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Family History Predicts Stress Fracture in Active Female Adolescents

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Abstract

OBJECTIVE—Increased physical activity and menstrual irregularity have been associated with increased risk for stress fracture among adult women active in athletics. The purposes of this study were to determine whether menstrual irregularity is also a risk factor for stress fracture in active female adolescents and to estimate the quantity of exercise associated with an increased risk for this injury.

PATIENTS AND METHODS—A case-control study was conducted of 13- to 22-year-old females diagnosed with their first stress fracture, each matched prospectively on age and self-reported ethnicity with 2 controls. Patients with chronic illnesses or use of medications known to affect bone mineral density were excluded, including use of hormonal preparations that could alter menstrual cycles. The primary outcome, stress fracture in any extremity or the spine, was confirmed radiographically. Girls with stress fracture had bone mineral density measured at the lumbar spine by dual-energy x-ray absorptiometry.

RESULTS—The mean $\pm$ SD age of the 168 participants was 15.9 ± 2.1 years; 91.7% were postmenarcheal, with a mean age at menarche of 13.1 ± 1.1 years. The prevalence of menstrual irregularity was similar among cases and controls. There was no significant difference in the mean hours per week of total physical activity between girls in this sample with stress fracture (8.2 hours/week) and those without (7.4 hours/week). In multivariate models, case subjects had nearly 3 times the odds of having a family member with osteoporosis or osteopenia. In secondary analyses, participants with stress fracture had a low mean spinal bone mineral density for their age.

CONCLUSIONS—Among highly active female adolescents, only family history was independently associated with stress fracture. The magnitude of this association suggests that further investigations of inheritable skeletal factors are warranted in this population, along with evaluation of bone mineral density in girls with stress fracture.

Keywords

stress fracture; adolescent health; bone mineral density; bone strength; exercise

Stress fractures can be defined as skeletal defects that result from the repeated application of a stress lower than that required to fracture a bone in a single loading.^{1,2} We have recently reported a 2.7% estimated lifetime prevalence of this injury in female adolescents,³ which compares favorably with estimates ranging from 1.0% to 2.6% among general collegiate athletes.^{4,5} Although these overall rates seem low, certain subgroups, such as college freshmen⁶ and other young adult women participating in track and field⁷⁻¹¹ may have rates of stress fracture between 6.9%⁶ and 21.1%.¹¹

Stress fractures are particularly concerning in active female adolescents and young adults because they may signify insufficiency of the bones to withstand repetitive loading. Although a “fracture threshold” is not yet defined for children and adolescents, ~80% to 90% of in vitro skeletal strength in adults is determined by bone mineral density (BMD).¹² A woman’s peak bone mass is achieved by her early 20s^{13,14} and is one of the strongest predictors of her long-term risk of osteoporosis.^{15,16} Understanding the risk factors that predispose to stress fracture in this population could, therefore, indirectly elucidate the risk factors for a low BMD.

To our knowledge, no data exist regarding risk factors for stress fracture in adolescents younger than age 17 years. We, therefore, constructed a pathogenetic model of stress fracture on the basis of studies in the adult literature and the observations of experienced clinicians. The risk factors deemed most important in our model included BMI, dietary intake of calcium and vitamin D, and heredity and were identified, a priori, as covariates to be measured in the study.

Even before the American College of Sports Medicine coined the term “female athlete triad” in 1992 to describe the interrelatedness of disordered eating, amenorrhea, and osteoporosis in young female athletes,^{17,18} another area of significant interest in women’s skeletal health has been menstrual irregularity (MI).^{19,20} Studies have inconsistently shown MI to be a risk factor for stress fracture in active adult women,²¹⁻²⁶ but information on menstrual history was not available from the large epidemiologic cohort that we analyzed previously.³

Inadequate skeletal load-bearing capacity, as caused by the factors just mentioned, is not a sufficient condition for stress fracture. By definition, repetitive loading of a bone, as caused by physical activity, is necessary as well. Identification of a threshold quantity of activity at which the risk of stress fracture increases would be valuable for physicians, certified athletic trainers, coaches, and others guiding athletes in their training regimens. Our previous work demonstrated that the quantity of physical activity is significantly associated with history of self-reported stress fracture diagnosis, with each hour/week of high-impact exercise increasing the odds of stress fracture by 5%, but we could not identify a threshold amount of physical activity above which the risk of stress fracture would be deemed unsafe.³

Therefore, to fill the gaps in knowledge about the risk factors for stress fracture in active female adolescents, we designed a case-control study to estimate the associations between a diagnosis of stress fracture with amount of physical activity and MI. Important covariates also included dietary intake of calcium and vitamin D, BMI, and family history of skeletal impairment.

PATIENTS AND METHODS

Overview

Active females aged 13 to 22 years presenting to outpatient clinics conducted at a tertiary care academic children's hospital medical center were eligible for participation. Subjects were enrolled prospectively and matched 2 control subjects for each case of stress fracture. As a secondary, exploratory objective, all of the case subjects and any control subjects who met criteria for MI subsequently completed BMD testing via dual-energy x-ray absorptiometry (DXA). The Children's Hospital Boston Committee on Clinical Investigation approved this project, with an informed consent or assent process completed by each participant complemented by parent or guardian consent for those participants under 18 years of age.

Assembly of Participants

Potential case subjects (adolescents with their first stress fracture) were referred to study investigators by the clinicians evaluating them. Clinicians were asked to refer adolescents with other musculoskeletal complaints as potential control subjects. Patients were eligible only if they participated in exercise that caused impact loading (eg, gymnastics, figure skating, running, dance, team sports, and aerobics; not swimming) no fewer than 3 days/week for a combined total of ≥ 3 hours/week during the 6 months before stress fracture for case subjects or the 6 months before recruitment for control subjects.

Exclusion criteria included the following: any history of a stress fracture diagnosed > 3 months before date of recruitment; presence of a chronic disease (eg, inflammatory bowel disease, rheumatologic disease, cystic fibrosis, etc); solid organ or bone marrow transplant recipient; lifetime total use of glucocorticoids (including inhaled), anticonvulsants, or gonadotropin-releasing hormone analogs totaling ≥ 3 months; use of oral contraceptive pills or monthly injected estrogen/progestin during the 12 months before stress fracture for case subjects or the 12 months before recruitment for control subjects; any use of depo-medroxyprogesterone; or persistent unexplained pain in the pelvis, spine, or any extremity in the 3 months before recruitment (to exclude potentially undiagnosed stress fractures). Patients were asked if they had any history of an eating disorder diagnosed by a clinician but were not excluded on this basis.

Case subjects were defined as patients diagnosed with their first ever stress fracture within the 3 months before presentation. Control subjects were defined as patients presenting to the same clinic for other musculoskeletal complaints, matched for the same age in years and same self-reported race/ethnicity as the index case subjects (to control for these other sources of potential bias), no later than 4 weeks after the identified case subjects (to control for seasonal variability in vitamin D status).

Exposures and Their Measurements

Activity was defined as average hours/week of physical activity in the 12 months before stress fracture (case subjects) or enrollment (control subjects). Data were obtained by a validated self-administered survey for adolescents, the Modifiable Activity Questionnaire for Adolescents,²⁷ enhanced by a semistructured interview by study personnel, yielding weeks/month, days/week, and minutes/day of impact-loading activities for the 12 months before the end point. For analyses, participants were categorized as "highly active" if they participated in an average of > 10 hours/week of activity. In addition, average weekly activity was categorized as 0 to 3.9, 4 to 7.9, 8 to 11.9, 12 to 15.9, 16 to 19.9, 20 to 23.9, 24 to 27.9, and ≥ 28 hours/week.

For MI, data were obtained by subject self-report via a semistructured health history interview. Subjects meeting any of the following criteria were categorized as having MI: primary amenorrhea (absence of menses by 15 years of age), secondary amenorrhea (absence of menses for ≥ 6 months in postmenarchal girls), or oligomenorrhea (≤ 4 total menstrual periods in the year before stress fracture [case subjects] or enrollment [control subjects]).

Because there were only 10 participants who met the criteria for MI in the sample, a second, more expansive, definition of MI, based on recent studies in the literature,²⁸ was created for analyses. This definition considered secondary amenorrhea as the absence of menses for ≥ 3 months in postmenarchal girls and oligomenorrhea as ≤ 9 total menstrual periods in the year before stress fracture (case subjects) or enrollment (control subjects). For all of the covariates, “time of presentation” was similarly defined as the date of diagnosis of stress fracture for case subjects and date of enrollment for control subjects.

In addition, an exposure called “menstrual ratio,” based on a published “menstrual index,”⁹ was developed. It was calculated as the ratio of the number of menstrual periods reported by a participant in the previous 2 years to her potential number of menstrual periods, based on her age at presentation and reported age at menarche. This ratio was then multiplied by 12 to yield a range of 0 to 12, a more understandable number to quantify the average number of yearly menses.

Covariates and Their Measurements

Subject demographics, such as age, age at menarche, smoking history, and history of diagnosis with an eating disorder, were obtained by subject self-report via a semistructured health history interview. BMI was defined as weight over height (kilograms/meter squared) obtained by direct measurement of height and weight on the same calibrated stadiometer and scale by research staff.

Average daily dietary intake of calcium and vitamin D was evaluated using the Youth/Adolescent Questionnaire, a validated self-administered semiquantitative food frequency questionnaire assessing intake over the past year.²⁹ The questionnaire asks participants how often, on average, they consumed each of the 131 foods listed. Response categories for foods ranged from less than once per month to ≥ 4 times per day. Nutrient intake was computed by multiplying the frequency of consumption of the foods by nutrient content, estimated from standard food composition sources.

Family history was obtained by subject self-report via a semistructured health history interview. For each first-degree relative (mother, father, and siblings) and select second-degree relatives (maternal and paternal grand-parents), the participant was asked whether the family member had a history of stress fracture (possible responses included “yes,” “no,” or “don’t know”) and at what age it was diagnosed. She was similarly asked about the family members’ history of osteoporosis, then separately about their history of osteopenia. To account for the families’ potential lack of access to their relatives’ medical charts, participants were additionally asked about the individual relatives’ histories of frequent fractures or “brittle bones” (to identify potentially unmeasured, and therefore undiagnosed, low bone mass) without the specific date of diagnosis. Parents who accompanied the participants were allowed to assist their daughters in answering the family history questions. We created 3 classifications for family history on the basis of participant responses to these 4 questions. A positive response for osteopenia or osteoporosis diagnosed in a family member (siblings, parents, or grandparents) was categorized as a positive “measured family history,” because these conditions are often quantified radiographically. A positive response for stress fracture or other frequent fractures was considered a positive “family history of

fracture.” Positive responses to any of these 4 conditions were combined into a general “positive family history.”

Outcome and Its Measurement

A stress fracture must have been diagnosed by a bone scan, plain radiograph, computed tomography, or MRI documented in the medical chart within the 3 months before presentation. Additional information of the body part injured was therefore collected for all of the stress fractures.

Secondary Outcome and Its Measurement

Bone mineral content (in grams) and areal BMD (bone mineral content/projected area of the region scanned, in grams/centimeter squared) were measured using a Hologic 4500 Elite DXA scanner (Hologic Inc, Waltham, MA). Anterior-posterior measurements were obtained of the lumbar spine and total hip. Comparisons with databases were then used to generate standardized scores with respect to age and gender (z scores) for the lumbar spine. BMD was dichotomized by z score for the lumbar spine as >0 or <0 . Algorithms for BMD z scores at the hip had not been developed for all of the participants; therefore, this measure was not used in analyses. Precision is monitored daily in the local DXA center using standardized phantoms provided by the manufacturer (Hologic, Inc). Reviewing data from the study time period, the in vitro precision, measured as coefficient of variation percentage (mean $\pm$ SD), was $0.454\% \pm 0.004\%$.

Data Analysis

Data were entered and stored in a password-protected Microsoft Access database (Microsoft Corp, Redmond, WA) after a quality assurance check by the principal investigator (Dr Loud). All of the analyses were conducted by using Stata 8 statistical software (Stata Corp, College Station, TX). Because McNemar’s testing could not be performed for 2:1 matching, Mantel-Haenszel odds ratios (mhodds in Stata) were generated by considering each case subject and her 2 matched control subject to be a stratum of 3. Conditional logistic regression modeling (clogit in Stata) was used for multivariate analyses to account for the effects of matching case subject and control subject. All of the covariates were controlled for BMI before entry into the final multivariate model.

Because menstrual ratio was undefined for the 14 participants who were not yet 15 years of age or who had not yet achieved menses, a sensitivity analysis was performed. Neither defining their menstrual ratio as 12 nor setting it equal to 0 significantly changed any results, so it was left as missing for subsequent analyses. For all of the analyses, a 2-tailed $P < .05$ was considered significant.

RESULTS

The mean age of the 168 participants was 15.9 years. The vast majority (91.7%) had achieved menses, with mean age at menarche 13.1 years (Table 1). This sample was 98.2% white. Only 2 participants (1.5%) reported a history of a clinically diagnosed eating disorder, and only 9 (6.8%) had a history of smoking cigarettes; both frequencies were too small to allow for meaningful associations with stress fracture.

The mean BMI of the cohort was 21.5 kg/m^2 , corresponding with a z score of 0.32 for the mean age of 15 years, 11 months. As subjects were matched on age and ethnicity, BMI z scores were not calculated for individual participants; 0.32 does not, therefore, represent the mean BMI z score for the sample. Nonetheless, case subjects had a significantly higher BMI than control subjects (22.3 vs 21.1 kg/m^2 ; $P = .03$).

The distribution of fractures was regionalized by body part (Table 2). The lumbar spine was the most commonly injured body part in the study sample. This injury, also defined as spondylolysis, was analyzed separately from other stress fractures. There were no significant differences from the main analysis; thus, these results are not presented here.

Physical Activity

Case subjects averaged 8.2 ± 5.6 ($\pm$ SD) hours/week of total physical activity, whereas control subjects averaged 7.4 ± 9.5 hours/week. This weekly difference was nonsignificant for this sample size ($P = .51$). The distribution of stress fractures appears bimodal, with the highest percentage of case subjects having participated in 4 to 7.9 hours/week of activity. The second mode occurs at 20.0 to 27.9 hours/week (Fig 1).

Reanalyzing activity level as either a categorical (as in Fig 1) or dichotomous variable ("high activity," >10 hours/week) did not demonstrate significant bivariate associations with stress fracture (Table 3), although each hour/week of dance was weakly associated ($P = .08$) with a 10% increase in the odds of stress fracture, controlling for other important factors (odds ratio [OR]: 1.10; 95% confidence interval [CI]: 0.99 to 1.23). Most participants were active in >1 sport, with running the most commonly reported activity, yet the sum of all running activities (running for exercise, running for team, running for sport training, and cross-country running) accounted for a mean of only 0.97 hours/week (range: 0–7 hours/week) in this sample.

MI

The mean ages at menarche among case and control subjects in this sample were 13.1 and 13.3 years, respectively. Only 10 participants (5.9% of the sample) met our criteria for MI (3 with secondary amenorrhea and 7 with oligomenorrhea). All 10 of these adolescents with strictly defined MI were case subjects. Ten case subjects compared with 0 control subjects is a strikingly significant difference (Fisher's exact test, $P < .0001$), but the magnitude of the association cannot be estimated because of the empty (0) cell. Twenty-eight participants (12 case subjects and 16 control subjects) met the expanded criteria for MI used in other recent studies,²⁸ but this construct was not significantly associated with stress fracture (OR: 1.64; 95% CI: 0.65 to 4.04; Table 3). The menstrual ratio construct was similarly not significant, with a mean of 10.5 in case subjects and 10.2 in control subjects (OR: 0.99; 95% CI: 0.86 to 1.14).

Other Covariates

Any positive family history (of osteoporosis, osteopenia, frequent fractures/brittle bones, or stress fracture itself) was significantly associated with stress fracture in the participants, with an unadjusted OR of 2.93 (95% CI: 1.43 to 6.00; Table 3). Examined separately, a positive "measured family history" (osteoporosis or osteopenia) remained significant (OR: 3.00; 95% CI: 1.50 to 5.99), whereas "family history of fractures" (frequent or stress) was not (OR: 1.00; 95% CI: 0.34 to 2.93). Including both subgroups of family history in a multivariate model resulted in a decrease in the magnitude of the association between a family history of fracture and stress fracture (OR: 0.69; 95% CI: 0.20 to 2.44), suggesting confounding (Table 4).

Multivariate Analyses

As noted in bivariate analyses, BMI was significantly associated with stress fracture (OR: 1.12; 95% CI: 1.01 to 1.24). Therefore, the exposures of interest (physical activity and MI), as well as significant covariates in stratified (Mantel-Haenszel) analyses, were reanalyzed, each controlling for BMI (Table 4). A final multivariate model was computed incorporating

BMI and the important exposures identified a priori (total activity and MI), as well as the components of positive family history (Table 4). Controlling for all variables, BMI was no longer significantly associated with stress fracture; only family history of osteoporosis or osteopenia was independently and strongly associated with stress fracture (OR: 2.96; 95% CI: 1.36 to 6.45).

Exploratory Analysis: BMD

In exploratory analyses of BMD, the mean BMD z score at the lumbar spine among the 56 participants with stress fracture was -0.41 (95% CI: -0.78 to -0.04). Because no control participants met the a priori criteria for MI, none had BMD testing performed, and there was no comparison group. Consistent with previous reports, BMI was moderately associated with BMD z score at the lumbar spine, with a Spearman correlation coefficient of 0.44 ($P = .008$).

DISCUSSION

Although neither quantity of exercise nor MI were significantly associated with stress fracture in this study, a family history of osteoporosis, osteopenia, frequent fracture, or stress fracture was a strong independent predictor for incident injury. Because a stress fracture can be defined as a repetitive stress injury, training volume (ie, amount of exercise), which is directly related to the number of repeated applications (or “strain cycles”), is thought to be a key component in the pathophysiology of stress fracture.³⁰ However, recent evidence³¹ has re-emphasized the observation that stress fracture results from an imbalance between the microfracture caused by repeated loading cycles and the skeleton’s own response to remodel the damaged region.^{30,32} Because remodeling is a constant, dynamic process, it may be an inadequate acceleration of this process that results in stress fracture. Therefore, the rate of increase in exercise volume may be a more informative activity parameter than the total volume of exercise as a predictor of stress fracture. Because the reactive forces transmitted from the ground to the skeleton depend on the composition of the playing or training surface, that parameter is also of significant interest. Future studies should examine these and other activity-related factors.

A cohort study of older adolescent Australian track- and-field athletes demonstrated that age at menarche was an independent risk factor for stress fracture, with earlier ages providing significant protection.¹⁰ Menarche occurs near the end of the pubertal growth spurt, which is accompanied by a rapid increase in bone mass and BMD, one of the main determinants of a bone’s ability to withstand loading.^{12,16} Other studies have not consistently replicated this finding, although none have suggested an inverse relationship between age at menarche and risk for stress fracture.²⁶ Numerous small studies have also consistently suggested that stress fractures are less common among athletes with regular menses²⁶; however, the studies have not been sufficiently large to afford adequate statistical power to reach firm conclusions. The presumed mechanism through which regular menses would offer protection against stress fracture is the improved BMD associated with a normal endogenous estrogen state. In the present study, a small proportion of participants met our a priori definition of MI, all of which were girls with stress fracture, a highly significant statistical finding. However, because the majority of both case and control subjects demonstrated regular menstrual histories, we have emphasized the nonsignificant findings with respect to the expanded MI definition as more clinically relevant.

The lack of significant associations of stress fracture with high activity levels or MI may be because of insufficient statistical power. In this sample, both case and control subjects participated in relatively high levels of activity, thereby reducing the variability in the exposure, which may make it more difficult to detect a real effect on the outcome. The

sample size of 168 participants yielded only 10.5% statistical power to detect a difference as small as 0.8 hour/week of activity and 22.4% statistical power to detect the difference in the prevalence in MI (expanded definition). We cannot exclude the possibility that the growing stigma of the female athlete triad led to a much lower proportion of girls reporting MI than expected. An additional limitation of the case-control design is the potential for recall bias; case subjects may have given greater thought to potential causes of their stress fractures, including family history. Thus, this study may have overestimated the magnitude of association between stress fracture and family history of skeletal abnormalities. However, the magnitude of this association was so robust (~3 times the odds of a positive family history among case subjects) that it is unlikely to have been because of recall bias alone.

To further clarify the relationships, we separated a family history of osteoporosis or osteopenia, the measurable indices of skeletal health, from a family history of frequent fractures or frank stress fractures, which are outcomes of the interaction between bone and the loads applied to it. It is noteworthy that this split resulted in only the measurable indices being significantly associated with stress fracture in the female adolescent. Osteoporosis and osteopenia lie on a spectrum of decreased BMD, the majority of which is determined by inherited factors.¹⁵ These factors, which are largely unidentified, could be transmitted to the adolescent, thereby increasing her risk for an insufficiency-type stress fracture. The history of an actual fracture depends to some degree on the activity pattern characteristics of the injured family member, few of which may be inheritable.

Although BMI was directly related to BMD in the secondary analysis of case subjects, this variable was not a significantly protective factor for stress fracture in the entire sample. In fact, each unit increase in BMI was associated with an unadjusted 12% increase in the odds of stress fracture. Recent work by Goulding et al³³ has suggested that children and adolescents with increased BMI exhibit an increased risk of fracture (at the distal radius). Some have hypothesized that heavier patients in that study, as determined by higher BMI, may have fallen with greater force than normal-weighted individuals, sustaining the traumatic wrist fractures. Others attribute the increased fracture rate to decreased BMD because of lower fitness in children with higher BMI. In athletic individuals, like those in the current cohort, lower fitness levels could translate to injury because of a lesser ability to absorb and withstand the effects of repetitive stresses. In a multivariate model including physical activity and menstrual ratio, however, BMI did not remain significantly associated with stress fracture, perhaps as both physical activity and BMI relate to fitness.

Mean daily intakes of calcium and vitamin D in this sample did not meet the daily recommended intake of 1300 mg for calcium but satisfied the American Academy of Pediatrics recommendation of 200 IU/day of vitamin D for female adolescents. Interestingly, however, neither dietary component was significantly associated with stress fracture.

As mentioned, we are unable to comment on any association between BMD and stress fracture. However, the BMD *z* score compares participants with a historical cohort of age- and ethnicity-matched female adolescents. A *z* score of -0.41 would suggest a lower mean BMD among case subjects in this study than among female adolescents in the general population. Although this mean *z* score is not in a range that elicits significant clinical concern (eg, either less than -1.0 or -2.0, depending on expert opinion), a BMD in active athletes lower than the normal BMD of the general population of female adolescents, many of whom are inactive, is concerning.

Other limitations must be acknowledged and considered. In addition to the potential for recall bias and limited statistical power mentioned earlier, this matched case-control design also precludes the ability to assess the impacts of matching factors age and ethnicity on

stress fracture risk. An additional limitation of this study is a lack of generalizability, because the sample is almost entirely white. However, this limitation is mitigated because whites are a group at increased risk for stress fracture,³⁴ so this cohort represents an enriched sample in which to study this particular injury. Similarly, in subgroup analyses of activity type, dance was suggestive of an effect on stress fracture risk in the current study. This finding may be explained by the fact that ballet dancers are particularly prone to the stress fracture of the lumbar spine known as spondylolysis, and the clinic where all of the participants were enrolled is a wellknown referral center for injured dancers.

The homogeneity of the current study sample reflects the characteristics of the population referred to the sports medicine center at this particular children's hospital: namely, active but generally healthy female adolescents. Given the relatively good levels of nutritional and menstrual health in the study population, many of the exposures potentially predictive of stress fracture in our pathogenetic model were too similar (eg, physical activity and calcium and vitamin D intake), too uncommon (eg, disordered eating and smoking), or both (eg, MI) to detect an effect on the outcome. Other factors known to affect BMD and potentially stress fracture risk, such as medication use and chronic diseases, were specifically excluded from the sample, whereas age was rendered nonpredictive by matching. That leaves heredity and BMI as the only factors potentially predictive of stress fracture in this study. The most proximate causes of stress fracture are thought to be excessive repetitive stress and insufficient load bearing capacity, or "bone strength." Bone strength is determined by both bone geometry and BMD. Because we did not measure bone geometry in this study, it is not surprising that only the inheritable, but as yet undefined, determinants of BMD account for the variability in stress fracture diagnosis in our clinics. In addition to prospective research that more closely examines the changes in amount and types of weekly exercise, as well as the types of training surfaces over time, studies of the relationship between stress fracture and genetic markers of skeletal health are, therefore, needed.

CONCLUSIONS

Girls in a high stratum of physical activity who sustained stress fracture were distinguished not by their ability to overwhelm the bone's remodeling capacity (ie, a "fatigue fracture") but by the intrinsic load-bearing properties of their bones (ie, "insufficiency fractures"). Because a "fracture threshold" remains undefined for adolescents, the relative contribution of low BMD to skeletal insufficiency is unknown, but identifying low BMD would still be crucial in this population, for whom exercise should improve peak bone mass and thereby decrease long-term risk of osteoporosis.^{35,36} Until the relationships among "bone strength," BMD, and their inheritable determinants are more fully understood, further clinical investigation of BMD is, therefore, warranted in active female adolescents who sustain stress fracture.

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Abbreviations

BMD	bone mineral density
MI	menstrual irregularity
DXA	dual-energy x-ray absorptiometry
OR	odds ratio
CI	confidence interval

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FIGURE 1.
Participants according to activity category.

TABLE 1
Age, Maturational Stage, Dietary Intake, and Activity of 168 Participants

Variable	Data
Age, mean (SD), y	15.9 (2.1)
BMI, mean (SD), kg/m ²	21.5 (3.2)
Age at menarche, mean (SD), y	13.1 (1.1)
Postmenarchal, % (<i>n</i>)	91.7 (154)
MI, % (<i>n</i>)	5.9 (10)
Calcium intake, mean (SD), mg/d	1096 (480)
Vitamin D intake, mean (SD), IU/d	253 (159)
Physical activity, % (<i>n</i>)	
0–3.9 h/wk	25.0 (42)
4–7.9 h/wk	42.3 (71)
8–11.9 h/wk	19.1 (32)
12–15.9 h/wk	8.3 (14)
16–19.9 h/wk	1.8 (3)
20–23.9 h/wk	1.2 (2)
24–27.9 h/wk	1.8 (3)
>28 h/wk	0.6 (1)

TABLE 2
Stress Fractures According to Regional Body Part

Fractured Body Part	Frequency, <i>n</i>	Percentage
Lumbar spine	34	60.7
Lower leg	14	25.0
Foot	5	8.9
Ankle	2	3.6
Hip/pelvis	1	1.8

TABLE 3
Unadjusted Measures of Association Between Major Exposures and Stress Fracture
(Mantel-Haenszel Stratified ORs)

Variable	Unadjusted OR (95% CI)	P
BMI, kg/m ²	1.12 (1.01 to 1.24)	.03
Total activity, h/wk	1.01 (0.97 to 1.05)	.56
High activity, >10 h/wk	1.79 (0.83 to 3.86)	.13
Postmenarcheal	0.88 (0.27 to 2.82)	.82
Age at menarche, y	1.02 (0.72 to 1.45)	.91
Menstrual irregularity, expanded def ^a	1.64 (0.65 to 4.04)	.24
Menstrual ratio, average menses/y	0.99 (0.86 to 1.14)	.85
Calcium intake, mg/d	1.00 (0.99 to 1.00)	.87
Vitamin D intake, IU/d	1.00 (0.99 to 1.00)	.21
Positive family history	2.93 (1.43 to 6.00)	.002
Measured family history, osteoporosis/penia	3.00 (1.50 to 5.99)	.001
Family history of fracture	1.00 (0.34 to 2.93)	.38

^aData are for the absence of menses for >3 months or <9 menses in previous year for post-menarchal females.

TABLE 4
Associations of BMI, Menstrual Ratio, Physical Activity, and Family History With Stress Fractur (From Conditional Logistic Regression Models)

Variable	Adjusted OR for BMI Only (95% CI)	Adjusted OR for All Covariates in Table (95% CI) ^a
BMI, kg/m ²	1.12 (1.01 to 1.25)	1.08 (0.97 to 1.22)
Total activity, h/wk	1.00 (0.96 to 1.04)	1.00 (0.96 to 1.04)
Menstrual ratio, average menses per y	0.99 (0.86 to 1.14)	0.93 (0.78 to 1.11)
Measured family history, osteoporosis/penia	2.74 (1.33 to 5.66)	2.96 (1.36 to 6.45)
Family history of fracture	1.17 (0.38 to 3.65)	0.69 (0.20 to 2.44)

^aData are for the final conditional logistic regression model including 149 participants with complete data.