Risk Factors for Stress Fracture among Young Female Cross-Country Runners

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ABSTRACT

KELSEY, J. L., L. K. BACHRACH, E. PROCTER-GRAY, J. NIEVES, G. A. GREENDALE, M. SOWERS, B. W. BROWN JR., K. A. MATHESON, S. L. CRAWFORD, and K. L. COBB. Risk Factors for Stress Fracture among Young Female Cross-Country Runners. Med. Sci. Sports Exerc., Vol. 39, No. 9, pp. 1457-1463, 2007. Purpose: To identify risk factors for stress fracture among young female distance runners. Methods: Participants were 127 competitive female distance runners, aged 18-26, who provided at least some followup data in a randomized trial among 150 runners of the effects of oral contraceptives on bone health. After completing a baseline questionnaire and undergoing bone densitometry, they were followed an average of 1.85 yr. Results: Eighteen participants had at least one stress fracture during follow-up. Baseline characteristics associated (P < 0.10) in multivariate analysis with stress fracture occurrence were one or more previous stress fractures (rate ratio [RR] [95% confidence interval] = 6.42 (1.80-22.87), lower wholebody bone mineral content (RR = 2.70 [1.26–5.88] per 1-SD [293.2 g] decrease), younger chronologic age (RR = 1.42 [1.05–1.92] per 1-yr decrease), lower dietary calcium intake (RR = 1.11 [0.98–1.25] per 100-mg decrease), and younger age at menarche (RR = 1.92 [1.15-3.23] per 1-yr decrease). Although not statistically significant, a history of irregular menstrual periods was also associated with increased risk (RR = 3.41 [0.69–16.91]). Training-related factors did not affect risk. Conclusion: The results of this and other studies indicate that risk factors for stress fracture among young female runners include previous stress fractures, lower bone mass, and, although not statistically significant in this study, menstrual irregularity. More study is needed of the associations between stress fracture and age, calcium intake, and age at menarche. Given the importance of stress fractures to runners, identifying preventive measures is of high priority. Key Words: BONE MASS, EPIDEMIOLOGY, FEMALE ATHLETES, LONG-DISTANCE RUNNERS

S tress fractures are common among young female competitive athletes, especially in track and field (17). Reported 1-yr incidence rates in competitive track and field athletes have ranged from 8.7% (22) to 21.1% (5) in females and males combined, the variation probably depending in part on the sensitivity of the methods used to detect stress fractures. Incidence rates appear to be

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0195-9131/07/3909-1457/0 MEDICINE & SCIENCE IN SPORTS & EXERCISE® Copyright © 2007 by the American College of Sports Medicine DOI: 10.1249/mss.0b013e318074e54b similar in female and male track and field athletes (5.22). It is generally agreed that current or past menstrual irregularity is a risk factor in female athletes (2,6,7,9,21,22). Results from studies of female or female and male athletes are contradictory regarding the associations of stress fractures with age (4), lower bone mineral density or lean body mass (6,7,9,22), late age at menarche (4,6,7,9,21), not using oral contraceptives (4,7,21), low body weight (7,22), disordered eating (6,7,22), and low calcium and dairy product intake (6,7,21). Individual studies have reported leg length discrepancy (6), low dietary fat intake (6), and a history of stress fracture (22) to be risk factors, but confirmation in other investigations is needed. Many of these results are based on small numbers of study subjects, some have collected information retrospectively, and most do not use multivariate methods of statistical analysis to determine which of these attributes are independent predictors of stress fracture. A recent review in fact concluded that data regarding the epidemiology of stress fractures in

1457

athletes are "lacking," except that stress fractures usually occur among those participating in sports with repetitive weight-bearing activity (29). Also, risk factors may not be the same for all athletes, so studies focusing on specific sports may provide particularly useful information for participants in that sport.

Studies of stress fracture in female or female and male military recruits and trainees have also produced somewhat inconsistent and tentative results. Possible risk factors include increasing age (19,27), a small thigh girth (1), lower aerobic fitness (24), no or only a small amount of lower extremity weight training in the past year (24), lack of menstrual cycles in past year (24), and, in a large prospective study (19), lower bone mineral density, weight loss, alcohol consumption of more than 10 drinks per week, cigarette smoking, weight bearing exercise, lower adult weight, corticosteroid use, use of depomedroxyprogesterone acetate, and lack of past regular exercise. Two retrospective studies have reported no association between stress fracture occurrence and bone mineral density or bone mineral content (1,10), and a few studies have found no association with menstrual frequency or age at menarche (1,19), calcium intake or dairy food consumption (10,19), and eating disorders (1). In addition to methodologic limitations in some of these studies, risk factors in military recruits and trainees may have limited relevance to women who have been running competitively for several years.

In this paper we use data collected during the course of a randomized trial of the effect of oral contraceptives on bone health to identify other factors that predict stress fractures in young female long-distance runners. Results of the randomized trial are presented in a companion paper.

METHODS

Study population. The study population for these analyses consists of 127 competitive female cross-country runners between the ages of 18-26 yr at baseline who participated in a randomized trial to examine whether use of oral contraceptives protects against loss of bone mass and stress fracture occurrence. Recruitment took place between August 1998 and September 2003. One hundred fifty runners had been recruited for the trial from intercollegiate cross-country teams, postcollegiate running clubs, and road race participants, of whom 127 (85%) provided some follow-up information. Of these, 57 were collegiate runners and 70 postcollegiate runners. At the time of recruitment, most lived in the vicinities of the sites at which bone densitometry was undertaken: Stanford, CA, Los Angeles, CA, West Haverstraw, NY, Ann Arbor, MI, and Boston, MA. To be eligible, women had to run at least 40 miles per week during peak training times, had to compete in races, could not have used oral contraceptives or other hormonal contraceptives within 6 months of entering the study, and had to be willing to be randomized and to have no contraindications to oral contraceptive use. The size of the

study population was based on the number needed to provide adequate statistical power for the randomized trial, not for the comparisons presented in this paper. Details of the study and testing procedures were explained to each subject, and a written, informed consent was obtained. The protocol was approved by the institutional review boards of Stanford University, the University of California Los Angeles, the University of Michigan, the Helen Hayes Hospital, the Massachusetts General Hospital, the U.S. Army Medical Research and Materiel Command, and the colleges at which participants were recruited.

Data collected at baseline. At each of the five clinical sites, height and weight were measured using standard stadiometers and balance-beam scales, respectively. Body mass index (BMI) $(kg \cdot m^{-2})$ was calculated from these measurements. Body composition (lean body mass and fat mass) and bone mineral content (g) and bone mineral density (g·cm⁻²) at the left proximal femur, spine, and whole body and were measured by dual-energy x-ray absorptiometry (DXA, QDR 4500A at four sites, 2000W at one site). The coefficient of variation for measuring the bone mineral density at the hip and spine in same person after leaving and then returning to the measuring table on the same day was less than 2% at each of the clinical sites. For most of the period of data collection, machines were cross-calibrated using a circulating Hologic anthropomorphic spine phantom, and each site maintained a quality-assurance program.

A self-administered baseline questionnaire was used to obtain information about several other variables of interest. Demographic information included age and race/ethnicity. Women were asked their age when they first started competing for a running team and number of cross country seasons in which they had competed. They were asked to record the number of miles they ran per week during each competitive season (fall cross-country, winter track, spring track) and off-season (summer) in the previous year. From this information an average number of kilometers run per week was computed for the past year. Participants were asked what percentage of the distance was on pavement or concrete.

Women were asked to give a complete history of previous stress fractures that had occurred prior to baseline. They had to report confirmation by x-ray, bone scan, or magnetic resonance imaging for the stress fracture to be counted in these analyses. Eighteen women did not know whether they had experienced a previous stress fracture. These women are assumed not to have had a stress fracture in the analyses presented here.

Participants were asked to record their age at menarche and the number of menses they had in the previous 12 months. Women were classified as having current menstrual irregularity if they were oligomenorrheic (defined as four to nine cycles in the past year) or amenorrheic (defined as fewer than four cycles in the past year). Women were also asked whether they had had 0, 1–3, 4–9, or 10–13 menses during each year after menarche. They were categorized as having a history of menstrual irregularity if they had ever been amenorrheic or oligomenorrheic since the year of menarche. Hormone concentrations were not measured, as this was beyond the scope of the study. A complete history of oral contraceptive use was obtained.

A modified version of the 97-item National Cancer Institute Health Habits and History food frequency questionnaire (8) was used to estimate usual nutrient intake during the previous six months. One of the modifications to the questionnaire was the inclusion of additional food items that were likely to be consumed by young athletes and that contained relatively high amounts of calcium. Only dietary calcium intake is included in the analyses presented in this paper. Use of calcium supplements tended to be inconsistent and of short duration, and was not measured precisely enough for inclusion in these analyses. Three subscales (drive for thinness, bulimic tendencies, and body dissatisfaction) of the Eating Disorder Inventory (EDI) were used to identify subclinical eating disorders (3,14,15). A total EDI score was computed by summing the scores on each of the three EDI subscales. In the present study Cronbach's alpha for the three subscales was 0.79, indicating that the scores for the three subscales were to a large extent consistent with the total score.

Ascertainment of stress fracture occurrence during follow-up. Participants were asked to record the occurrence of a possible stress fracture on a monthly calendar and also to report their occurrence to us immediately. The fracture had to be confirmed by x-ray, bone scan, or magnetic resonance imaging to be counted in this study. All reported stress fractures were in fact confirmed. The study paid for the imaging as needed. Participants were also queried periodically about the occurrence of stress fractures by e-mail, phone, and on their questionnaires. No additional stress fractures were reported as a result of these queries. No physical examinations were undertaken if a possible stress fracture was not reported.

Other aspects of follow-up. Participants were asked to return for bone densitometry and measurement of body composition, height, and weight 1 and 2 yr after baseline measurements. At this time they were asked to fill out a questionnaire covering most of the areas included at baseline, and every six months they filled out another food frequency questionnaire. This information is not, however, used in the present analyses. Because the data were updated only at yearly intervals (or in the case of dietary intake at six month intervals), it was generally not possible to know whether any changes preceded or followed stress fracture occurrence, and therefore it was impossible to differentiate cause from effect.

In addition, in this young, mobile, and preoccupied population, not all participants had measurements made at the time requested. As mentioned above, no follow-up information at all was available for 23 (15%) of the original 150 women seen at baseline, and some were followed for less than 2 yr. Baseline characteristics of those lost to follow-up were generally similar to those retained in the cohort, except that those lost to follow-up were more likely to have a history of stress fracture prior to baseline (52 vs 32%, P = 0.05). Among those who continued to participate in the study, we set a 4-yr limit as to how long we would wait for them to report for their follow-up visits. Only four runners had their final follow-up visit during the fourth year. Also, we included stress fractures that occurred up to one month after the final follow-up visit.

Statistical analysis. Analyses were carried out with the SAS statistical package, version 8.02 (SAS Institute, Cary NC). Cox proportional hazards models were used to compute rate ratios for the rate of a first stress fracture during follow-up among those with a given characteristic divided by the rate of a first stress fracture during follow-up among those without the characteristic. Cox models were also used to estimate rate ratios according to the level of a characteristic and to compute rate ratios for one variable while controlling for the effects of other characteristics. Except for descriptive information on the study population, all analyses controlled for clinical assessment site and group to which a participant was randomized. Additional control on actual oral contraceptive use during follow-up did not materially change any of the results. An examination of the degree of skewness of the variables indicated that none needed to be transformed.

RESULTS

The 127 participants were followed for stress fracture occurrence for a total of 2824 months, or an average of 1.85 yr per woman. The age at baseline of the 127 runners ranged from 18 to 26 yr, with a mean of 22.0 yr. Table 1 provides other descriptive statistics on the cohort at baseline. About 83% were white, and their average body mass index was 21.2 kg·m⁻². Almost 31% reported having previously had one or more definite stress fractures, 57% had a history of menstrual irregularity, and 40% had previously used oral contraceptives.

Eighteen of the 127 runners had at least one stress fracture, for an average of 7.7 first stress fractures during the followup period per 100 person-years of follow-up. Ten of the first stress fractures occurred in the tibia, six in the foot, and two in the femur. Four runners had a second stress fracture: two in the tibia, one in the foot, and one in the femur.

Various factors were associated with elevated rate ratios for stress fracture during the follow-up period (Table 2). Women with a previous stress fracture had more than a fivefold higher rate of stress fracture during follow-up than women without such a history. Various indicators of lower bone mass were associated with an increased rate of stress fracture. For instance, for each standard deviation decrease (293.2 g) in whole-body bone mineral, the rate of stress fracture increased almost twofold. Other factors associated (P < 0.10) with an increased rate of stress fracture were lower average daily dietary calcium intake and daily

TABLE 1. Mean ± SD c	r percentage with s	elected characteristic	at baseline.
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	Mean \pm SD or Percentage
Age (yr)	$22.0~\pm~2.6$
Height (cm)	165.9 ± 6.1
Weight (kg)	58.3 ± 6.7
Body mass index $(kg \cdot m^{-2})$	21.2 ± 1.9
Percent body fat	$23.0~\pm~5.3\%$
Race/ethnicity	
White	83.5%
Hispanic	3.9%
Asian/Pacific Islander	8.7%
Black	0.8%
Other	3.1%
Age started running competitively (yr)	$14.2~\pm~3.5$
Total number seasons run competitively	$11.9~\pm~6.8$
Average distance run per week, past year (km)	55.5 ± 18.0
Percent of distance on pavement or concrete	65.6 ± 22.1%
History of one or more stress fractures	30.7%
Age at menarche (yr)	13.1 ± 1.5
History of menstrual irregularity ^a	57.1%
Menstrual irregularity (past year) ^b	33.1%
Ever used oral contraceptives	39.7%
Total eating disorder inventory score ^c	11.8 ± 12.4
Whole-body bone mineral content (g)	2169.3 ± 293.2
Bone mineral density (g⋅cm ⁻²)	
Hip	0.986 ± 0.116
Spine	0.988 ± 0.108
Whole body	1.111 ± 0.084
Daily dietary calcium intake (mg)	1357.5 ± 681.4

^a No more than nine menstrual periods in any year, excluding the year of menarche.
^b No more than nine menstrual periods in the year before baseline.

 $^{\rm c}$ Total eating disorder inventory score, which can range from 0 to 69, is the sum of the scores from three subscales. See Garner and Olmsted (14).

servings of dairy products, younger age at menarche, lower lean body mass, and lower weight. Younger age, shorter height, lack of previous oral contraceptive use, and a history of menstrual irregularity were also associated with increased rates of stress fracture, but these trends were not statistically significant. Little association was seen for current menstrual irregularity, percent body fat, BMI, age started running competitively, total competitive seasons run, kilometers run per week in past year, and total eating disorder inventory score from the three subscales.

We attempted to examine whether previous stress fractures at certain sites were particularly strong predictors of stress fracture during follow-up. Numbers were small and confidence intervals very wide, but for the most common sites of previous stress fracture the point estimates of the rate ratio were quite similar: previous foot fracture 6.11 (2.11–17.68); previous tibia fracture: 7.91 (2.77–22.59); previous femur fracture: 6.78 (1.60–28.74); and previous fibula fracture: 6.98 (0.63–77.09).

We used a multivariate Cox model to identify variables that predicted stress fracture independently of the other variables under consideration. The various indicators of bone mass at different skeletal sites were highly correlated with each other, and we selected whole-body bone mineral content for our primary multivariate model because of the strength of its association with stress fracture, the multiple skeletal sites at which stress fractures can occur, and the limitations of using bone mineral density as a measure of bone mass, particularly when growth is still occurring (16). We subsequently present another model in which hip bone

mineral density is used in place of whole-body bone mineral content because some readers will have a preference for that measure. Daily calcium intake and servings of dairy products were highly correlated (r = 0.83), and we chose dietary calcium intake for the multivariate model. Lean body mass was sufficiently highly correlated with bone mineral content that it could not be included in the same model. Accordingly, age, height, weight, history of stress fracture, age at menarche, history of menstrual irregularity, whole-body bone mineral content, and daily calcium in the diet were considered for inclusion in a multivariate model, along with certain other variables. Those significant at P < 0.10, and also a history of menstrual irregularity, for which the rate ratio was consistent with other studies even though P > 0.10, were included in the model presented here.

In the multivariate analysis (Table 3), a history of stress fracture was still a strong predictor of a future stress fracture, along with lower whole-body bone mineral content, decreasing age, younger age at menarche, and lower dietary

TABLE 2. Adjusted rate ratios (and 95% confidence interval) for associations between selected characteristics and stress fracture.

	Rate Ratio (95% CI)
Age (per vear vounger)	1.12 (0.89, 1.41)
Height (per centimeter shorter)	1.04 (0.96, 1.12)
Weight (per kilogram decrease)	1.08 (0.99, 1.16)
Body mass index (per decrease in kilograms	1.20 (0.90, 1.61)
per meter squared)	
Percent body fat (per 5% increase)	1.16 (0.71, 1.89)
Lean body mass (per kilogram decrease)	1.14 (1.01, 1.28)
Age started running competitively (per year younger)	1.01 (0.93, 1.10)
Total number competitive seasons (per season)	1.01 (0.93, 1.10)
Average distance run per week, past year	1.08 (0.81, 1.45)
(per 10-km increase)	
Percent distance on pavement or concrete (per 5% decrease)	1.05 (0.94, 1.18)
History of one or more stress fractures (yes/no)	5.24 (1.88, 14.49)
Number of previous stress fractures (per each	1.59 (1.15, 2.19)
previous fracture)	
Age at menarche (per year younger)	1.37 (0.97, 1.92)
History of menstrual irregularity ^a (yes/no)	1.90 (0.66, 5.51)
Menstrual irregularity in past year ^b (yes/no)	1.05 (0.38, 2.89)
Never used oral contraceptives (yes/no)	2.22 (0.65, 7.69)
Total eating disorder inventory score ^c (per 5 units)	1.03 (0.86, 1.24)
Whole-body bone mineral content	1.79 (1.02, 3.13)
(per standard deviation decrease,	
where one standard deviation = 293.2 g)	
Hip bone mineral content (per standard deviation	1.69 (0.95, 2.94)
decrease, where one standard deviation = 5.78 g)	
Spine bone mineral density (per standard	1.89 (1.04, 3.45)
deviation decrease, where one standard	
deviation = 0.11 g·cm ⁻²)	
Hip bone mineral density (per standard	1.45 (0.81, 2.56)
deviation decrease, where one standard	
deviation = 0.12 g·cm ⁻²)	
Whole-body skeletal area (per standard	1.89 (1.06, 3.33)
deviation decrease, where one standard	
deviation = 166.8 cm ²)	
Daily dietary calcium intake (per 100-mg decrease)	1.08 (0.99, 1.18)
Daily servings of dairy products (per one-serving	1.41 (1.01, 1.96)
decrease)	

Rate ratios are adjusted by Cox proportional hazards model for clinical site and treatment group assignment.

^a No more than nine menstrual periods in any year, excluding the year of menarche.

^b No more than nine menstrual periods in the year before baseline.
^c Total eating disorder inventory score, which can range from 0 to 69, is the sum of the scores from three subscales. See Garner and Olmsted (14).

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TABLE 3. Multivariate adjusted rate ratios (and 95% confidence intervals) for associations between selected characteristics and stress fracture, with whole-body bone mineral content used as a measure of bone mass.

	Rate Ratio (95% CI)
Age (per year younger) History of one or more stress fractures (yes/no) Whole-body bone mineral content (per standard deviation decrease, where one standard	1.42 (1.05, 1.92) 6.42 (1.80, 22.87) 2.70 (1.26, 5.88)
deviation = 293.2 g) Daily dietary calcium intake (per 100-mg decrease) Age at menarche (per year younger) History of menstrual irregularity ^a (yes/no)	1.11 (0.98, 1.25) 1.92 (1.15, 3.23) 3.41 (0.69, 16.91)

Rate ratios are adjusted by Cox proportional hazards model for clinical site, treatment group assignment, and all the other variables in the table.

^a No more than nine menstrual periods in any year, excluding the year of menarche.

calcium intake. A history of irregular periods was also associated with an increase rate of stress fracture, although not statistically significantly so. Height, weight, BMI, percent body fat, age started running competitively, total competitive seasons run, kilometers run per week in past year, and total eating disorder inventory score did not predict stress fracture occurrence when entered into the multivariate analysis.

When hip bone mineral density was substituted for whole-body bone mineral content in the multivariate model, similar results were obtained (Table 4).

DISCUSSION

To our knowledge only one other study in runners, presented in abstract form (22), has examined whether a history of stress fracture predicts future stress fracture, and a positive association was found. A study in military recruits (24) reported an increase in risk that did not reach statistical significance. The rate ratio of 6.42 (1.80-22.87) associated with one or more previous stress fractures in the multivariate analysis here indicates that particular attention should be paid to this history, as these individuals appear to be at especially high risk of additional stress fractures. Our results also indicate that a history of stress fractures is a marker of susceptibility above and beyond its association with bone mineral content or density and the other variables included in the multivariate analyses. Runners and their coaches should be made aware of the high risk for additional fractures, should try to identify the reason for the high risk, and should make changes so as to reduce that risk.

Our finding that lower bone mass is associated with an increased risk for stress fracture is consistent with other prospective studies carried out in competitive athletes (6,22) and military recruits (19). Thus, it is likely that lower bone mass is indeed predictive.

Several previous studies in competitive athletes and military recruits have reported that current or past menstrual irregularity is associated with an increased risk for stress fracture (2,6,7,9,21,22,24). Our rate ratio of 3.41 (0.69–16.91), although not statistically significant, is consistent with these other reports. Studies not finding this association had very small numbers of amenorrheic participants (19) or had participants with only short periods of amenorrhea (10). Menstrual irregularities often occur in association with low serum estrogen concentrations and are known to be related to low bone mineral density and low serum concentrations of bone formation markers (12,20,23,30). The results of our multivariate analysis suggest that a history of menstrual irregularity may have additional adverse effects on bone health beyond its associations with lower bone mineral content and density. Efforts should be made to identify reasons for the menstrual irregularities, such as inadequate diet, and appropriate changes made.

Low calcium and dairy product intake has been associated with decreased bone mineral density in young adult women (25). One previous study in competitive athletes found lower calcium and dairy product intake to be associated with an increased risk for stress fracture (21). Also, a report available in abstract form (18) from a recent randomized trial of supplementation with 2000 mg calcium and 800 international units (IU) of vitamin D among female Navy recruits in basic training, found that in just eight weeks the supplemented group had a 27% lower incidence of stress fracture than the non-supplemented group, using a per protocol statistical analysis. On the other hand, another observational study in track and field athletes (6) and other observational studies in military recruits (10,19) have not shown any protective effect. Among the studies showing no effect, the prospective study of Bennell et al. (6) reported that most of the track and field athletes had high intakes of dietary calcium, and were thereby possibly already receiving whatever protection dietary calcium provides against stress fracture. The questionnaire used in another study (19) assessed only whether the recruits had at least one serving of milk, cheese, or yogurt per day, and thus did not attempt to collect detailed quantitative information on calcium intake. The other study (10) asked soldiers to recall diet during adolescence, and errors in recall would have been likely. Thus, uncertainty remains about the role of lower calcium intake on stress fracture occurrence. In our study, lower dietary calcium and dairy product intake were associated with an increased risk of stress fracture independently of their association with bone mineral content or density. Some other aspect of bone strength may be affected by calcium intake as well. For instance, insufficient dietary

TABLE 4. Multivariate adjusted rate ratios (and 95% confidence intervals) for associations between selected characteristics and stress fracture, with hip bone mineral density used as a measure of bone mass

	Rate Ratio (95% CI)
Age (per year younger)	1.42 (1.03, 1.95)
History of one or more stress fractures (yes/no)	6.71 (1.93, 23.35)
Hip bone mineral density (per standard	2.16 (1.04, 4.48)
deviation decrease, where one standard	
deviation = 0.12 g·cm ⁻²)	
Daily dietary calcium intake (per 100-mg decrease)	1.09 (0.97, 1.23)
Age at menarche (per year decrease)	1.61 (1.04, 2.49)
History of menstrual irregularity ^a (yes/no)	3.10 (0.70, 13.74)

Rate ratios are adjusted by Cox proportional hazards model for clinical site, treatment group assignment, and all the other variables in the table.

^a No more than nine menstrual periods in any year, excluding the year of menarche.

calcium would also be expected to result in inadequate repair of microdamage (21) or may have a detrimental effect on some aspect of bone geometry, such as cortical thickness (26), and thereby increase the risk for stress fractures.

Increasing calcium intake in those consuming inadequate amounts would be a relatively easy preventive measure to implement, so determining its importance with more certainty is of high priority. More research should be undertaken to determine the optimal level of calcium intake of distance runners and of athletes in general. The protection indicated by the randomized trial of 2000 mg per day of calcium with 800 IU·d⁻¹ of vitamin D in Navy recruits (18) might indicate that among highly active young women such as military recruits and competitive distance runners, higher levels of calcium intake are needed than the recommended dietary allowance of 1300 mg·d⁻¹ for those of ages 9–18 yr and 1000 mg·d⁻¹ for those of age 19 yr and older in the general population.

Whether increasing age is associated with a greater risk, a reduced risk, or no change in risk for stress fracture has been controversial (4). Across the age range of 18–26 yr considered in this study, it would be expected that younger runners would have higher stress fracture rates because bone mass is still gained through the third decade of life (25). It should also be noted that the decreasing stress fracture rate with increasing age in the present study was seen only in the multivariate analysis when we accounted for a history of stress fracture.

Other studies of athletes in this age group (4,6,7,9,21)have found either a positive association between age at menarche and stress fracture risk or no association. In contrast, we found that younger age at menarche was associated with a higher rate of stress fracture. Most studies, but by no means all (see Bennell et al. (4) and Eastell (13 for reviews), have found that age at menarche is inversely correlated with bone mineral density and bone mineral content, but in the present study we found that age at menarche had only a slight inverse correlation with wholebody bone mineral density (r = -0.13, P = 0.12), but no correlation with whole-body bone mineral content (r = 0.03, P = 0.76). If later age at menarche results in later maturation and consolidation of bone, one would expect higher rates of stress fracture with later age at menarche, as reported by others. It is possible that some other aspect of bone strength associated with late age at menarche is playing a role in the decreased risk found in our study. Among the determinants of bone strength are bone size, cortical thickness and porosity, the number of trabeculae, trabecular thickness and connectedness, tissue mineral content, the presence of microfractures, and the direction and extent of cross-linking of collagen (28). Further studies are needed before any definitive conclusions are reached.

Although we previously reported an association at baseline between disordered eating and low bone mineral density among eumenorrheic runners (11), no association between disordered eating and subsequent stress fracture occurrence was seen in these analyses. Numbers of stress fractures, however, were too small to consider the rates of stress fracture by menstrual status and eating disorder status simultaneously.

Finally, we did not find training-related factors to be important, including age started running competitively, total competitive seasons run, miles run per week in past year, and miles run on concrete or pavement. The number of stress fractures was too small to enable us to examine these factors in detail, but the results of the present study are consistent with those reported by others (6,21). Although it does not seem that training-related factors are important in the etiology of stress fracture at least among athletes who have been participating in their sport for several years, more study with larger numbers of stress fractures and with more variation in length and type of training is needed before definitive conclusions are reached.

Our prospective study had the advantage of collecting information on possible risk factors before the occurrence of the stress fractures, thus eliminating the possibility of biased recall once a stress fracture has occurred. In addition, all participants were from one sport, cross-country running, thus eliminating sport as a potential source of variation. On the other hand, our study population was of modest size, and the number of stress fractures was only 18. Accordingly, we could not identify small increases or decreases in risk. Because of limited resources, physical examinations were not conducted on those who did not report possible stress fractures, and measurements of serum hormone concentrations were not made on any participants. Also, despite our best efforts, we had no follow-up information on 15% of the original participants. We found this age group, with its high degree of mobility and changing interests over time, to be particularly challenging to retain in a longitudinal study. Because the major objective was to conduct a randomized trial of the effect of oral contraceptives, we did not collect information on a wide spectrum of possible risk factors. In addition, it should be emphasized that we did focus on only one sport. None of the risk factors identified is specific to cross-country track, and evaluating these risk factors in athletes in other sports could give wider applicability to our findings.

In conclusion, the results of our study and those of others indicate that young female runners with previous stress fractures, lower bone mass, and a history of irregular menstrual periods are at high risk for stress fracture and should be carefully monitored. Although the evidence is not definitive, high calcium intake should be encouraged. The relation between age at menarche and risk for stress fracture is unclear, and needs further study.

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REFERENCES

- 1. ARMSTRONG, D. W., J-P. H. RUE, J. H. WILCKENS, and F. J. FRASSICA. Stress fracture injury in young military men and women. *Bone* 35:806–816, 2004.
- 2. BARROW, G. W., and S. SAHA. Menstrual irregularity and stress fractures in collegiate female distance runners. *Am. J. Sports Med.* 16:209–215, 1988.
- 3. BEALS, K. A., and M. M. MANORE. Behavioral, psychological, and physical characteristics of female athletes with subclinical eating disorders. *Int. J. Sport Nutr. Exerc. Metab.* 10:128–143, 2000.
- BENNELL, K., G. MATHESON, W. MEEUWISSE, and P. BRUKNER. Risk factors for stress fractures. *Sports Med.* 28:91–122, 1999.
- BENNELL, K. L., S. A. MALCOLM, S. A. THOMAS, et al. The incidence and distribution of stress fractures in competitive track and field athletes: a twelve-month prospective study. *Am. J. Sports Med.* 24:211–217, 1996.
- BENNELL, K. L., S. A. MALCOLM, S. A. THOMAS, et al. Risk factors for stress fractures in track and field athletes. A twelve-month prospective study. *Am. J. Sports Med.* 24:810–818, 1996.
- BENNELL, K. L., S. A. MALCOLM, S. A. THOMAS, et al. Risk factors for stress fractures in female track-and-field athletes: a retrospective analysis. *Clin. J. Sport Med.* 5:229–235, 1995.
- 8. BLOCK, G., A. M. HARTMAN, C. M. DRESSER, et al. A data-based approach to diet questionnaire design and testing. *Am. J. Epidemiol.* 124:453–469, 1986.
- CARBON, R., P. N. SAMBROOK, V. DEAKIN, et al. Bone density of elite female athletes with stress fractures. *Med. J. Aust.* 153:373–376, 1990.
- CLINE, A. D., G. R. JANSEN, and C. L. MELBY. Stress fractures in female army recruits: implications of bone density, calcium intake, and exercise. J. Am. Coll. Nutr. 17:128–135, 1998.
- COBB, K. L., L. K. BACHRACH, G. GREENDALE, et al. Disordered eating, menstrual irregularity, and bone mineral density in female runners. *Med. Sci. Sports Exerc.* 35:711–719, 2003.
- DRINKWATER, B. L., K. NILSON, C. H. CHESNUT III, W. J. BREMNER, S. SHAINHOLTZ, and M. B. SOUTHWORTH. Bone mineral content of amenorrheic and eumenorrheic athletes. *N. Engl. J. Med.* 311: 277–281, 1984.
- 13. EASTELL, R. Role of oestrogen in the regulation of bone turnover at the menarche. *J. Endocrinol.* 185:223–234, 2005.
- GARNER, D. M., and M. P. OLMSTED. Manual for Eating Disorders Inventory. Odessa, FL: Psychological Assessment Resources, Inc., 1984.
- GARNER, D. M., M. P. OLMSTED, and J. POLIVY. Development and validation of a multidimensional eating disorder inventory for anorexia nervosa and bulimia. *Int. J. Eat. Disord.* 2:15–34, 1983.

- HEANEY, R. P. BMD: the problem. Osteoporos. Int. 16:1013–1015, 2005.
- JOHNSON, A. W., C. B. WEISS, Jr., and D. L. WHEELER. Stress fractures of the femoral shaft in athletes—more common than expected. *Am. J. Sports Med.* 22:248–256, 1994.
- LAPPE, J. M., D. M. CULLEN, K. THOMPSON, and R. AHLF. Calcium and vitamin D supplementation reduces incidence of stress fractures in Navy recruits. Paper presented at: 53rd Annual Meeting of the Orthopaedic Research Society; February 11–14, 2007; San Diego, CA. Paper 0016.
- LAPPE, J. M., M. R. STEGMAN, and R. R. RECKER. The impact of lifestyle factors on stress fractures in female army recruits. *Osteoporos. Int.* 12:35–42, 2001.
- MARCUS, R., C. CANN, P. MADVIG, et al. Menstrual function and bone mass in elite women distance runners. Endocrine and metabolic features. *Ann. Intern. Med.* 102:158–163, 1985.
- MYBURGH, K. H., J. HUTCHINS, A. B. FATAAR, S. F. HOUGH, and T. D. NOAKES. Low bone density is an etiologic factor for stress fractures in athletes. *Ann. Intern. Med.* 113:754–759, 1990.
- NATTIV, A., J. C. PUFFER, J. CASPER, et al. Stress fracture risk factors, incidence, and distribution: a 3 year prospective study in collegiate runners. *Med. Sci. Sports Exerc.* 32(Suppl. 5):S347, 2000.
- NELSON, M. E., E. C. FISHER, P. D. CASTOS, C. N. MEREDITH, R. N. TURSKOY, and W. J. EVANS. Diet and bone status in amenorrheic runners. *Am. J. Clin. Nutr.* 43:910–916, 1986.
- 24. RAUF, M. J., C. A. MACERA, D. W. TRONE, R. A. SHAFFER, and S. K. BRODINE. Epidemiology of stress fracture and lowerextremity overuse injury in female recruits. *Med. Sci. Sports Exerc.* 38:1571–1577, 2006.
- RECKER, R. R., K. M. DAVIES, S. M. HINDERS, R. P. HEANEY, M. R. STEGMAN, and D. B. KIMMEL. Bone gain in young adult women. *JAMA* 268:2403–2408, 1992.
- RUFFING, J. A., F. COSMAN, M. ZION, et al. Determinants of bone mass and bone size in a large cohort of physically active young adult men. *Nutr. Metab.* 3:14, 2006.
- SCHMIDT BRUDVIG, T. J., T. D. GUDGER, and L. OBERMEYER. Stress fractures in 295 trainees: a one-year study of incidence as related to age, sex, and race. *Mil. Med.* 148:666–667, 1983.
- SEEMAN, E. Periosteal bone formation—a neglected determinant of bone strength. N. Engl. J. Med. 394:320–323, 2003.
- SNYDER, R. A., M. C. KOESTER, and W. R. DUNN. Epidemiology of stress fractures. *Clin. Sports Med.* 25:37–52, 2006.
- ZANKER, C. L., and I. L. SWAINE. Relation between bone turnover, oestradiol, and energy balance in women distance runners. *Br. J. Sports Med.* 32:167–171, 1998.

STRESS FRACTURES IN YOUNG FEMALE RUNNERS