

# Stress Fracture in Military Recruits: Gender Differences in Muscle and Bone Susceptibility Factors

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A total of 693 female U.S. Marine Corps recruits were studied with anthropometry and dual-energy X-ray absorptiometry (DXA) scans of the midthigh and distal third of the lower leg prior to a 12 week physical training program. In this group, 37 incident stress fracture cases were radiologically confirmed. Female data were compared with male data from an earlier study of 626 Marine recruits extended with additional cases for a total of 38 stress fracture cases. Using DXA data, bone structural geometry and cortical dimensions were derived at scan locations and muscle cross-sectional area was computed at the midthigh. Measurements were compared within gender between pooled fracture cases and controls after excluding subjects diagnosed with shin splints. In both genders, fracture cases were less physically fit, and had smaller thigh muscles compared with controls. After correction for height and weight, section moduli ( $Z$ ) and bone strength indices ( $Z/\text{bone length}$ ) of the femur and tibia were significantly smaller in fracture cases of both genders, but patterns differed. Female cases had thinner cortices and lower areal bone mineral density (BMD), whereas male cases had externally narrower bones but similar cortical thicknesses and areal BMDs compared with controls. In both genders, differences in fitness, muscle, and bone parameters suggest poor skeletal adaptation in fracture cases due to inadequate physical conditioning prior to training. To determine whether bone and muscle strength parameters differed between genders, all data were pooled and adjusted for height and weight. In both the tibia and femur, men had significantly larger section moduli and bone strength indices than women, although women had higher tibia but lower femur areal BMDs. Female bones, on average, were narrower and had thinner cortices (not significant in the femur,  $p = 0.07$ ). Unlike the bone geometry differences, thigh muscle cross-sectional areas were virtually identical to those of the men, suggesting that the muscles of the women were not relatively weaker. (Bone 27:437–444; 2000) © 2000 by Elsevier Science Inc. All rights reserved.

**Key Words:** Bone mass; Bone geometry; Bone strength; Muscle strength; Muscle size; Stress fracture susceptibility; Dual-energy X-ray absorptiometry (DXA); Gender differences in bone strength.

## Introduction

Stress fractures are a relatively uncommon but costly problem for military recruits and elite runners and dancers. Despite the infrequency of stress fractures, studies of the phenomenon under the controlled conditions of military training are scientifically attractive because they can provide insight into how bone strength differs among otherwise healthy young individuals.

Mechanistically, stress fracture is a form of fatigue damage resulting from repetitive skeletal loading<sup>6</sup> and usually occurs in the weight-bearing lower extremities or pelvic girdle.<sup>15</sup> Strenuous activities associated with stress fracture cause torsional and bending stresses concentrated in the cortex.<sup>13</sup> These stresses are generally highest on the subperiosteal surface, that is, the sites of stress fracture. In elite military training programs, exercise conditions can be considered to be reasonably uniform yet consistently a small fraction of trainees suffer stress fractures, and presumably these individuals have biomechanical differences that heighten their susceptibility. Because stress fractures are also more common in females<sup>7,14</sup> this would suggest that there may be gender differences in those susceptibility factors.

From a mechanical perspective, strength of a bone may differ in either the material properties that govern its ability to withstand loading stress, or in the structural geometry that determines the magnitudes of those stresses within it. There is little reason to suspect that reduced bone strength might be due to deficient bone material properties in young healthy adults; however, it has been shown that stress fracture cases have bone geometries that should lead to higher bending and torsional stresses. Studies on Israeli Army Recruits used radiographic methods to show that fracture cases had narrower tibiae,<sup>12</sup> and smaller tibial mediolateral cross-sectional moments of inertia.<sup>18</sup> In a previous study of male U.S. Marine Corps recruits using a dual-energy X-ray absorptiometry (DXA) method, we similarly found that stress fracture cases had lower mediolateral cross-sectional moments of inertia and section moduli in both the distal third of the tibia and the midshaft of the femur.<sup>3</sup> Fracture cases in our study of men were, on average, physically smaller in body weight and anthropometric dimensions; however, after bone shaft geometries were corrected for body size (weight), diaphyseal dimensions remained significantly smaller in fracture cases, although joint dimensions were not different.<sup>3</sup> Because diaphyses are more environmentally

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labile than articulations,<sup>20</sup> this suggested that stress fractures could result from poorer physical conditioning, and thus weaker diaphyses, prior to recruit training. It has been reported that stress fracture cases are relatively less physically fit.<sup>14</sup>

Because fitness also influences muscle strength, it is conceivable that there may also be a muscle factor in stress fracture susceptibility. Not only are skeletal loading forces mainly mediated through muscle contraction,<sup>4</sup> but certain muscle groups function to oppose bending and torsional stresses under load. Weaker muscles may possibly fatigue more easily thus degrading this protective function under repetitive loading.

To investigate these musculoskeletal strength issues we employed male and female data sets from prospective studies of U.S. Marine Corps recruits. The male data set has been reported previously<sup>3</sup> and is supplemented here with additional fracture cases. Here we compare the male data with those from a new prospective study of female Marine Corps recruits. Our main objectives were to investigate differences that might provide biomechanical explanations for why stress fracture susceptibility varies among different individuals and between genders. Due to the small incidence of stress fractures, there are practical constraints on the design of prospective studies. For example, our population samples are not large enough to generate enough cases to permit breakdown by fracture location or ethnicity. In the current study, we therefore looked for generalized, biomechanically relevant differences between pooled cases and controls within gender. We then looked at how these biomechanical factors varied between the genders to determine whether differences help to explain gender differences in stress fracture rates.

As in our previous study we employed DXA-based methods to measure bone mineral density (areal BMD) and bone structural properties at the midthigh and distal third of the lower leg. DXA measurements were extended to include estimates of cortical dimensions as well as thigh muscle mass. Consistent with the previous study, we employed a series of anthropometry measurements and supplemented them with physical fitness data taken from military records.

## Materials and Methods

### Subjects

The study design was prospective; the Marine Corps recruits were enrolled after appropriate institutional review board approval for human subject research. Female recruits were studied at the Parris Island recruit training facility in Beaufort, SC, between June 1995 and September 1996. Recruit volunteers were given a consent form during the first week of training and then administered a questionnaire on general background information (diet, exercise, menstrual and smoking histories, and previous skeletal injury) for the purposes of a larger separate study. A subset of these recruits was randomly selected for DXA scans and anthropometry. At the end of data accrual in September 1996 a total of 693 female recruits were enrolled for anthropometric measurements. Of these recruits, 671 received DXA scans. Enrollees ranged in age from 17 to 32 years, with an average age of 19 years.

The previously described male study group of 624 enrolled subjects<sup>3</sup> ranged in age from 17 to 28 years, with an average age of 19 years. To improve case statistics (stress fracture incidence is low), additional male fracture cases were added from a substudy conducted in June 1994 over the same time period and location as our previous work. In the substudy, a streamlined version of the project enrollment was followed where some anthropometry measures were excluded, and DXA scans were done only on the thigh. Because some prescreening criteria were

used in substudy enrollment, “normal” subjects were not necessarily representative and were not used here.

The female cohort was followed through the 12 weeks of training to ascertain the incidence of stress fractures and other musculoskeletal injuries, discovered by self-referral to sick call. Because self-referral resulted in a 40% underreporting of stress fractures in our male study,<sup>3</sup> a follow-up procedure was conducted at the end of training to determine whether the actual stress fracture rate differed from that self-reported to sick call. As in the male study, this procedure employed a questionnaire on symptoms of stress injury followed by a medical examination of those reporting symptoms. Fracture case definitions conformed to strict ICD-9-CM Expanded Orthopedic classifications and were confirmed by radiograph and/or nuclear bone scan using criteria described previously.<sup>3</sup>

### Anthropometric Measurements

Anthropometric measurements included height, weight, and girths of the neck, waist, hip (women only), thigh, and calf. Lengths were measured of the upper and lower right leg, and mediolateral widths were measured on the pelvis between the iliac crests, the hips between the greater trochanters (women), and the right knee at the level of the femoral condyles.

### Physical Fitness Data

Military records obtained on enrolled recruits included physical fitness scores based on numbers of repetitions of certain exercises and times recorded to run a specific distance, determined at the beginning and at regular intervals during training. It was our intent to use fitness scores recorded at the beginning of training; however, during study accrual, female distance-run requirements were increased from 0.75 to 1.5 miles, which made retrospective scores difficult to interpret. For women, we instead used run scores recorded after 2 weeks of training, which used a constant run distance. A comparable substitution could not be done in men because only initial run scores were recorded.

### Bone and Muscle Measurements

DXA scans were done with a conventional Norland XR26 scanner (Norland Medical Systems Inc., Fort Atkinson, WI) over narrow (5-mm-wide) “cross-sectional” regions across the mid-length of the right thigh and across the lower right leg at one third the length from its distal end.<sup>3</sup> Using programs described previously,<sup>3</sup> DXA data were used to derive areal BMD as well as mediolateral bone widths, cross-sectional areas (surface area of bone within cross-section), and section moduli of the femur and tibia at both scan locations. In addition, the “whole bone strength index,” after Selker and Carter,<sup>22</sup> was calculated as the ratio of section modulus to bone length. This index is based on the observation that strength of a bone under bending or torsion is inversely dependent on bone length and directly related to the section modulus. To make units more convenient, bone strength indices were multiplied by 100. As before,<sup>3</sup> section modulus was calculated as the ratio of cross-sectional moment of inertia to half of the mediolateral bone width. Estimates of mean cortical thickness were obtained as well, based on a simple model of the cross section as a circular annulus:

$$t_c = \frac{w}{2} - \sqrt{\left(\frac{w}{2}\right)^2 - \frac{A}{\pi}} \quad (1)$$

where  $w$  is the measured mediolateral bone width and  $A$  is the measured cross-sectional area. Note that this expression is mathematically equivalent to that used by Sievanen et al.<sup>23</sup>

In geometry measurements reported previously,<sup>3</sup> a coding error resulted in an overestimation of bone tissue density and a 39% underestimation of cross-sectional areas and section moduli. The current algorithm corrects effective tissue density to 1.05 g/cm<sup>3</sup>.<sup>16</sup> Although the error had no bearing on previous conclusions it has been corrected here.

The standard Norland software was used to measure relative lean mass—that is, the ratio of lean to total soft tissue mass within the thigh region-of-interest. The measurement was done only at the thigh, because the distal location of the lower leg region, away from major muscle (belly) groups, was frequently uninterpretable. Muscle strength can be quantified by physiological cross-sectional area<sup>1</sup>; this quantity is based on knowledge that strength of a muscle bundle is a function of the number and lengths of muscle fibers within the muscle organ. We estimated muscle cross-sectional area of the midthigh in the following manner. First, the total soft-tissue cross-sectional area was computed from the measured circumference and the total bone subperiosteal area computed from measured subperiosteal width was subtracted. The resulting soft tissue cross-sectional area was then multiplied by the relative lean mass fraction of the thigh scan region.

#### Statistical Analysis

Statistical analysis of results was done with STATVIEW for the Macintosh (version 5.0, SAS Institute, Inc., Cary, NC). Adjusted means of pooled data within gender were computed in STATVIEW using residuals from the multiple regression on height and weight, summed to the average value of the parameter. The same procedure was followed in the direct gender comparison using pooled data for both genders. Differences between fracture cases and controls and between genders were examined by unpaired, two-tailed Student's  $t$ -test with a 0.05 level of significance.

## Results

#### Fracture Incidence

A total of 37 women suffered stress fractures during the training period, corresponding to a fracture rate of 5.3%. Unlike the male study group, self-reporting of stress fracture was accurate in women, because no additional fractures were discovered at follow-up. Of the 37 female recruits with fractures, 11 fractured at two sites, and 1 recruit suffered four stress fractures. A total of 13 women had at least one stress fracture of the foot (tarsals or metatarsals), and 10 each had at least one stress fracture of the pelvic girdle, lower leg (tibia or fibula), or femur. Of the fractures in the pelvic girdle, one was in the sacrum, while the rest were localized to inferior or superior pubic rami. As previously noted, numbers of cases were too few to permit stratification by fracture location, hence cases were pooled and measured parameters were compared with those of nonfracture cases. In addition to stress fractures, a total of 37 recruits were diagnosed with shin splints or other skeletal stress reactions, 6 of which were later diagnosed with stress fracture. Consistent with the male study, subjects with shin splints were excluded from the control group.<sup>3</sup> Shin splints included overuse injuries, usually to the tibia, that did not meet all fracture criteria. This exclusion left a total of 626 female recruits diagnosed with neither stress fracture nor shin splints for comparison with 37 fracture cases.

The previously unreported male substudy yielded a total of 15 additional stress fracture cases, 4 of which were located in the

tibia, and 11 in the foot. Together with the 23 previously reported cases,<sup>3</sup> a total of 38 male recruits with stress fractures were available for comparison with the original 587 male controls after exclusion of 16 cases of shin splints. The distribution of the 38 male stress fractures was 41% in the foot, 40% in the lower leg, and 19% in the femur. Interestingly, above-the-knee fractures constituted nearly half (46%) of the observed cases in women, but only 19% in men, none of which was in the pelvis.

#### Fracture Cases Vs. Controls

**Anthropometric variables and physical fitness.** Means and standard deviations for age and anthropometric and fitness variables measured at baseline in cases and controls of both genders are listed in **Table 1**. As we found previously for male stress fracture cases,<sup>3</sup> women with stress fracture were, on average, smaller in height, weight, and most dimensional measurements; however, unlike their male counterparts, differences were slight and did not reach statistical significance.

After adding 15 more cases to the original male data, the same anthropometric variables that were significantly smaller in fracture cases in our earlier study remained significant. However, the differences in height, weight, body mass index [weight in kg/(height in m)<sup>2</sup>], and most girth dimensions were somewhat smaller than those reported previously.<sup>3</sup> Pelvic widths as an index of skeletal size were narrower in male cases than in controls, but not in females, whereas bicondylar breadth, a measure of joint size, was essentially identical in cases and controls of both genders.

Stress fracture cases of both genders were, on average, less physically fit; cases were able to do fewer sit-ups and run times were significantly slower.

**Bone geometry and mass variables.** As we showed previously,<sup>3</sup> areal BMD and bone structural properties are dependent on body size, hence these parameters were size corrected before comparison. In men we previously found that body weight was the best single descriptor of body size, with the highest correlations with skeletal geometry compared with other anthropometric measurements. The same finding was observed in females. Coefficients of determination from regressions of geometric dimensions and areal BMD on body weight explained from 8% to 51% of the measured variance in those variables; all correlations were significant at the  $p < 0.05$  level. Correlations with height were also independently significant, although weaker, in most of the parameters measured. For comparison purposes, mean bone and muscle measurements were adjusted for both height and weight.

After adjustment for body size, one male fracture case with a body mass index (BMI) in the 99th percentile (31.4 kg/m<sup>2</sup>) appeared to skew the size-adjusted tibia averages. This subject, who suffered one of the few male femoral stress fractures, had an adjusted tibia strength index that was 2.4 standard deviations above that of male controls. Consistent with his fracture location, however, his adjusted femoral strength index was lower, within 1 standard deviation of control values, although higher than the average of fracture cases. Because his adjusted tibia values appeared to be inconsistent with either fracture cases or controls, his tibia (only) measurements were excluded from adjusted means.

Height- and weight-adjusted means are compared between cases and controls in **Table 2**. Note that dimensions are reported in centimeters to facilitate comparison with literature values, and also that male cross-sectional measurements were linearly scaled to correct the calibration error in the original work (see *Materials and Methods*). Because the additional male cases were not scanned in the lower leg, the tibia values are as reported previously (after scaling correction and conversion to centimeters),<sup>3</sup>

**Table 1.** Means and standard deviations of age, anthropometric dimensions, and exercise scores in stress fracture cases and controls of both genders measured at the beginning of training

Parameter	Men						Women					
	Controls (N = 587)		Cases (N = 38)		Percent difference	Significance	Controls (N = 626)		Cases (N = 37)		Percent difference	Significance
	Mean	SD	Mean	SD			Mean	SD	Mean	SD		
Age (yr)	19.28	±1.81	18.90	±1.80	−2.0%	(0.19)	19.07	±1.98	19.65	±2.82	3.1%	(0.09)
Weight (kg)	75.39	±11.0	70.27	±14.5	−6.8%	0.007	57.95	±7.20	55.89	±8.62	−3.6%	(0.10)
Height (cm)	175.04	±6.64	172.8	±6.72	−1.3%	0.046	162.8	±6.55	161.2	±6.04	−1.0%	(0.15)
Body mass index (kg/m <sup>2</sup> )	24.58	±3.18	23.38	±3.81	−4.9%	0.027	21.83	±2.08	21.43	±2.52	−1.8%	(0.27)
Neck girth (cm)	38.59	±2.25	37.31	±2.33	−3.3%	0.0007	31.89	±1.54	31.72	±1.43	−0.5%	(0.53)
Waist girth (cm)	85.08	±8.61	82.63	±10.8	−2.9%	(0.10)	68.86	±5.16	67.76	±5.13	−1.6%	(0.21)
Hip girth (cm)	—	—	—	—	—	—	94.05	±5.45	92.63	±6.54	−1.5%	(0.13)
Pelvic width (cm)	28.46	±2.44	27.63	±3.14	−2.9%	(0.67)	27.94	±2.01	27.61	±2.05	−1.2%	(0.34)
Trochanter width (cm)	—	—	—	—	—	—	31.63	±1.90	31.39	±2.18	−0.8%	(0.46)
Femur bicondylar breadth (cm)	10.45	±0.77	10.39	±0.79	−0.6%	(0.62)	8.94	±0.51	8.89	±0.43	−0.6%	(0.60)
Thigh length (cm)	52.17	±3.02	52.67	±3.42	1.0%	(0.33)	50.92	±3.06	50.55	±3.40	−0.7%	(0.48)
Tibia length (cm)	40.76	±2.47	39.74	±2.31	−2.5%	0.014	37.11	±2.35	36.52	±2.39	−1.6%	(0.14)
Thigh girth (cm)	54.49	±4.55	52.24	±5.96	−4.1%	0.004	52.23	±3.99	51.80	±4.02	−0.8%	(0.58)
Calf girth (cm)	37.33	±2.72	35.10	±2.53	−6.0%	0.0002	34.52	±2.25	33.80	±2.77	−2.1%	(0.11)
Number of sit-ups	57.2	±13.3	51.8	±10.8	−9.5%	0.022	35.0	±6.45	32.7	±6.64	−6.6%	0.05
Run scores (secs)	1086	±111	1157	±123	6.6%	0.0004	1215	±110	1269	±90.0	4.4%	0.007

Values in parentheses not significant at the  $p = 0.05$  level (two tailed  $t$ -test).

but strength indices and cortical dimensions are added. Femur averages reflect the larger set of 38 male fracture cases.

Interestingly, size-adjusted male, but not female, fracture cases have wider pelvis and longer femora than controls (Table 2). Differences in tibia length and bicondylar breadths (not shown) were not significant in either gender after size correction.

Areal BMD differences in men were eliminated by size correction but this was not the case in women. This apparent anomaly becomes clearer with a closer look at adjusted cortical dimensions (Table 2). Only female cases showed thinner corti-

ces; male cases showed somewhat narrower subperiosteal diameters, but little difference in cortical thickness. Thus, the percentage of cortical bone within the subperiosteal envelope was smaller in female cases, but not in males cases, leading to significantly smaller areal BMD in female fracture cases. Bone strength, as depicted by section modulus or bone strength index, was smaller in fracture cases of both genders. The reduced section modulus in women was due to thinner cortices, but in men it was due to narrower subperiosteal diameters. Note that a relatively longer femur was a contributor to lower bone strength indices in male fracture cases, whereas, in the tibia and in both

**Table 2.** Means and standard deviations of tibia and femur geometries, pelvic and bicondylar widths, and muscle size after correction for height and weight (all measurements recorded at the beginning of training)

Parameter	Men						Women					
	Controls (N = 587)		Cases (N = 38)		Percent difference	Significance <sup>a</sup>	Controls (N = 626)		Cases (N = 37)		Percent difference	Significance <sup>a</sup>
	Mean	SD	Mean	SD			Mean	SD	Mean	SD		
Pelvic breadth	28.42	±2.09	29.23	±1.98	2.7%	0.026	27.92	±1.61	27.85	±1.62	−0.3%	(0.79)
Thigh length (cm)	52.2	±1.87	53.3	±2.223	2.0%	0.001	50.9	±2.17	51.0	±2.50	0.3%	(0.66)
Thigh muscle CSA (cm <sup>2</sup> )	204.3	±16.4	196.0	±16.2	−4.0%	0.003	168.9	±16.2	162.7	±11.9	−3.7%	0.047
Tibia BMD <sup>b</sup> (g/cm <sup>2</sup> )	1.526	±0.125	1.493	±0.096	−2.2%	(0.22)	1.440	±0.146	1.366	±0.127	−5.2%	0.0033
Subperiosteal diameter <sup>b</sup> (cm)	2.172	±0.150	2.098	±0.092	−3.4%	0.023	1.886	±0.141	1.860	±0.147	−1.4%	(0.29)
Mean cortical thickness <sup>b</sup> (cm)	0.353	±0.038	0.346	±0.028	−2.0%	(0.36)	0.342	±0.047	0.320	±0.038	−6.4%	0.0073
Section modulus <sup>b</sup> (cm <sup>3</sup> )	0.718	±0.111	0.662	±0.062	−7.8%	0.018	0.503	±0.089	0.466	±0.086	−7.3%	0.018
Bone strength index <sup>b</sup> (×100)	1.764	±0.267	1.643	±0.159	−6.9%	0.037	1.350	±0.229	1.261	±0.218	−6.5%	0.029
Femur BMD (g/cm <sup>2</sup> )	2.155	±0.161	2.137	±0.152	−0.8%	(0.51)	1.937	±0.144	1.852	±0.126	−4.4%	0.0007
Subperiosteal diameter (cm)	2.479	±0.158	2.419	±0.152	−2.4%	0.022	2.201	±0.130	2.159	±0.107	−1.9%	(0.062)
Mean cortical thickness (cm)	0.533	±0.059	0.532	±0.061	−0.2%	(0.97)	0.481	±0.052	0.454	±0.042	−5.7%	0.0033
Section modulus (cm <sup>3</sup> )	1.315	±0.178	1.245	±0.144	−5.3%	0.018	0.924	±0.125	0.860	±0.098	−7.3%	0.0019
Bone strength index (×100)	2.509	±0.337	2.334	±0.263	−6.9%	0.0018	1.815	±0.258	1.691	±0.222	−6.9%	0.0060

Abbreviations: BMD, bone mineral density; CSA, cross-sectional area.

<sup>a</sup>Values in parentheses not significant ( $p > 0.05$ , two-tailed  $t$ -test).

<sup>b</sup>Tibial statistics exclude one male femoral fracture case (see text).



**Table 3.** Body size-adjusted means and standard deviations of anthropometric dimensions, bone mineral density (BMD) and bone geometry compared between male and female Marine Corps recruits

Height- and weight-adjusted parameter	Men		Women		Percent difference	Significance <sup>a</sup>
	Mean	SD	Mean	SD		
Femur bicondylar breadth (cm)	9.945	±0.650	9.563	±0.406	-3.8%	<0.0001
Thigh girth (cm)	52.75	±2.14	54.31	±2.54	3.0%	<0.0001
Calf girth (cm)	35.94	±1.63	36.15	±1.63	0.6%	0.032
Pelvic breadth	27.67	±2.12	28.61	±1.70	3.4%	<0.0001
Tibia length (cm)	38.83	±1.45	38.73	±1.45	-0.3%	(0.23)
Thigh length (cm)	50.85	±1.99	52.18	±2.29	2.6%	<0.0001
Thigh muscle cross-sectional area (cm <sup>2</sup> )	188.4	±16.9	187.9	±15.7	-0.3%	(0.64)
Tibia BMD (g/cm <sup>2</sup> )	1.47	±0.124	1.49	±0.145	1.4%	0.036
Subperiosteal diameter (cm)	2.05	±0.15	1.99	±0.14	-2.9%	<0.0001
Mean cortical thickness (cm)	0.342	±0.038	0.350	±0.046	2.3%	0.0018
Section modulus (cm <sup>3</sup> )	0.618	±0.108	0.591	±0.088	-4.4%	<0.0001
Bone strength index (×100)	1.58	±0.267	1.51	±0.230	-4.4%	<0.0001
Femur BMD (g/cm <sup>2</sup> )	2.05	±0.162	2.03	±0.144	-1.0%	0.008
Subperiosteal diameter (cm)	2.35	±0.154	2.32	±0.126	-1.3%	0.0002
Mean cortical thickness (cm)	0.508	±0.060	0.502	±0.052	-1.2%	(0.067)
Section modulus (cm <sup>3</sup> )	1.13	±0.171	1.089	±0.125	-3.6%	<0.0001
Bone strength index (×100)	2.21	±0.340	2.082	±0.269	-5.8%	<0.0001

All measurements were recorded at the beginning of training. Also listed are the percent differences in the adjusted parameter expressed as the percent difference from male value for women.

<sup>a</sup>Significantly different by unpaired *t*-test (*p* < 0.05).

bones in women lower strength indices were due only to smaller section moduli.

As shown in Table 2, size-adjusted muscle cross-sectional areas were smaller in fracture cases in both genders. In summary, stress fracture cases appeared to have weaker lower limb bones and smaller thigh muscles than nonfractured controls and, consistent with previous reports,<sup>14</sup> they were also significantly less physically fit.

#### Gender Differences, Pooled Cases, and Controls

**Anthropometric variables.** To determine whether there were apparent musculoskeletal differences between the genders the data were pooled (fracture and shin splint cases + controls) for the men and women. Analyses of covariance indicated that there was no significant interaction between gender and height or weight (*p* > 0.05) for any anthropometric or musculoskeletal measurement. This suggested that the geometric properties could be reasonably adjusted for body size differences between the genders to determine whether there were remaining gender differences. The adjusted mean values of anthropometric dimensions, areal BMD, and bone geometry are listed in Table 3, together with the standard deviations and percent differences between the genders (relative to male values).

After adjusting for body size, women had narrower knee joints (bicondylar breadths) but wider pelves and longer femora than men in the pooled sample. These latter dimensions may be relevant in the higher female stress fracture rate, because male fracture cases had proportionately wider pelves and longer femora. Women had larger thigh circumferences but thigh muscle cross-sectional areas were comparable to men. Areal BMD differences were somewhat paradoxical, with higher values in the tibia and lower values in the femur among women. Geometry differences in both bones were more consistent with lower strength in women, because section moduli and strength indices were smaller, subperiosteal diameters were narrower, and corti-

ces were thinner among female recruits (not significant in the femur, *p* = 0.067).

#### Discussion

Studies of stress fracture among otherwise healthy young men and women military trainees are of scientific interest because they can provide insight into individual differences in bone strength within gender and also between genders. The strength in bending of a long bone shaft subject to bending and torsional stresses should be proportional to its section modulus and inversely related to its length. Indeed, the current study shows that, independent of body size, those who suffer stress fracture, in both genders, have smaller section moduli in the femur and tibia. Moreover, when section moduli are normalized to bone length in the strength indices, values remain 7% lower in cases of both men and women and in both bones when compared to controls. These observations are consistent with our earlier work on bone geometry<sup>3</sup> as well as those of Giladi and colleagues.<sup>11,12,18</sup> The results of this study support the hypothesis that stress fracture occurs because fracture cases experience relatively higher skeletal stresses than do those who do not fracture.

An important finding in the current study is that stress fracture cases not only had relatively smaller bone geometries but relatively smaller thigh muscles as well. There are two aspects to this observation:

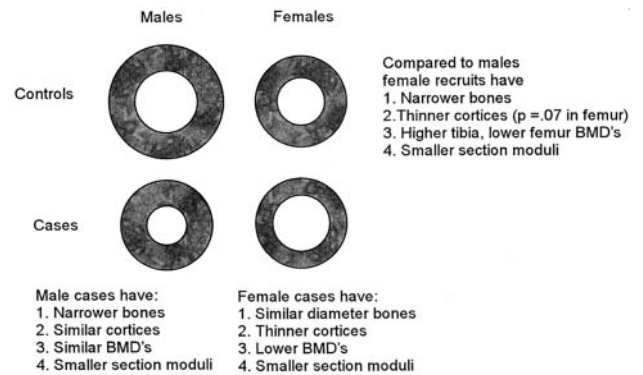
1. Measurements recorded in these studies were acquired at the beginning of training, and thus reflect the physical condition of the recruit upon arrival. Taken together with the poorer physical conditioning of fracture cases, this suggests that smaller bone geometries may be the result of inadequate conditioning of the bones and muscles prior to arrival at training.
2. The fact that muscles are smaller in fracture cases suggests

that weaker muscles may themselves contribute to bone fatigue damage under repetitive loading.

With regard to the first issue, the Marine Corps recruits in these cohorts had an average age of 19 in both genders. At this age, long bone joints have generally reached adult dimensions and can no longer adapt to environmental changes in skeletal loading. Indeed, knee joint widths are not different between cases and controls in these data. The shafts of long bones, however, retain the ability to adapt to changes in loading throughout adult life.<sup>20</sup> Generalized models of physical adaptation of long bones, as proposed by Beaupre et al.<sup>2</sup> and later refined by van der Meulen et al.,<sup>26</sup> assume that bones adapt to produce stress magnitudes corresponding to a specific normal range of strains, consistent with the “mechanostat” of Frost.<sup>9</sup> These generalized models are based on the view that the maximum strain that can be generated in a given bone is proportional to the strength of the muscles acting on that bone. Individuals vary in muscle strength, and if muscle forces are indeed the osteogenic stimulus for adaptation, those with weaker muscles should also have weaker bones. In the current study, thigh muscle cross-sectional area was positively correlated with both femur and tibia section moduli, explaining 41% and 27% of the variability ( $R^2$ ) in femur section modulus and 33% and 22% of variability in tibia section modulus for men and women, respectively. Smaller muscle cross-sectional areas in fracture cases would generate lower peak forces (osteogenic stimuli), consistent with their smaller bone geometries. Those beginning training with weaker muscles and smaller bone geometries would thus be more susceptible to bone failure during that training. This relationship was articulated by Frost as “In otherwise comparable people, a femur with less bone mass and strength than another usually became that way because weaker muscles put smaller forces on it, regardless of how often those forces were applied.”<sup>10</sup> Ultimately this issue should be settled with a longitudinal study comparing muscle and bone dimensions recorded prior to physical training to those recorded afterwards.

The second issue—that weaker muscles may contribute to fatigue damage under repetitive loading—is supported by recent work in humans by Milgrom and colleagues.<sup>17</sup> These investigators implanted rosette strain gauges on tibiae of five male and three female military recruits and then recorded strains and strain rates during free walking on a treadmill, before and after a muscle-fatiguing 2 km run.<sup>17</sup> In both genders, there was a significant increase in both strain rates and magnitudes following the 2 km run; moreover, the increase was greater in women than in men. Increased bone strains following muscle fatigue in a dog model was also shown experimentally by Yoshikawa et al.<sup>27</sup> Taken together with our findings of smaller muscles and poorer physical condition in fracture cases, this suggests that muscles serve a protective role in resisting those mechanical stresses leading to stress fracture. We conjecture that the protective mechanism works by contraction of muscles attached to the terminal ends of long bones during repetitive activities. Contractions should oppose bending and perhaps torsion as well, converting more harmful tensile and shear stresses to compression. Such an adaptation would be advantageous, because bone is intrinsically stronger in compression than in tension or shear.<sup>13</sup> Muscle fatigue would diminish this protective function, resulting in higher bone stresses, as observed by others.<sup>17,27</sup>

Finally, it should be realized that muscle adapts to changing load much faster than bone. Those with smaller bone section moduli may experience higher mechanical strains during training due to the mismatch between the rates of adaptation of muscle and bone. Progressively greater muscle forces in strengthening



**Figure 1.** Depiction of observed differences in bone geometry and areal BMD between cases and controls of each gender (vertical pairs), and between genders (horizontal). Differences are exaggerated for clarity.

muscles are likely to outstrip the ability of bone to adapt during the recruit training period.

#### *Gender Differences in Fracture Susceptibility and in Strength Indices*

The overall differences in bone geometry and areal BMD between cases and controls and between genders are summarized in **Figure 1**.

In both men and women, fracture cases had relatively smaller section moduli and thigh muscles. Female cases, however, had relatively thinner cortices, whereas male cases had relatively narrower subperiosteal diameters. This finding may be in part a function of gender differences in relative skeletal maturity. There is evidence that the subperiosteal surface of long bones is most sensitive to alterations in mechanical loading during childhood and early adolescence, but the endocortical surface is more sensitive thereafter.<sup>21,23,24</sup> A similar conclusion was made by Uthoff in a disuse dog model.<sup>25</sup> Cast-generated disuse in the forelimb of immature dogs retarded subperiosteal bone apposition, then restored it upon reloading. In adult dogs, bone loss was mainly on the endosteal surface, and restoration of loading resulted in contraction of the endosteal diameter. This difference may be related to more general developmental changes in bone modeling/remodeling that occur during adolescence but which occur earlier in women than in men.<sup>8</sup> While men and women in our study were the same absolute age (Table 1), the female skeleton would be, on average, relatively more developmentally advanced. Thus, if physical inactivity explains at least part of the smaller bone dimensions in our fracture subjects, then it is possible that this had a greater effect on the endocortical surface of the more developmentally mature women, and on the subperiosteal surface of the less mature men. This interpretation is consistent with our geometric results, in which female fracture cases had relatively thinner cortices (i.e., wider medullary cavities), but male fracture cases had relatively narrower subperiosteal diameters. These results also caution against the use of areal BMD alone in mechanical interpretations, because areal BMD is confounded by changes on subperiosteal and endocortical surfaces, and differences in areal BMD may or may not represent differences in structural strength.<sup>19,23</sup> Ideally, a longitudinal study should be conducted to examine the effects of intense physical activity on bone geometry in young male and female subjects selected for poor initial levels of physical conditioning.

Female recruits are more likely to suffer stress fractures<sup>7,14</sup> and those fractures are more likely to occur in the femur and

pelvis as compared with their male counterparts. This would suggest that women have relatively weaker bones overall and that skeletal weakness is more likely to extend to the femur and pelvic girdle in women. When we compared geometries between the genders after correction for body size we found that section moduli (Table 3) were 4% smaller, on average, in women. The gender difference in the femur increased to 6% after normalizing to the relatively longer femoral shafts of women, which is consistent with the greater likelihood of femoral fractures in women. Among men, those with a wider pelvis were more likely to suffer a stress fracture. A wider pelvis may incur a mechanical disadvantage, because, on average, women have wider pelves than men (Table 2), and only women suffer pelvic stress fractures. On the other hand, size-adjusted thigh muscle cross-sectional areas were not smaller in women than in men. These gender differences must be interpreted with some caution, because, in the U.S. Marine Corps, men and women do not train together and, although training conditions are extremely vigorous for both genders, they cannot be objectively compared as equivalent. Furthermore, it is possible that the higher stress fracture incidence among women may be due to relatively poorer initial physical conditioning rather than an intrinsic strength difference. We did not have a robust measure of physical conditioning that would permit a valid comparison between genders in the current study. The geometric differences in the pelvis and femur would, however, suggest that there may be a mechanical disadvantage to the wider pelvis and longer femora in women, as evidenced by their greater incidence of above-the-knee stress fractures.

There are a number of limitations of this work. First, like some other stress fracture studies,<sup>11,18</sup> bone geometries were measured in a single plane and are thus relevant mainly to frontal plane stresses. Dynamic loading of the lower limb is known to produce significant stresses in the sagittal plane as well.<sup>5</sup> Another limitation of this work is that, for technical reasons, skeletal measurements at the femur or lower leg were assumed to be broadly representative of bone strength at other lower extremity locations. Certainly there is heterogeneity in the geometry between lower extremity locations in the same individual, and fractures often occurred at sites that were not specifically measured. Moreover, our sample size of stress fracture cases was not large enough to permit separate analysis by fracture location, nor was it feasible to measure at all potential fracture locations. Conceivably a larger study, with more stress fracture cases could provide greater insight into bone strength differences between fracture sites, but the small incidence of stress fractures makes this an expensive prospect. Another limitation of our work is that we relied on military records for assessment of physical fitness levels; in retrospect, an objective assessment under controlled conditions would have provided better stratification of initial physical condition and would better elucidate gender differences in physical condition.

This study further illustrates that relevant structural information is present in bone mass data, although the implications of that information can be obscured by conventional areal BMD/BMC presentation where bone is regionally averaged. In fairness, current DXA scanners are better suited to measurement of areal BMD where dimensional errors are less problematic than they are to the measurement of geometry. The dimensional differences between cases and controls in this study were quite small; for example, the relatively large 15% average difference in uncorrected male femoral sectional modulus (Table 2) was attributable to only 1 mm in subperiosteal breadth. Other dimensional differences, such as cortical thicknesses, were even smaller. The coefficient of variation in bone widths with our measurement averaged about  $\pm 0.2$  mm.<sup>3</sup> It is therefore likely that the ability of current DXA technology to detect small

differences in bone geometry in *individuals* would be limited. Also, while DXA scanners can be used to determine lean muscle mass, our crude estimate of muscle cross-sectional areas could be improved with better technology, ad hoc software, scanning protocols, and suitable calibration. Direct comparisons with objectively measured muscle strength should also be done.

## Conclusions

In conclusion, evidence for an environmental component of stress fracture susceptibility is quite strong. In both genders, those who do not fracture have significantly larger bone cross-sectional geometries, indicative of stronger bones. Fracture cases of both genders have smaller thigh muscles and, consistent with other reports,<sup>14</sup> are less physically fit than noncases. Higher fitness levels and larger muscles in controls imply that bone geometric differences are an adaptation response to physical conditioning prior to the initiation of basic training.

Female stress fracture cases show thinner cortices than controls but similar subperiosteal diameters, whereas male cases show narrow subperiosteal diameters but similar cortical thicknesses compared with controls. This may indicate a gender difference in the bone response to physical training among young (19 years) adults, where women respond by building bone on the endocortical surface and men respond on the subperiosteal surface. When male and female data were pooled and adjusted for body size differences, areal BMD values were equivocal, approximately 1% higher in the tibia but 1% lower in the femur among women compared with men. Section moduli, however, were significantly smaller in women, indicating relatively lower bending strengths. Size-adjusted thigh muscle sizes were virtually identical between genders, suggesting that biomechanical differences may be more evident in bone than in muscle properties.

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