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Vitamin D, Calcium, and Dairy Intakes and Stress Fractures Among Female Adolescents

Kendrin R. Sonneville, ScD, RD, **Catherine M. Gordon, MD, MSc**, **Mininder S. Kocher, MD, MPH**, **Laura M. Pierce, BA**, **Arun Ramappa, MD**, and **Alison E. Field, ScD**
Division of Adolescent/Young Adult Medicine, Department of Medicine, Children's Hospital Boston and Harvard Medical School, Boston, MA (KS, CM, LP, AF). Channing Laboratory, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA (AF). Department of Epidemiology, Harvard School of Public Health, Boston, MA (AF). Department of Endocrinology, Children's Hospital Boston, Boston, MA (CG). Division of Sports Medicine, Department of Orthopedic Surgery, Beth Israel Deaconess Medical Center, Boston, MA (AR). Department of Orthopedic Surgery, Children's Hospital Boston, and Harvard Medical School, Boston, MA (MK).

Abstract

Objective—To identify whether calcium, vitamin D, and/or dairy intake are prospectively associated with stress fracture risk among female adolescents.

Design—Prospective cohort study.

Setting—Adolescent girls living throughout the United States.

Participants—A total of 6712 girls ages 9 to 15 years at baseline in the Growing Up Today Study, an ongoing prospective cohort study.

Main Exposure—Dairy, calcium, and vitamin D intake assessed by food frequency questionnaire every 12-24 months between 1996 and 2001.

Main Outcome Measures—Incident stress fracture that occurred between 1997 and 2004, as reported by mother's of the participants in 2004. Cox proportional hazards models were used to examine associations.

Results—During 7 years of follow-up, 3.9% of females developed a stress fracture. Dairy and calcium intake were unrelated to risk of developing a stress fracture. However, vitamin D intake was inversely related to stress fracture risk. The multivariable-adjusted hazard ratio (HR) of stress fracture for the highest versus the lowest quintile of vitamin D was 0.49 (95% CI=0.24-1.01; p_{trend}=0.07). We conducted a stratified analysis to estimate the association between vitamin D intake and stress fracture risk among girls participating in ≥1 hour/day of high-impact activity, among whom 90% of the stress fractures occurred, and found that higher vitamin D intake predicted significantly lower risk of stress fracture (p_{trend}=0.04)

Corresponding Author/Requests for Reprints: Dr. Kendrin Sonneville, Children's Hospital Boston, Division of Adolescent/Young Adult Medicine, 300 Longwood Avenue (AU-514), Boston, MA 02115, Phone: (617) 355-0922, Fax: (617) 730-0004, kendrin.sonneville@childrens.harvard.edu.

All of the authors were involved in the concept and design. Drs. Sonneville and Field were responsible for the analysis and interpretation of data and drafting of the manuscript. All authors contributed to revising the manuscript.

Dr. Sonneville, Ms. Pierce, Dr. Ramappa, and Dr. Field have no conflicts of interest to declare.

Conclusions—Vitamin D intake is associated with lower stress fracture risk among adolescent girls who engage in high levels of high-impact activity. Neither calcium nor dairy intake were prospectively associated with stress fracture risk.

Introduction

As participation in organized sports and athletic specialization among children and adolescents has increased, so too has the recognition of overuse injuries[1,2]. Stress fractures, which occur when stresses on bone exceed the bone's capacity to withstand and heal from those forces, are a particularly common type of injury seen in both competitive and recreational athletes[3]. We have previously reported that nearly 4% of the adolescent and young adult girls in our cohort developed a stress fracture during 7 years of follow-up[4].

The risk of stress fracture is influenced by extrinsic (training regimen, type of sport), intrinsic (gender, race/ethnicity), biomechanical, anatomic, and hormonal factors[3]. Nutritional intake, particularly calcium, which is needed for bone mineralization, and vitamin D, which is needed for maintaining calcium homeostasis and bone remodeling, have been suggested as protective against stress fractures[3]. Although calcium and calcium-rich dairy products are routinely encouraged for optimal bone health, the evidence for this recommendation has been challenged[5,6]. Further, while vitamin D deficiency is relatively common among adolescents[7,8], data are lacking on the role of vitamin D intake, whether sufficient or in excess of recommended intake[9], on bone health[10,11].

Adolescence is the most critical period for bone mineral accrual[12-16] and therefore, is considered an important window for the prevention of long-term consequences of low bone mineral content, such as postmenopausal osteoporosis. The relationship between dietary intake during adolescence and short-term consequences of low bone mineral content, however, is understudied. In a cross-sectional analysis of adolescent girls, dairy, calcium, and vitamin D intake were all unrelated to stress fractures after controlling for age[17]. Because bone mineral is accrued over time, however, the contribution of long-term dietary exposure on stress fracture risk cannot be examined in cross-sectional studies or studies of short duration.

Physical activity is the primary modifiable stimulus for increased bone growth and development in adolescents[5] and weight-bearing activity during childhood and adolescence seems to be a more important factor for peak bone mass than dietary intake[18]. Despite known benefits of physical activity on bone mineral content[19], there is a threshold over which the risk of stress fracture increases significantly among adolescent girls[17]. The combined effects of diet and exercise on bone health are still unknown. More research is needed to explore whether protective dietary factors could mitigate the risk of stress fractures among adolescents who regularly engage in high-impact activities.

Stress fractures are a source of significant morbidity among female athletes during adolescence[17]. However, few studies have identified modifiable risk factors for stress fractures among female adolescents, other than participation in high-impact sports[4,17]. As such, prospective studies are needed to identify other modifiable risk factors for stress fractures among this population. The aim of the current study was to identify dietary factors that are prospectively associated with risk of stress fractures among female adolescents and, in particular, those who are at highest risk for stress fractures.

Subjects and Methods

Participants were members of the Growing Up Today Study (GUTS), an ongoing cohort study of adolescents throughout the United States that was established in 1996. Participants in GUTS are the offspring of women in the Nurses' Health Study[20]. Mothers of children who were between the ages of 9 and 14 years in 1996 were sent a detailed letter that outlined the purposes of GUTS and were asked to provide parental consent for their children to enroll. Of those invited, 68% of their daughters (n = 9039) returned completed questionnaires, thereby assenting to participate in the cohort. Additional details of enrollment are reported elsewhere[21].

Exposures

Dietary intake, including intake of dairy foods and soda, was assessed annually from 1996 through 1999 and again in 2001 using the previously validated Youth/Adolescent Questionnaire (YAQ)[22,23]. The YAQ is a self-administered, semi-quantitative, food frequency questionnaire that assesses intake over the past year using portion sizes for foods that are appropriate for each age as determined from analyses of national nutrition data[22,23]. The development, reproducibility, and validation of the YAQ has been previously described[22,23]. Briefly, participants were asked how frequently they used a typical portion size of specified foods on average during the past year. Nutrient intakes were computed by multiplying the frequency of consumption of each unit of food and the nutrient content of the specified portions based on the nutrient values in foods obtained from US Department of Agriculture sources and food manufacturers and includes calcium or vitamin D in foods routinely fortified with these nutrients[24].

Participants also reported calcium supplement and multivitamin use, physical activity, menstrual status, weight, and height annually from 1996 through 2001. We calculated body mass index (BMI) from self-reported weight and height information. Despite concern that self-reported weight, and thus BMI, are biased, a strong correlation between BMI calculated from self-reported versus measured height and weight has been observed in adolescent samples[25,26].

Total number of hours of physical activity per week was assessed by asking participants to report the number of hours they spent doing 18 different types of physical activity in each of the 4 seasons. Reported physical activity that exceeded 40 hours per week was considered implausible and was not used in the analysis. High-impact activity was computed as the sum of the average hours per week a participant reported engaging in basketball, running, soccer, tennis, cheerleading, or volleyball[17]. Girls who reported participating in an average of ≥1 hour/day of high-impact activity were defined as having high levels of high-impact activity.

On each questionnaire, girls were asked whether their menstrual periods had started and, if yes, how old they were when their periods began. Girls were classified as having a family history of low bone density or osteoporosis if their mothers indicated having a history of low bone density or osteoporosis on the 2005 Nurses' Health Study questionnaire.

Outcome

Incident stress fracture was the primary outcome. Stress fractures were reported in 2004 by the participants' mothers, who were registered female nurses participating in the Nurses' Health Study II. Mothers were asked whether a doctor had ever said that their child had a stress fracture and were asked to report age and site (foot, arm, leg, wrist, or other) of the stress fracture.

Sample for Analysis

After excluding cases that occurred prior to enrollment in GUTS in fall of 1996 and reports of a stress fracture without an age at diagnosis, 6712 girls whose mothers responded to the question about stress fractures were included in the analysis.

Ethics

GUTS was approved by the Human Subjects Committee at Brigham and Women's Hospital. This analysis was approved by that committee and by the Committee on Clinical Investigation at Children's Hospital Boston.

Statistics

Cox proportional hazards models were used for all multivariate analyses. We modeled calcium and vitamin D intake two ways: calcium and vitamin D from dietary intake only and calcium and vitamin D from both dietary and supplement intake. Calcium and vitamin D were modeled as quintiles with the lowest quintile serving as the reference. Dairy intake was modeled as servings per day (0, 1, 2, and ≥ 3) with 0 servings as the reference.

All models controlled for age. Fully-adjusted models additionally controlled for known predictors of bone mineral content or stress fracture in children including BMI, age at menarche, physical activity, and family history[5,13]. Models assessing the association with quintiles of calcium intake additionally adjusted for vitamin D intake (as a continuous variable centered at the mean) and models assessing the association with vitamin D intake additionally adjusted for calcium intake (as a continuous variable centered at the mean). In secondary analyses we further controlled for soda intake, which has been suggested as a potential confounder of a calcium-bone health association.

Because we have previously shown that high levels of high-impact activity increases the risk of developing a stress fracture[4], we investigated whether associations with dietary intake were modified by activity level. In these analyses we stratified by level of high-impact activity (<1 hour/day of high-impact activity, ≥1 hour/day of high-impact activity).

We report hazard ratios (HR) and 95% confidence intervals (CI) using the lowest intake category as the referent group, as well as the *p* for trend. All analyses were conducted with the SAS statistical software package (version 9.1; SAS Institute, Cary, NC).

Results

Among the 6712 girls, 9% were underweight and 20% were overweight or obese (Table 1). Approximately 30% of the girls engaged in ≥ 1 hour per day of high-impact activity. The majority of the sample (94%) was white and 10% had a mother with a history of low bone density or osteoporosis. The girls consumed a mean (SD) of 2.0 (1.3) servings of dairy foods per day. At baseline, mean (SD) calcium (1182 [478] mg) and vitamin D (376 [183] IU) intakes were below the Recommended Dietary Allowance (RDA) for girls between the ages of 9 and 18, 1300 mg and 600 IU, respectively. As expected, dairy intake was strongly correlated to calcium (r=090, p <0.0001) and vitamin D (r=0.79, p <0.0001) intake. Calcium and vitamin D intake were also highly correlated (r=0.84, p<0.0001).

During 7 years of follow-up, 3.9% of girls developed a stress fracture. Most (90%) of the stress fractures occurred in girls who were participating in ≥1 hour/day of high-impact activity. There was no evidence of a protective association between dairy intake and stress fracture risk. Girls consuming 3 or more servings per day of dairy were no more likely (hazard ratio (HR)=1.02, 95% confidence interval (CI)=0.65, 1.61) than their peers consuming no dairy to develop a stress fracture (Table 2). Similarly, there was no suggestion that higher calcium intake from both dietary sources and supplements was protective against stress fractures. Girls in the highest quintile were no less likely (HR=1.57, 95%=CI 0.77, 3.17) than girls in the lowest quintile to develop a stress fracture.

Although there did not appear to be an association between vitamin D and fracture risk in age-adjusted models, after adjusting for confounders, there was a suggestion that vitamin D from both dietary sources and supplements was protective against stress fractures. Girls in the highest quintile of vitamin D intake had a 50% lower risk of stress fractures compared to those who were in the lowest quintile (HR=0.49, 95% CI=0.24-1.01; p_{trend}=0.07).

In an analysis stratified by level of high impact activity, vitamin D was associated with lower risk of incident stress fracture among girls who participate in ≥1 hour/day of high-impact activity (Table 3). Among these highly active participants, girls in the highest quintile vitamin D intake levels had a 52% lower risk of stress fractures compared to those who were in the lowest quintile (HR=0.48, 95% CI=0.22, 1.02; p_{trend}=0.04). High dairy intake was unrelated to stress fracture risk among the highly active girls (HR=1.15, 95% CI=0.71, 1.84), whereas, highly active girls with high calcium intake were at increased risk of fracture (HR=2.14, 95% CI=0.98, 4.69).

When the analyses were further adjusted for soda intake, the results were virtually unchanged (data not shown). Moreover, when the analyses were restricted to calcium and vitamin D intake from foods only (i.e., not including supplement intake), the results were not different from the finding reported for models including calcium and vitamin D from both dietary sources and supplements.

Comment

We found that, among 6712 preadolescent and adolescent girls living throughout the United States, vitamin D intake was predictive of a lower risk of developing a stress fracture, particularly among those girls who participated in ≥1 hour/day of high-impact activity and thus were at increased risk of fracture. In contrast, there was no evidence that calcium or dairy intake were protective against developing a stress fracture, nor that soda intake was predictive of an increased risk of stress fractures or confounded the association between dairy, calcium, or vitamin D intake and fracture risk. In a stratified analysis, we observed that high calcium intake was associated with greater risk of developing stress fractures. This unexpected finding warrants further inquiry.

Our findings support the Institute of Medicine’s recent increase in the RDA for vitamin D for adolescents from 400 IU to 600 IU[9]. We observed a linear trend for lower stress fracture risk with increasing vitamin D intake such that those in the highest quintile had about 50% the risk of developing a stress fracture compared to those in the lowest quintile. Because too few participants had a vitamin D intake above 600 IU, we were unable to explore the potential benefits of vitamin D intake in excess of the RDA. Moreover, at the time the data were collected, vitamin D supplements were uncommon and, thus, we were unable to assess whether intakes in excess of 800 to 1000 IU, which have been recommended by some experts[27-29], lowered risk of stress fracture. Future research is needed to ascertain whether the risk of stress fracture can be lowered further with higher doses of vitamin D.

No previous longitudinal studies have examined the influence of dietary intake on the risk of developing a stress fracture among a general population of female adolescents. Thus, it is challenging to compare our results to prior studies, many of which have focused on specialized high risk populations, such as competitive athletes. Our findings are not consistent with those reported in a prospective study of 125 young adult female competitive distance runners which found that higher intakes of calcium and dairy products predicted lower rates of stress fracture and higher intakes of vitamin D, calcium, and dairy foods were all associated with significant gains in hip bone mineral density over the 2-years of follow-up[30]. The discrepancy in results could be due to the fact that our sample included preadolescents and adolescents, which are critical windows in bone development. Our findings are supported by related evidence from genomic analyses[31] which have reported a relationship between vitamin D receptor gene polymorphisms and bone mineral density in a sample of adolescent girls[32] and risk of stress fracture in an adult sample[33].

Our findings are supported by several studies which have found no association between dairy intake and bone health in children and adolescents[5,6]. While two randomized trials report a positive relationship between dairy product consumption and measures of bone health[34,35], most cross-sectional, retrospective, and prospective studies do not[36-42]. A review of calcium, dairy products, and bone health found that the vast majority of controlled studies of dairy supplementation or total dietary calcium intake show that, although very low calcium intakes may be harmful to bone development, increases in dairy or total dietary calcium intake above 400–500 mg/day are not correlated with nor represent a predictor of bone mineral density or fracture rate in children or adolescents[5]. This review concluded that there is no empirical evidence for the recommendation to increase dairy intake in children and adolescents to promote bone mineralization[5]. One cross-sectional study of bone mass among pubertal girls in Beijing, however, found a significant correlation between milk consumption and bone mineral content and reported that vitamin D was the most important nutrient in milk[43]. Further, low vitamin D status was associated with lower bone mineral density of the forearm in a study of 12 and 15 year old girls[44].

This study is subject to several limitations. Although the participants in the GUTS cohorts reside across the United States, the sample is not representative of the US population, therefore potentially limiting the generalizability of our findings. Because the participants are children of registered nurses, female subjects of low socioeconomic status are underrepresented. Further, our sample lacks the racial/ethnic diversity needed to further explore racial differences in stress fracture risk, which one would expect given the known racial difference in calcium retention and bone health[45-48]. Finally, GUTS participants have high levels of physical activity and thus may be a select sample of youth. Although the prevalence of stress fractures could have been overestimated because cases were reported by mothers, the misclassification would likely bias the results towards the null, thus we may have presented conservative estimates. We report an association between vitamin D intake, not vitamin D status, of our participants and risk of stress fracture. Because vitamin D status is only partly dependent upon dietary intake of vitamin D[49], the association between vitamin D status and stress fracture risk should be explored in future studies to help elucidate the mechanism through which vitamin D may alter stress fracture risk. The strengths of our study, including its prospective design, geographically diverse sample, validated measures, and large sample size, far outweigh the limitations. Moreover, characteristics of our sample which limit generalizability enhance our ability to study stress fractures because whites and those participating in high levels of physical activity are at highest risk for developing this type of fracture. Future studies are needed to distinguish stress fractures from other overuse injuries and, if possible, to include radiographic confirmation of the fractures.

Stress fractures are a frequent cause of injury in recreational athletes with consequences ranging from delayed return to full sport participation and reoccurrence in injury[50]. Given the limited knowledge of modifiable risk factors for stress fractures among adolescent girls, the results of this study provide important information regarding the role of dietary factors in the prevention of stress factors. Among the dietary factors studied, only vitamin D appeared to be related to lower risk of stress fractures among female adolescents. The protective association was seen among girls at increased risk of stress fracture due to their high activity levels. Future studies are needed to ascertain whether vitamin D from supplements confers a similarly protective effect as vitamin D consumed through dietary intake.

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Table 1

Baseline demographics and lifestyle characteristics of 6712 preadolescent, adolescent, and young adult females in the Growing Up Today Study

Mean (SD) age (years)	11.6 (1.6)
% White	93.6%
Mean (SD) body mass index (kg/m^2)	19.0 (3.3)
% Overweight or obese	19.8%
% Underweight	8.6%
Mean (SD) age at menarche (years)	12.3 (1.2)
% Maternal history of low bone density or osteoporosis	10.4%
Mean (SD) calcium intake (mg/day)	1181.5 (478.1)
Mean (SD) vitamin D intake (IU/day)	376.2 (183.0)
Mean (SD) daily servings of dairy	2.0 (1.3)
Mean (SD) hours/week of high-impact activity[a]	5.2 (4.1)

[a]Sum of basketball, running, soccer, tennis, cheerleading, and volleyball.

TABLE 2

Age-adjusted and fully-adjusted associations of dairy, vitamin D, and calcium intake with stress fracture among all girls in GUTS

	Age-adjusted Hazard Ratio (95% CI)	Fully-adjusted[a] Hazard Ratio (95% CI)
Dairy intake (servings/day)		
0 servings	--	--
1 serving	1.28 (0.87, 1.89)	1.21 (0.81, 1.81)
2 servings	0.98 (0.64, 1.52)	0.91 (0.58, 1.43)
3 or more servings	1.13 (0.72, 1.75)	1.02 (0.65, 1.61)
p for trend	0.83	0.82
Vitamin D intake quintile (quintile mean [SD])		
Quintile 1 (107 [46])	--	--
Quintile 2 (210 [56])	0.93 (0.59, 1.49)	0.95 (0.59, 1.55)
Quintile 3 (324 [43])	0.86 (0.53, 1.38)	0.72 (0.42, 1.24)
Quintile 4 (433 [55])	0.92 (0.58, 1.47)	0.78 (0.44, 1.39)
Quintile 5 (663 [149])	0.72 (0.44, 1.19)	0.49 (0.24, 1.01)
p for trend	0.25	0.07
Calcium intake quintile (quintile mean [SD])		
Quintile 1 (541 [124])	--	--
Quintile 2 (825 [86])	0.93 (0.56, 1.54)	0.94 (0.55, 1.61)
Quintile 3 (1111 [93])	1.12 (0.69, 1.83)	1.28 (0.74, 2.22)
Quintile 4 (1398 [93])	0.87 (0.52, 1.44)	0.99 (0.54, 1.81)
Quintile 5 (1891 [298])	1.22 (0.76, 1.94)	1.57 (0.77, 3.17)
p for trend	0.52	0.29

[a]Hazard ratios above are from Cox proportional hazards models adjusted for age, BMI, age at menarche, maternal history of low bone density or osteoporosis, and level of high-impact physical activity. Calcium model additionally adjusted for mean-centered vitamin D intake. Vitamin D model additionally adjusted for mean-centered calcium intake.

TABLE 3

Fully-adjusted associations of dairy, vitamin D, and calcium intake with stress fracture stratified by level of high-impact activity among all girls in GUTS

	Participants with ≤1 hour high-impact activity/day	Participants with ≥1 hour high-impact activity/day
	Fully-adjusted[a] Hazard Ratio (95% CI)	**Fully-adjusted[a] Hazard Ratio (95% CI)**
Dairy intake (servings/day)		
0 servings	--	--
1 serving	0.54 (0.15, 1.97)	1.35 (0.88, 2.07)
2 servings	0.85 (0.26, 2.78)	0.94 (0.57, 1.53)
3 or more servings	0.29 (0.04, 2.37)	1.15 (0.71, 1.84)
p for trend	0.28	0.90
Vitamin D intake quintile		
Quintile 1	--	--
Quintile 2	0.45 (0.08, 2.36)	1.04 (0.62, 1.73)
Quintile 3	0.66 (0.11, 3.93)	0.74 (0.41, 1.33)
Quintile 4	2.24 (0.56, 8.98)	0.71 (0.38, 1.32)
Quintile 5	0.72 (0.07, 7.99)	0.48 (0.22, 1.02)
p for trend	0.55	0.04
Calcium intake quintile		
Quintile 1	--	--
Quintile 2	0.15 (0.02, 1.02)	1.29 (0.71, 2.37)
Quintile 3	0.15 (0.02, 1.28)	1.79 (0.97, 3.30)
Quintile 4	0.48 (0.10, 2.25)	1.24 (0.62, 2.49)
Quintile 5	0.22 (0.01, 3.83)	2.14 (0.98, 4.69)
p for trend	0.20	0.11

[a]Hazard ratios above are from Cox proportional hazards models adjusted for age, BMI, age at menarche, maternal history of low bone density or osteoporosis, and level of high-impact physical activity. Calcium model additionally adjusted for mean-centered vitamin D intake. Vitamin D model additionally adjusted for mean-centered calcium intake.