

## ONLINE FIRST

# Prospective Study of Physical Activity and Risk of Developing a Stress Fracture Among Preadolescent and Adolescent Girls

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**Objective:** To identify predictors of developing a stress fracture among adolescent girls during a 7-year period.

**Design:** Prospective cohort study.

**Setting:** Adolescent girls living throughout the United States.

**Participants:** A total of 6831 girls aged 9 to 15 years at baseline in the Growing Up Today Study, an ongoing prospective cohort study.

**Main Exposures:** Exposures were assessed by self-report questionnaires completed by adolescent girls in 1996, 1997, 1998, 1999, 2000, 2001, and 2003. The adolescent girls' history of stress fracture, including age when fracture occurred and site, were reported by their mothers, who are registered nurses, in 2004. Cox proportional hazards models were used in the analysis.

**Main Outcome Measure:** Incident stress fracture that occurred between 1997 and 2004.

**Results:** During 7 years of follow-up, 267 girls (3.9%) developed a stress fracture. Independent of age, age at menarche, family history of fracture, and hours per week of low- and moderate-impact activity, hours per week of running (hazard ratio=1.13; 95% confidence interval, 1.04-1.23), basketball (hazard ratio=1.12; 95% confidence interval, 1.03-1.23), and cheerleading/gymnastics (hazard ratio=1.12; 95% confidence interval, 1.02-1.22) were significant predictors of developing a stress fracture. No other type of high-impact activity was associated with an increased risk.

**Conclusion:** Girls who engage in running, basketball, cheerleading, or gymnastics should be encouraged to include varied training in lower-impact activities to decrease the cumulative amount of impact in order to minimize their risk of stress fractures.

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**D**URING ADOLESCENCE, more than half of adult bone calcium is acquired; peak bone mineral density (BMD), a major determinant of a woman's long-term risk of osteoporosis,<sup>1,2</sup> is thought to be achieved by early adulthood.<sup>3,4</sup> Although BMD is genetically determined to a large extent,<sup>5</sup> physical activity is an important modifiable determinant of bone health. However, the relationship between activity and BMD is complex. Weight-bearing activity stimulates bone remodeling and thus increases BMD,<sup>6,7</sup> but very high levels of activity may be detrimental to bone health<sup>8,9</sup> and increase the risk of stress fracture.

Among females, other suspected risk factors for developing a stress fracture include disordered eating<sup>10</sup> and irregular menstrual cycles, both of which may result in a deficient estrogen status that can

counteract the beneficial effects of exercise on BMD.<sup>11-14</sup> Delayed menarche has also been shown to be associated with deficits of the peripheral and axial skeleton, implicating estrogen deficiency as detrimental for bone accretion.<sup>15,16</sup> Although stress fractures are relatively uncommon, they affect as many as 20% of young female athletes and military recruits.<sup>17</sup>

Despite a growing concern about suboptimal bone health in adolescents, particularly among girls and athletes, few prospective studies have been conducted.<sup>18</sup> Most have used specialized samples, so it is unclear to whom their results are generalizable. Moreover, few studies have been conducted in samples of adolescent athletes, and no prospective studies to our knowledge have examined factors related to stress fractures in girls younger than 18 years. Therefore, the prevalence and predictors of stress fracture among children and adolescents are essen-

tially unknown. In addition, the results from studies of older adolescent girls have not been consistent with those of adult women.<sup>19-24</sup> As adolescence is a sensitive period for bone health, high levels of physical activity, particularly when accompanied by inadequate caloric intake, can result in suboptimal growth.<sup>8</sup> However, high levels of activity before puberty may result in greater BMD.<sup>25,26</sup> Thus, adolescence may be the most important period for examining factors predictive of stress fracture.

Although there is a dearth of prospective research on stress fracture, the results on sex differences from cross-sectional studies clearly demonstrate that female athletes have a much greater risk of sustaining stress fracture than do male athletes. In a large retrospective study of 2989 athletes seen over a 14-year period, Iwamoto et al<sup>27</sup> observed female track-and-field athletes to have a more than 4-fold greater risk of developing stress fractures than their male counterparts. Similar sex differences have been observed in Israeli military recruits.<sup>28</sup>

Athletic participation by females has increased dramatically since the Title IX legislation was enacted in 1972. Current estimates are that 3 million girls in the United States participate in high school sports,<sup>29</sup> but little is known about their risk of stress fracture. Because youth sports have become more specialized and training programs have become more rigorous and extend over multiple seasons, it is of critical importance to understand the activity patterns that increase risk of stress fracture. The aim of our investigation was to assess the relationship between the type and quantity of physical activity and the risk of developing a stress fracture over a 7-year period among 6831 preadolescent, adolescent, and young adult girls in the Growing Up Today Study (GUTS).

## METHODS

### OVERVIEW

The Growing Up Today Study was established by recruiting the children of women participating in the Nurses' Health Study II (NHS II); these children were aged 9 to 14 years in 1996. Using NHS II data, a detailed letter was sent to identified mothers who had children between the ages of 9 and 14 years. The purposes of GUTS were explained, and the mothers were asked to provide parental consent for their children to enroll. Additional details have been reported previously.<sup>30</sup> Approximately 68% of the girls (n=9039) and 58% of the boys (n=7843) returned completed questionnaires, thereby assenting to participate in the cohort. The GUTS project and the analyses using data from GUTS participants and their mothers in the NHS II were approved by the Human Subjects Committee, Brigham and Women's Hospital; this study was approved by that committee as well as the Committee on Clinical Investigation, Children's Hospital Boston.

### MEASURES

In fall 1996 through 2003, the GUTS participants received a questionnaire every 12 to 18 months assessing a variety of factors. Self-reported weight, height, and age at menarche were assessed on all questionnaires.

Body mass index (BMI; calculated as weight in kilograms divided by height in meters squared) was calculated using self-

reported weight and height information. Children were classified as overweight or obese based on the International Obesity Task Force cutoffs,<sup>31</sup> which are age and sex specific and provide comparability in assessing overweight and obesity from adolescence to adulthood. The validity of self-reported weight and height among preadolescents and adolescents has been investigated by several groups of researchers,<sup>32-34</sup> and the results show that young people provide valid information on weight and height.

Menstrual status was assessed annually from 1996 through 2005. Girls were asked whether their menstrual periods had started. Girls who answered yes were asked for the age when periods began (age at menarche).

Weight control behaviors were assessed with questions adapted from the Youth Risk Behavior Surveillance System questionnaire.<sup>35</sup> Purging was assessed with 2 questions: "during the past year, how often did you make yourself throw up to keep from gaining weight?" and "during the past year, how often did you take laxatives to keep from gaining weight?" The purging questions have been validated in the GUTS cohort. Among the girls, the specificity and negative predictive values of self-reported purging (0.87 and 0.99, respectively) were high, thereby demonstrating that the questionnaire did an excellent job at classifying girls who did not purge.

Physical activity was assessed with 17 questions on hours per week within each of the 4 seasons that a participant engaged in a specific activity (eg, volleyball, soccer). Hours per week of moderate and vigorous activity were computed as the sum of average hours per week engaged in basketball, baseball, biking, dance/aerobics, hockey, running, swimming, skating, skateboarding, soccer, tennis, cheerleading/gymnastics, lifting weights, volleyball, and karate (copies of the questionnaire can be seen at <http://gutsblog.com/links/questionnaires.html>). Reports of an average of more than 40 hours per week were considered implausible and therefore set to missing and not used in the analysis. High-impact activity was computed as the sum of average hours per week engaged in basketball, running, soccer, tennis, cheerleading/gymnastics, and volleyball. Medium-impact activity was computed as the sum of average hours per week engaged in baseball, dance/aerobics, hockey, and karate.<sup>36</sup> Nonimpact activity was computed as the sum of average hours per week engaged in biking, swimming, skating, skateboarding, and lifting weights.

History of low BMD and osteoporosis was collected in 2005 as part of the NHS II. Girls whose mothers reported a history of low BMD or osteoporosis were classified as having a family history of low BMD or osteoporosis.

### OUTCOME

The outcome was incident stress fracture. In 2004, the mothers of the GUTS participants, who are registered nurses participating in the ongoing NHS II, were sent a brief questionnaire. They were asked whether a doctor has ever said that their child had a stress fracture. If the mother indicated that her child had a history of stress fracture, she was asked to report the age at diagnosis, site (foot, arm, leg, wrist, or other), whether the stress fracture was sports related, and the time off from playing sports (no time off, <1 month, 1-2 months, or ≥3 months). Cases were defined as GUTS participants whose mothers reported that they were diagnosed with a stress fracture at an age older than when they entered the GUTS cohort in fall 1996. Children who were the same age at diagnosis and entry into GUTS were classified as prevalent cases and were not included in the analysis. Reports of a stress fracture without an age at diagnosis were excluded from the analysis because it would be impossible to know whether the cases occurred in the eligible period.

## SAMPLE

Participants included 9039 girls who completed 1 or more questionnaires. Girls were excluded if the mother did not respond to the 2004 mothers' questionnaire (n=2109), the mother reported that her daughter had a stress fracture in 1996 (n=58), or the mother did not report information on stress fracture (n=41). Furthermore, girls were excluded if they did not provide plausible information or were missing information on physical activity or if they were missing plausible information on weight or height. After these exclusions, 6831 girls aged 9 to 15 years in 1996 remained for analysis.

## DATA ANALYSIS

All analyses were conducted with SAS version 6 statistical software (SAS Institute, Inc, Cary, North Carolina). Cox proportional hazards models were used for all multivariate analyses. Statistical models controlled for age and family history of low BMD or osteoporosis.

Hours per week of moderate or vigorous activity were initially divided into 8 groups: less than 1.0, 1.0 to 3.9, 4.0 to 7.9, 8.0 to 11.9, 12.0 to 15.9, 16.0 to 19.9, 20.0 to 24.9, and 25.0 or more hours per week. Owing to small group sizes, for the purpose of analysis the highest 3 categories were collapsed into 1 group, for a total of 6 groups. For multivariate analyses, the lowest 2 categories were also collapsed, giving 5 total groups (<4.0, 4.0-7.9, 8.0-11.9, 12.0-15.9, and  $\geq$ 16.0 hours per week). Participants who reported less than 4.0 hours per week of moderate or vigorous activity were used as the reference group. All *P* values are 2-sided, with *P* < .05 considered statistically significant.

## RESULTS

In 1996, the mean age of the girls was 12.0 years and 44.1% of the girls had achieved menarche. The mean BMI of the girls was 19.0; 8.6% of the girls were underweight and 19.8% were overweight or obese. Approximately 2.5% of the girls engaged in disordered eating. Among the girls, 96.4% engaged in moderate or vigorous activity for at least 4.0 hours per week (**Table 1**).

During 7 years of follow-up, 267 girls (3.9%) developed a stress fracture. The older a girl was at menarche, the higher her risk of developing a stress fracture was. Each 1-year delay in onset of menarche was associated with an approximate 30% increase in risk (hazard ratio [HR]=1.32; 95% confidence interval [CI], 1.11-1.57). Family history of osteoporosis or low BMD was strongly related to the risk of incident stress fracture. Girls reporting a family history of osteoporosis or low BMD were almost twice as likely to develop a stress fracture (HR=1.95; 95% CI, 1.24-3.07). In addition, risk of stress fracture increased with time spent engaged in physical activity (**Table 2**). Adjusting for age, age at menarche, and history of low BMD increased the associations. Girls who engaged in 8.0 or more hours of activity per week were twice as likely as their peers who engaged in less than 4.0 hours of activity to develop a stress fracture.

The association of hours per week of moderate or vigorous activity with risk of developing a stress fracture was driven by the impact of activities (**Table 3**). Neither non-impact activity (HR=0.98; 95% CI, 0.93-1.04) nor medium-impact activity (HR=1.01; 95% CI, 0.94-1.09) was predictive of risk, but each hour of high-impact activity (basketball,

**Table 1. Baseline Demographic and Lifestyle Characteristics of 6831 Preadolescent, Adolescent, and Young Adult Girls in the Growing Up Today Study**

Characteristic	Value (N=6831)
Age, mean (SD), y	12.0 (1.6)
BMI, mean (SD)	19.0 (3.3)
Age at menarche, mean (SD), y	11.8 (1.0)
Postmenarcheal, No. (%)	3008 (44.1)
Underweight, No. (%)	570 (8.6)
Overweight or obese, No. (%)	1309 (19.8)
Disordered eating, No. (%)	169 (2.5)
Family history of low BMD or osteoporosis, No. (%)	707 (10.4)
Moderate or vigorous activity, No. (%), h/wk <sup>a</sup>	
<1.0	12 (0.2)
1.0-3.9	222 (3.4)
4.0-7.9	918 (14.0)
8.0-11.9	1310 (19.9)
12.0-15.9	1239 (18.8)
16.0-19.9	988 (15.0)
20.0-24.9	734 (11.2)
$\geq$ 25.0	1033 (15.7)
Activity, mean (SD), h/wk	
Nonimpact	4.7 (3.3)
Intermediate impact	2.2 (2.4)
High impact <sup>b</sup>	5.2 (4.1)

Abbreviations: BMD, bone mineral density; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared).

<sup>a</sup>Sum of basketball, baseball, biking, dance/aerobics, hockey, running, swimming, skating, skateboarding, soccer, tennis, cheerleading/gymnastics, lifting weights, volleyball, and karate.

<sup>b</sup>Sum of basketball, running, soccer, tennis, cheerleading/gymnastics, and volleyball.

**Table 2. Associations of Age at Menarche and Activity With Incident Stress Fracture Among 6831 Preadolescent, Adolescent, and Young Adult Girls in the Growing Up Today Study**

Predicting Variable	HR (95% CI)	
	Adjusted for Age and Family History	Fully Adjusted <sup>a</sup>
Age at menarche, y	1.32 (1.11-1.57)	1.34 (1.12-1.62)
Activity, h/wk <sup>b</sup>		
<4.0	1 [Reference]	1 [Reference]
4.0-7.9	1.27 (0.67-2.43)	1.40 (0.70-2.80)
8.0-11.9	1.65 (0.88-3.11)	1.94 (0.98-3.83)
12.0-15.9	2.41 (1.28-4.54)	2.78 (1.41-5.47)
$\geq$ 16.0	2.67 (1.46-4.85)	2.65 (1.37-5.12)

Abbreviations: CI, confidence interval; HR, hazard ratio.

<sup>a</sup>The HRs are from Cox proportional hazards models adjusted for age, body mass index, family history of low bone mineral density or osteoporosis, and the covariates listed in the first column.

<sup>b</sup>Sum of basketball, baseball, biking, dance/aerobics, hockey, running, swimming, skating, skateboarding, soccer, tennis, cheerleading/gymnastics, lifting weights, volleyball, and karate.

running, soccer, tennis, cheerleading/gymnastics, and volleyball) increased the risk of stress fracture by approximately 8% (HR=1.08; 95% CI, 1.05-1.12).

When considered individually, risk of stress fracture was associated with only 3 types of high-impact activity. Running (HR=1.13; 95% CI, 1.04-1.23), basketball (HR=1.12; 95% CI, 1.03-1.23), and cheerleading/

**Table 3. Associations of Nonimpact, Medium-Impact, and High-Impact Activity With Incident Stress Fracture Among 6831 Preadolescent, Adolescent, and Young Adult Girls in the Growing Up Today Study**

Predicting Variable	HR (95% CI)	
	Adjusted for Age and Family History	Adjusted for All Covariates in Model <sup>a</sup>
Age at menarche, y	1.32 (1.11-1.57)	1.34 (1.11-1.61)
Activity, h/wk		
Nonimpact <sup>b</sup>	0.98 (0.92-1.03)	0.98 (0.93-1.04)
Medium impact <sup>c</sup>	1.02 (0.95-1.09)	1.01 (0.94-1.09)
High impact <sup>d</sup>	1.09 (1.06-1.13)	1.08 (1.05-1.12)

Abbreviations: CI, confidence interval; HR, hazard ratio.

<sup>a</sup>The HRs are from Cox proportional hazards models adjusted for age, body mass index, family history of low bone mineral density or osteoporosis, and the covariates listed in the first column.

<sup>b</sup>Sum of biking, swimming, skating, skateboarding, and lifting weights.

<sup>c</sup>Sum of baseball, dance/aerobics, hockey, and karate.

<sup>d</sup>Sum of basketball, running, soccer, tennis, cheerleading/gymnastics, and volleyball.

**Table 4. Associations of Type of Activity With Incident Stress Fracture Among 6831 Preadolescent, Adolescent, and Young Adult Girls in the Growing Up Today Study**

Predicting Variable	HR (95% CI)	
	Adjusted for Age and Family History	Adjusted for All Covariates in Model <sup>a</sup>
Age at menarche, y	1.32 (1.11-1.57)	1.35 (1.12-1.63)
Family history	1.95 (1.24-3.07)	1.81 (1.10-2.99)
Activity, h/wk		
Nonimpact	0.98 (0.92-1.03)	0.96 (0.90-1.02)
Medium impact	1.02 (0.95-1.09)	0.99 (0.92-1.07)
Specific activity		
Running	1.14 (1.06-1.22)	1.13 (1.04-1.23)
Basketball	1.19 (1.10-1.28)	1.12 (1.03-1.23)
Soccer	1.09 (1.01-1.18)	1.05 (0.96-1.15)
Cheerleading/gymnastics	1.12 (1.04-1.21)	1.12 (1.02-1.22)
Tennis	0.85 (0.66-1.10)	0.86 (0.66-1.12)
Volleyball	1.07 (0.96-1.20)	1.04 (0.92-1.18)

Abbreviations: CI, confidence interval; HR, hazard ratio.

<sup>a</sup>The HRs are from Cox proportional hazards models adjusted for age, body mass index, family history of low bone mineral density or osteoporosis, and the covariates listed in the first column.

gymnastics (HR=1.12; 95% CI, 1.02-1.22) were the only activities independently predictive of developing a stress fracture (**Table 4**).

Being underweight (HR=1.35; *P*=.40), being overweight (HR=0.96; *P*=.90), and engaging in disordered eating (HR=0.92; *P*=.88) were not associated with the risk of developing a stress fracture.

## COMMENT

Our study, which to our knowledge is the first large general population-based study of incident stress fractures among adolescent and young adult girls, found that 3.9% of the girls developed a stress fracture. Because it is the first prospective study in a general population sample,

it is difficult to compare our results with estimates from other studies. Not surprisingly, we observed a lower incidence than has been observed in smaller studies of collegiate athletes,<sup>22</sup> who represent a high-risk group.

Age at menarche was a significant predictor of risk of developing a stress fracture. The older a girl was when menses began, the higher her risk was. This result was not unexpected because there is a pronounced increase in BMD toward the end of the pubertal growth spurt, which is typically when menses begin.<sup>2</sup> Bone mineral density is one of the main determinants of a bone's ability to withstand loading.<sup>2,17</sup> Moreover, a later age at menarche would cause a prolonged period of low serum estrogen levels, which should increase the risk of developing a stress fracture. However, the results from other studies have been mixed. Bennell et al<sup>22</sup> prospectively studied a small sample of young adult female track-and-field athletes and found that lower BMD and a history of menstrual disturbances were significant predictors of stress fracture. On the other hand, a prospective study of 50 US collegiate track-and-field athletes found that menstrual history was not predictive of stress fracture.<sup>24</sup> Other studies have been too small to detect associations.<sup>37,38</sup>

Despite our large sample size, we did not observe associations between weight status (ie, being underweight or overweight) or disordered eating and risk of stress fracture. Thus, our results are not consistent with those from some previous cross-sectional<sup>39</sup> and case-control<sup>38</sup> studies. Barrack et al<sup>40</sup> failed to observe an association between disordered eating and low BMD among adolescent girls. Because low BMD is related to fracture risk in children,<sup>41</sup> our findings are consistent with several other studies that did not find an association between disordered eating and stress fracture or high risk of stress fracture. Moreover, only lowest adult weight, but not current weight, was associated with risk of stress fracture in a prospective study of 3758 female military recruits undergoing basic training.<sup>42</sup> It is possible that we did not observe an association with disordered eating or body weight because we had a relatively small number of girls who were underweight or engaging in disordered eating; also, we controlled for family history of low BMD and osteoporosis, which others have found to be a strong predictor of risk.<sup>38</sup> Approximately 80% of the variability in BMD is attributable to genetic factors.<sup>2</sup> Thus, if the risk associated with being underweight is small and correlates with weight and maternal history of low BMD or osteoporosis, controlling for family history would attenuate the association with stress fracture.

Our strongest findings relate to the association between physical activity and fracture risk. These results have important practical implications. We observed that girls engaging in 8.0 or more hours of activity per week were about twice as likely as their less active peers to develop a stress fracture. The association was driven by hours per week engaged in 3 activities: running, basketball, and cheerleading/gymnastics. These results are consistent with other studies that have observed high rates of stress fracture among collegiate female runners.<sup>43</sup> Previous studies of gymnasts and cheerleaders have been too small to have sufficient statistical power, but there is a biological plausibility to such an association. Cheerleading and gym-

nastics involve repeatedly jumping and landing, which cause particularly high stresses on bone<sup>44</sup>; thus, there is physiological support for our observed association. Our results imply that clinicians, athletic trainers, coaches, and others who supervise athletic programs for young female runners, basketball players, gymnasts, and cheerleaders should promote including varied training in non-impact or intermediate-impact activities to decrease the cumulative amount of impact as well as reducing the hours spent training in their high-impact sport.

This study has several limitations. Our cohort is more than 90% white, and it is not clear whether the results are generalizable to nonwhite female adolescents and young adults. However, white individuals are at high risk for stress fracture<sup>45</sup> and are thus an important group to study. In addition, we relied on self-reports from the mothers of the participants to ascertain stress fracture. This may have resulted in some misclassification, with a small number of individuals mistakenly included as cases and a small number of cases that the mother did not know about and therefore did not report. However, requiring radiographic confirmation, which would have been extremely difficult to obtain in this sample living throughout the United States, might also result in some misclassification because of the difficulty in distinguishing stress fractures from stress reactions. Nevertheless, the misclassification due to self-reported stress fracture likely slightly biased our results toward the null. Also, we did not have information on some of the other predictors of stress fracture, such as factors related to biomechanics and bone microarchitecture. The strengths of the study, however, far outweigh the limitations. To our knowledge, this is the first large prospective study of stress fracture. Moreover, this is the largest prospective study of adolescents. Another strength is that exposure information was collected every 12 to 24 months and was ascertained before the onset of the stress fracture. We also had information on the mother's history of low BMD and osteoporosis as well as information from the participant on age at menarche, body weight, disordered eating, and physical activity.

Our study observed that high-impact activities, specifically basketball, running, and gymnastics/cheerleading, significantly increase risk for stress fracture among adolescent girls. Thus, there is a need to establish training programs that are rigorous and competitive but include varied training in lower-impact activities to decrease the cumulative amount of impact in order to reduce the risk of stress fracture.

More research is needed to understand whether dietary intake, disordered eating, and weight history affect risk. Physical activity during childhood and moderate activity during adolescence may increase BMD and thus help to protect against osteoporosis in adulthood. Therefore, clinicians, parents, and coaches should continue to promote activity to young girls but should make sure that training hours are not excessive, thereby not compromising bone health. This is particularly critical since youth sports have moved away from playing a different sport in each season to focusing on a single sport throughout the year.

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