners and nonrunners within each sex were consistent for bone sites.

RESULTS

Figures 2–5 show the data of all bone indicators studied along the tibiae for the four groups, within the regions at which they could be determined according to the technical specifications described in the "Materials and Methods" section. The statistical significance of every intergroup difference described below, as determined by the factorial ANOVA tests within every range of values defined in the graphs, is indicated in the corresponding figures. A description of the group differences found for each type of bone property evaluated by the indicators studied follows.

Bone Mass Indicators

Total BMC. In men, the total BMC was greater in the runners than in the physically inactive people along the whole diaphysis (S20–S90, significantly between S25 and S75). Of note, these differences tended to be more pronounced in the distal than in the proximal part of the tibia. In females, there were no significant differences between runners and nonrunners throughout the tibia (Fig. 2A).

Cortical BMC. In the men, the cortical BMC values were greater in the runners than in the physically inactive group in the distal half of the tibia only (from S10 to S45). From S65 onward, the curves for runners and nonrunners tended to be very similar. Again, there were no significant differences detected between the female groups (Fig. 2B).

Bone Design Indicators

Periosteal perimeter. In men, runners had greater periosteal perimeter values than nonrunners from S55 to S75. No significant differences were found between the female groups (Fig. 3A).

Endocortical perimeter. In males, the endocortical perimeter was found to be greater in the runners than in the nonrunners in the proximal bone (between S45 and S75), whereas it was lower in runners than in nonrunners in the distal bone (between S20 and S40). No significant differences were detected between the female groups (Fig. 3B).

Cortical thickness. Cortical thickness likewise showed a reciprocal pattern of group differences along the tibia in males, with greater values in runner than nonrunner men in the distal region (significant between S10 and S40) but lower values in runner than nonrunner individuals in the

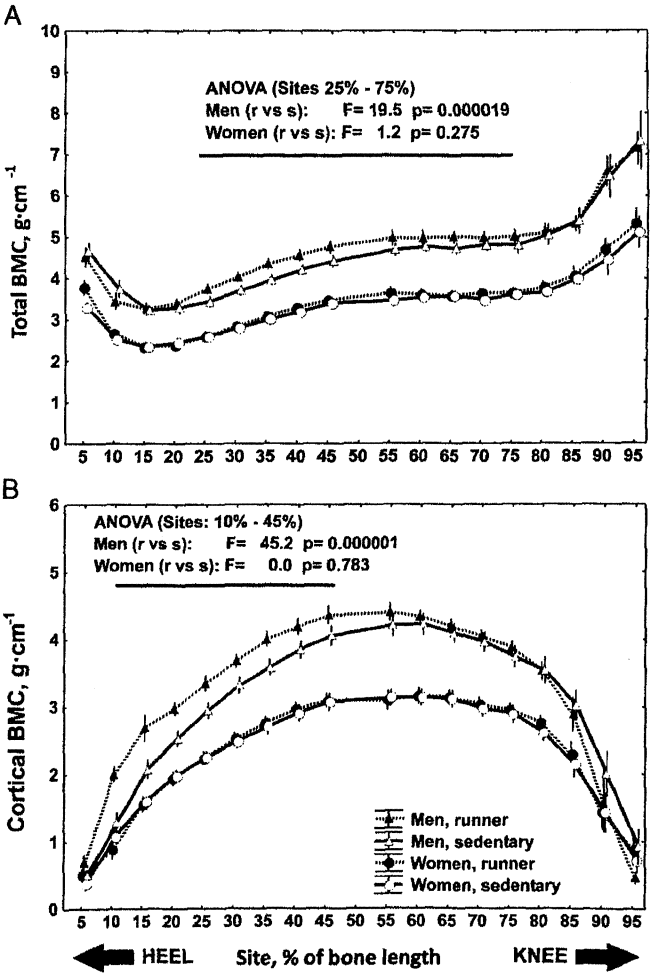

FIGURE 2—Means and SDs of the bone mass indicators, total (A) and cortical (B) BMC of all the bone sites studied. The *horizontal bars* indicate the sequences of bone sites along which the factorial ANOVA tests showed a statistical significance of differences between runners and nonrunners within each sex.

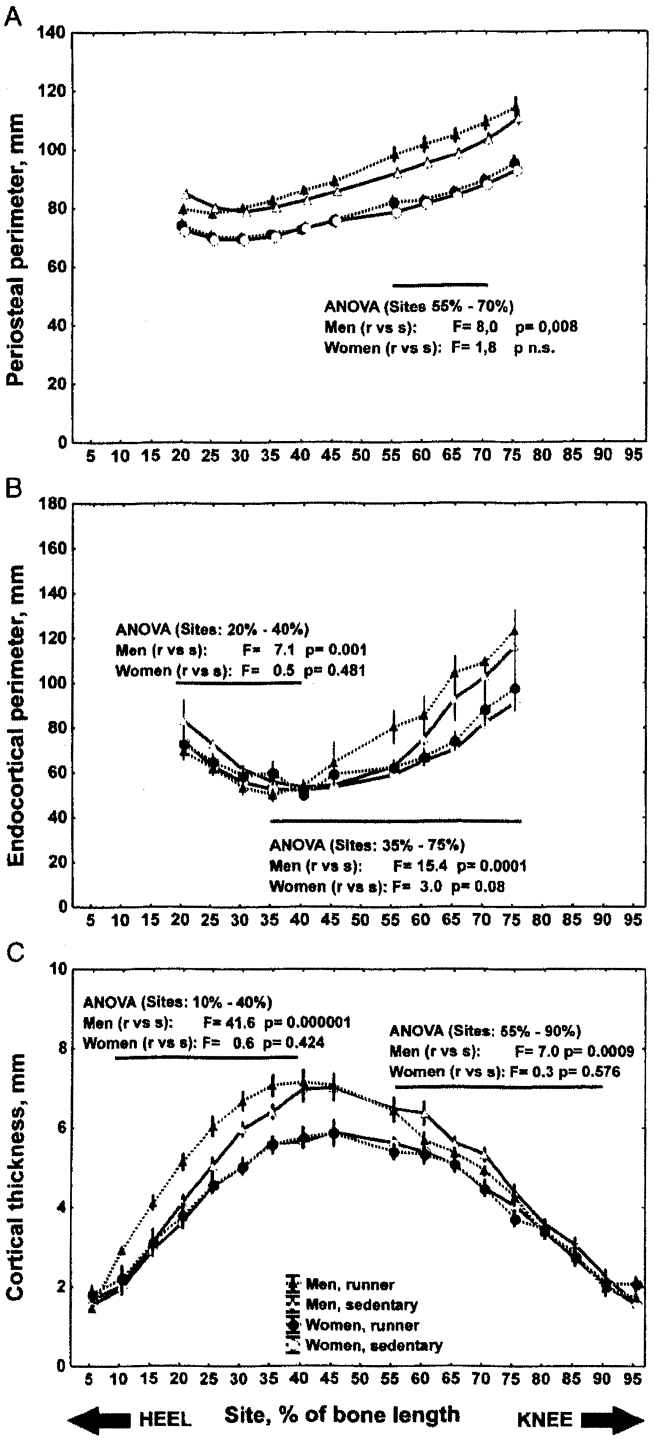

FIGURE 3—Means and SDs of the bone design indicators, periosteal (A) and endocortical (B) perimeters of the tibia sections from S20 to S75 and of the cortical thickness (C) from S5 to S95. The *horizontal bars* indicate the sequences of bone sites along which the factorial ANOVA tests showed a statistical significance of differences between runner and sedentary individuals within each sex as referred to in the text.

proximal part (significant between S60 and S90). No significant differences were detected between the female groups (Fig. 3C).

Cross-sectional circularity. No group differences were found in cross-sectional bone circularity, either between the men's groups or between the women's groups (always $P > 0.05$) (no illustration).

CSMIs. CSMIs were greater in runner than in nonrunner men from S35 upward. In the women, the differences

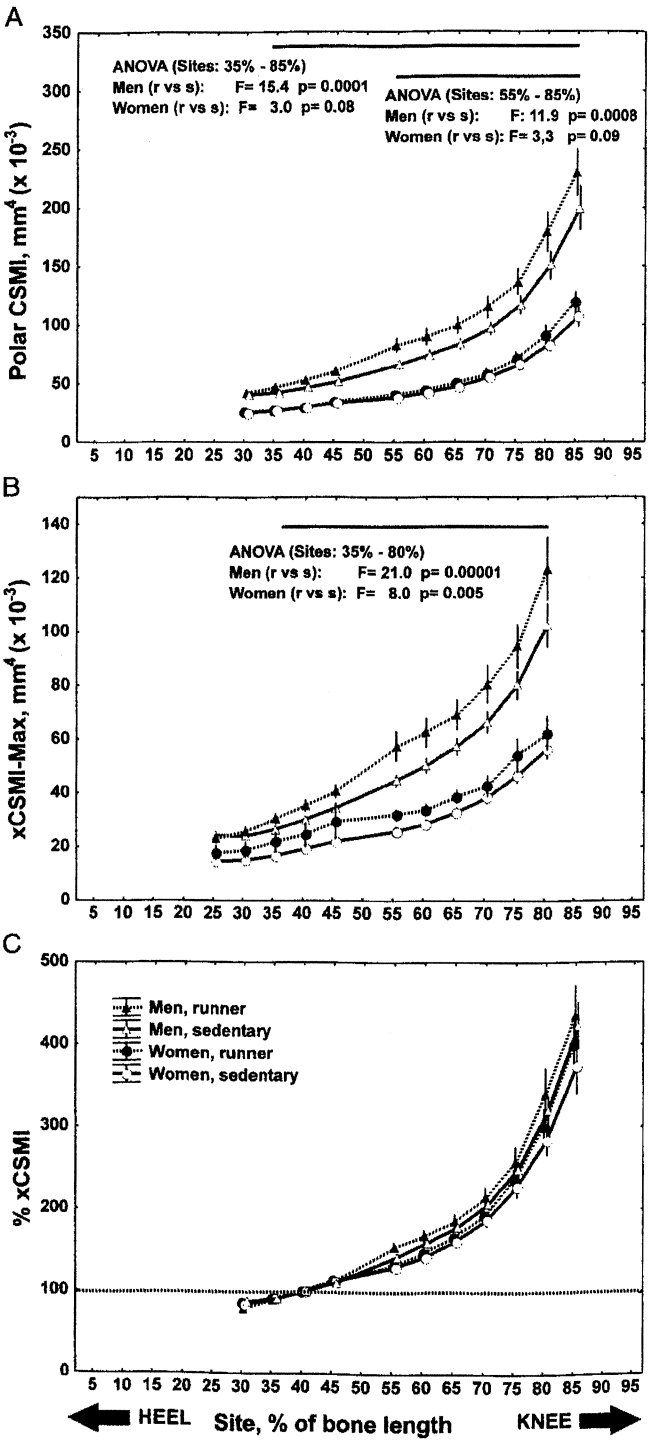

FIGURE 4—Means and SDs of the bone design indicators, polar CSMI (A), $xCSMI_{max}$ (B), and %pCSMI of the tibia sections (C) at the indicated bone sites. The *horizontal bars* indicate the sequences of bone sites along which the factorial ANOVA tests showed a statistical significance of differences between runner and sedentary individuals within each sex. No significant differences in %pCSMI were found between groups throughout the bones as referred to in the text.

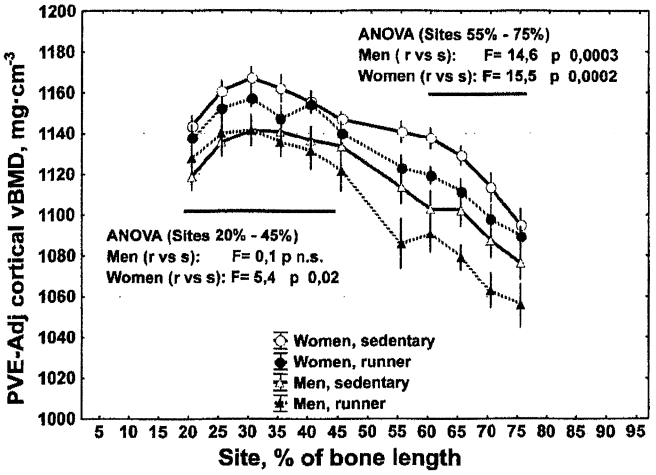

FIGURE 5—Means and SDs of the bone material "quality" indicator (17), partial volume effect-adjusted cortical vBMD from S20 to S75. The *horizontal bars* indicate the sequences of bone sites along which the factorial ANOVA tests showed a statistical significance of differences between runner and sedentary individuals within each sex as referred to in the text.

between runners and nonrunners were generally in the same direction as in men, with some trend to reach statistical significance. This was similar across xCSMI, yCSMI, and pCSMI. The latter is shown in Figure 4A. The $xCSMI_{max}$ values (Fig. 4B) behaved similarly as those of the xCSMI, but the differences in $xCSMI_{max}$ between runners and nonrunners were significant from S35 upward for both men and women. Importantly, all the %CSMIs showed virtually identical values in all groups between S30 and S45. The %pCSMI values throughout the bones in all groups are shown in Figure 4C.

Buckling ratio. There were no significant group differences found in this study (always $P > 0.05$) (no illustration).

Bone Material "Quality" (Intrinsic Stiffness) Indicator

Partial volume effect–adjusted vBMD of cortical bone. This variable (regarded as an indirect indicator of the intrinsic stiffness or elastic modulus of the mineralized tissue) (10) was the only variable in this study that was found to be significantly higher in women than in men. Also in contrast to the other indicators studied, the cortical vBMD was consistently lower in runners as compared with nonrunners, regardless of the sex or the region of the tibia (Fig. 5).

DISCUSSION

This study has yielded two main results, both of which are in some contrast to our initial expectations. First, the exercise-induced changes observed in all the different bone (mass, design, quality, strength) indicators were not reflected by general homogeneous effects throughout the bones but rather as site- or region-specific effects, with special characteristics for every indicator studied. Where group differences existed, they were specific to certain variables and regions of the tibia. These results are of some importance for how we regard the long-term effects of exercise upon bone. Second and even more importantly, there were few or no group differences found between the female groups, whereas some very pronounced differences existed between male runners and nonrunners, despite their similar anthropometric traits. This adds some new data to an ongoing debate on how (running) exercise may affect bone in women.

Specificity versus generality of differences. For the sake of clarity, we are initially focusing on the effects observed in the male groups in this section. As already stated, a striking feature of this study is that runners did seem to have stronger bones but that this effect was limited to specific areas and that the region specificity varied between variables. Cortical bone mass, for example, seemed to be elevated in runners only in the distal part of the tibia (Fig. 2B). This elevated bone mass is a result of a thicker cortex, which in turn seems to be an effect of a reduced endocortical perimeter in the runners, as previously observed by others in the distal humerus of the active arms in young postpubertal (female) tennis players (2,11,14). Mechanically, this implies an increased rigidity of the distal tibia in compression (11). It is interesting here to note that we had concluded from our previous study that the distal tibia would be mainly loaded in compression, rather than in bending or torsion, given that the distal part depicts minimal values of total mineral content, maximal circularity, and minimal CSMIs, particularly around S15 (7).

Another salient difference between runners and nonrunners relates to the enhanced CSMIs in the midshaft (Fig. 4). Technically, this difference is made up by a progressive increase in both periosteal and endocortical perimeters, rather than by an endocortical contraction. Others have reported significant increases in cortical bone mass, periosteal apposition, cortical thickness, and CSMIs in male and female tennis players (2,19,24). In our study, the changes in diaphyseal perimeters were notably associated with a progressive thinning of the cortex. However, the present data suggest that these changes did not induce an undue risk to buckle, and it therefore transpires that the CSMI group difference helps mainly to enhance the bending and/or torsional stiffness of the tibia midshaft in runners. Again, this is in line with the interpretation of our previous study to regard the tibia's midshaft as being more profoundly exposed to bending and/or torsional stresses (7). More proximally, the CSMIs' values increased in an even more pronounced fashion. However, this would reflect just a side effect of the necessary enlargement of the whole bone CSA (i.e., enlarged periosteal perimeters) and the total BMC (including a large proportion of trabecular bone) to cope with the biaxial compression stress pattern to be stood toward the knee, rather than to deal with larger bending or torsion loads. We are unable to discriminate between these two combined effects as per the indicators determined in this study.

Taking the two findings together (greater cortical bone mass in the distal part only, plus greater CSMI values in the midshaft) demonstrates that the tibia's enhanced mechanical competence in our runners is specific to location as well as to function. It is prudent to say that group differences were quite inconspicuous toward the proximal end of the bone, except perhaps for the finding that runners tended to have larger outer bone diameters than nonrunners, i.e., greater knee joint circumference. Considering also this third essential nonfinding, we feel that explaining the observed differences between the runner and nonrunner groups on pure genetic (or epigenetic) grounds, i.e., via the *anlagen*, is futile. As a much more parsimonious mode of explanation, we propose to interpret the observed differences as an adaptation of the tibia to bone strains that emerge from contractions of the plantar flexor muscles and in particular of the soleus muscle. This muscle originates from the dorsal aspect of the tibia's midshaft. It therefore causes both bending and torsional moments within the tibia because the muscle's line of action is, albeit aligned with the tibia's main axis, shifted from it by several centimeters. These bending and torsional moments must be expected to become less important as we move along the tibia toward its distal end, where indeed it was only compressive (thus directly relating to ground reaction forces) but not torsional or bending rigidity that was enhanced in runners.

Sex-related differences. The most important finding of this study is the virtual absence of any strong difference between the female groups in the presence of the eminent intergroup differences discussed in the previous section. As the only positive exercise effect in the tibiae, our female runners showed mildly but significantly larger tibial xCSMIs than their untrained controls. Other authors have reported some positive effects of racquet sports playing on bone size and strength in the humeral shaft of young female tennis players because of a periosteal enlargement of the bone cortex, more evident in the young starters (24). It was also shown that the combined independent influence of muscle performance and joint moments induced by different disciplines can improve the long bones' structure in female athletes, depending on the impact loading modality (29).

We are emphasizing here that the training characteristics and the amount of physical activity per week were comparable between male and female runners (Table 1). We would therefore argue that the observed nondifferences in bone mass and design indicators between the women's groups are an expression of a mitigated adaptation of bone modeling to running exercise in the female runners. Both mechanical and nonmechanical factors could explain the observed relative lack of response to mechanical stimulation in our female runners (34), as discussed below.

Concerning the mechanical factors, the significant differences in body weight between men and women in this study could be primarily regarded as a significant factor. However, the mechanostat theory (17) proposes that the structure of every bone is biomechanically adapted to the stresses determined by habitual usage, including those derived from weight bearing as well as from the contractions of the regional muscles, including those derived from walking, running, etc., in all vertebrates. This adaptation has been reflected in the linear correlations observed in many studies between bone mass and muscle mass or strength, which showed always similar slopes in men and women (6,9,16). Thus, regardless of the sex, a lesser body weight (or muscle mass) of any individual could determine a proportionally lower loading pattern of his or her weight-bearing bones, but there is no reason to propose that a low body weight (or muscle mass) by itself should also determine a lower relationship between loads and stresses, between stresses and strains, or between strains and adaptive modeling drifts in his/her bones. Therefore, the sex-related differences in body weight in this study could well explain the large differences observed in all the allometrically associated bone indicators determined in males and females, but they could hardly account for the striking differences in the skeletal responses to the mechanical environment in the studied men and women. In fact, many specifically designed studies of weight-bearing (tibiae) and nonbearing bones (radii, humeri) in individuals of a wide range of ages, trained or untrained in different disciplines (2,3,11,13,14,19,24,26), suggest that the bone structural adaptation to exercise can be shown beyond any influence of the bearing condition of the bones. Other factors, such as differences in gait patterns or in the dynamic loads during running (not specifically investigated in this study) may have played some role, however (29).

Concerning the nonmechanical factors, the hormonal environment is known to be a strong, relevant factor to the manifestation of sex-related differences in both bone geometry and exercise effects on bones (17,35). Many pQCT studies in trained or untrained individuals (2,3,11,14,19,24) suggest that the known inhibitory effect of estrogens on bone periosteal apposition (5,12,33,34) can interfere with bone adaptation to exercise. In young individuals, it was generally observed that the distal regions of long bones (tibiae, humeri) respond to exercise with a periosteal expansion in boys and with an endocortical contraction in girls, whereas the mid-diaphyseal regions of the same bones use to develop only a periosteal expansion, more evidently in boys than in girls. In the present study, in partial contrast with those observations, we have found an indication for endocortical contraction of the distal region and also a periosteal expansion of the midproximal region of the tibiae, but these two effects were restricted to only the male runners, yet a mild increase in the CSMIs at the mid-diaphyses (will require different line break) was also observed in our female runners. Whereas some authors argue that the very nature of estrogenic responses critically depend on the presence of specific estrogen receptors (25), other studies suggest that bones become nonresponsive to running exercise in female rats once they become fertile (22,23). A more recent study on adult rats suggests that estradiol protects trabecular bone against ovariectomy via the estrogen α-receptor, whereas

running seems to affect bone in these ovariectomized animals via the β-receptor (21).

There is probably more evidence to suggest some estrogen effect in our data, namely, the bone material quality indicator, cortical vBMD, which was the only indicator that yielded smaller values in men than women in this study. We and others have reported this observation repeatedly (3,5,26,30,34,35), and it is in consonance with the known ability of estrogens to inhibit intracortical (haversian) remodeling (27). The consistent reduction in cortical vBMD that was observed in both male and female runners in this study is likely to reflect an increase in haversian remodeling and thus in intracortical microporosity in response to the generation of microdamage through the vigorous mechanical usage of the runners' legs (4,18). Perhaps the estrogen-induced protection against intracortical remodeling has been the chief determinant of the striking finding that women have a significantly higher whole-body bone mass per unit of lean mass than men, as reported by us in several large dual energy x-ray absorptiometry studies (6,9,16). As long as the cortical vBMD is related to the stiffness of the cortical tissue (10), it can be further proposed that in fertile women, bones could manifest lesser levels of strain than in men under the action of similar loads, thus lessening the cortical-thickening modeling response to the usage-derived stress (17) as an additional mechanical factor to the estrogen-induced inhibition of periosteal growth.

CONCLUSIONS

The present study extends our previous observations in the tibiae of physically inactive men and women (7) to people who follow a more athletic lifestyle. Results in the habitual runners studied here are compatible with the view that both tibia bone mass and design are affected by long-distance running. However, this effect does not express itself in a general "scaling" factor, by which runners' bones would just uniformly be stronger by a given amount. Rather, we observed three different effect traits, which seem to be in good agreement with how the tibia is loaded as a mechanical structure:

1. In the distal third of the tibia, running was associated with enhanced total and cortical mass and cortical thickness (i.e., improved resistance to compression) but not with any effect upon bone diameters, cross-sectional circularity, or CSMI values.
2. In the tibia's midshaft, running was associated with improvements in all the CSMIs (i.e., improved resistance to bending/torsion), an effect which was evident even in the women group, whereas bone mass and other measures related to compression were unaffected.
3. In the proximal third, running was associated with exaggerated cortical thinning but with enhanced bone diameters and total (mostly trabecular) bone mass, thus allowing for a wider area of support for the articular cartilage. These changes should have contributed to maintain the customary pattern of compressive stress (force expressed by units of joint area) on the joint surface in the runners, despite of the increased loading of the legs during running.

In addition, we have identified the following consequences from the study:

a. The decrease in cortical vBMD induced by running in both men and women should correspond to an increase in intracortical porosity derived from the stimulated haversian remodeling of bone affected by exercise-induced microdamage. This effect should have increased the density of stress raisers within the bone tissue; thus, it may have impaired its intrinsic toughness. Certainly, both microdamage repair and the improvements in bone mass and design induced by running could counteract that negative effect within some extent (18). Nevertheless, in the absence of a method to assess bone microdamage directly and evaluate its repercussion on the integrity of bone structure, the evaluation of the combined effect of these opposite biomechanical effects on the whole-bone strength is beyond the scope of this study.
b. Most importantly, the observed sex-related incongruences (i.e., the virtual lack of exercise effects in the female runners, with the exception of a small effect on the CSMIs) strongly suggest that exercise-induced effects upon bone can be overrun by other factors. Beyond the natural influence of body weight bearing on the leg bones' structure, the collected evidence suggests that an obvious candidate mechanism could have been the endocrine environment within which the skeleton finds itself. On the other hand, there could be sex-related differences in the mechanical interfaces to the bone, e.g., in the tendons or joint cartilage. In any case, the present finding seems to be highly important. First, it supports the notion that the mechanostat function is embedded within the organismic physiological context of our body. Second, it is of obvious relevance to the prescription of physical interventions to enhance bone health, as the chances of success for such strategies may be smaller than expected in women during their reproductive phase of life.

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