

Is Caffeine Associated with Bone Mineral Density in Young Adult Women?

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Background. By increasing the urinary excretion of calcium, caffeine consumption may reduce bone mineral density (BMD) and subsequently increase the risk for osteoporotic fracture. Although negative associations between caffeine consumption and BMD have been reported for postmenopausal women, in particular for those who consume low amounts of dietary calcium, the relation between caffeine and BMD in younger women is unclear. Therefore, we evaluated the association between caffeine consumption and BMD in a cross-sectional study of 177 healthy white women, age 19-26 years, who attended a Midwestern university.

Methods. Average caffeine intake (milligrams per day) was calculated from self-reports of the consumption of coffee, decaffeinated coffee, tea, colas, chocolate products, and select medications during the previous 12 months (mean caffeine intake = 99.9 mg/day). BMD (grams per square centimeter) at the femoral neck and the lumbar spine was measured by dual-energy X-ray absorptiometry.

Results. After adjusting in linear regression models for potential confounders, including height, body mass index, age at menarche, calcium intake, protein consumption, alcohol consumption, and tobacco use, caffeine consumption was not a significant predictor of BMD. For every 100 mg of caffeine consumed, femoral neck BMD decreased 0.0069 g/cm² (95% confidence interval [CI] = -0.0215, 0.0076) and lumbar spine BMD decreased 0.0119 g/cm² (95% CI = -0.0271, 0.0033). No single source of caffeine was significantly associated with a decrease in BMD. Furthermore, the association between caffeine consumption and BMD at either site did not differ significantly between those who consumed low levels of calcium (≤ 836 mg/day) and those who consumed high levels of calcium (>836 mg/day).

Conclusions. Caffeine intake in the range consumed by young adult women is not an important risk factor for low BMD.

Key Words: BMD; caffeine; calcium; osteoporosis.

INTRODUCTION

Osteoporosis, a disease characterized by low bone mineral density (BMD), affects 6 to 7 million women 50 years old or older in the United States [1]. Low BMD increases the risk of bone fracture [2], and those with fractures suffer increased mortality rates as well as significant morbidity from long-term disability [3]. Low BMD as an older adult may partially reflect the failure to achieve peak BMD [4], most of which is obtained before the age of 30 [5,6]. Therefore, determining what factors influence the BMD of young women could help identify behaviors that, when modified, could reduce a woman's future risk of fracture. One behavior that may negatively influence BMD is high caffeine consumption.

Caffeine consumption is hypothesized to affect BMD by increasing calcium excretion [7-9]. Some [10-16], but not all [17-22], epidemiological studies of postmenopausal women suggest that high caffeine consumption is associated with poor bone health. At least two suggest that this negative effect is limited to women who consume low levels of calcium [14,16]. In contrast, for premenopausal women, none of the studies that examined the association between caffeine consumption and BMD found an association [23-28]. It is possible that age-related differences in calcium absorption efficiency explain the disparity in results between post- and premenopausal women [29]. However, among the studies of premenopausal women, four failed to account for potential covariates such as calcium intake and body size [23,24,26,27], and only one examined the effect of caffeine on BMD in women who consumed low levels of calcium [27], a dietary factor that may modify the association between caffeine consumption and BMD.

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This study [27] limited its evaluation to BMD at the lumbar spine. No studies have evaluated whether low calcium intake modifies the effect of caffeine consumption on BMD at the femoral neck, a site of costly fracture in the elderly.

Therefore, in a cross-sectional analysis of young healthy women age 19–26, we asked the following questions:

1. After accounting for covariates, is caffeine consumption associated with BMD at the lumbar spine and the femoral neck?
2. Is the association between caffeine intake and BMD stronger for women who consume low levels of calcium?

METHODS

Study Design and Population

The 177 participants in our study were recruited from a random sample ($n = 863$) of white female students, age 19–26, registered for the 1991 fall term at a Midwestern university. Of the 863, 614 (70%) responded to a short questionnaire administered over the telephone to determine eligibility for the study. To be eligible, women had to be nulligravid, between 80 and 150% of their ideal body weight, and to have reached menarche before age 19. They also had to be free of the following: amenorrhea (experiencing no menstrual periods during the previous 12 months); a history of chronic medical conditions that could affect BMD, including Type 1 or Type 2 diabetes, thyroid or kidney problems, and rheumatoid arthritis; a history of conditions that could alter nutrient absorption, including eating disorders and disorders of the digestive tract; a history of using drugs that could affect BMD, including seizure medications and glucocorticoids; and significant limitations in their physical activity during the previous month because of injury or illness. Of those contacted, 444 (60%) were eligible for the study. Among this group, 182 (41%) agreed to participate. Data on four women who participated in the study were dropped from this analysis because information on the consumption of one or more caffeinated items was missing. Data on a fifth participant whose daily intake of caffeine was more than eight standard deviations from the population mean was also dropped from the study. There were no significant differences ($P < 0.05$) between eligible persons participating and eligible persons not participating in the study with regard to age, height, weight, body mass index, or age at menarche (data not shown). This study was approved by the University of Michigan Institutional Review Board.

Measurement of Bone Mineral Density

A single technician measured each participant's BMD at the lumbar spine and the proximal femur using dual-energy X-ray absorptiometry (DPX-L, Lunar, Madison,

WI) and following standard protocols as described by the instrument manual. The machine was calibrated daily, and no more than five persons were scanned each day. Weekly scans of an aluminum spine phantom were completed to determine the precision of the machine over time; all values were within 2% of the standard phantom value over the 13-month study.

Caffeine Data Collection

To characterize caffeine consumption from foods, we asked participants to report how frequently during the previous year (times per day, week, month, or year) they consumed the following items: coffee, tea (excluding herbal tea), decaffeinated coffee, caffeinated soft drinks, hot chocolate, and chocolate bars. Participants were also asked whether their typical serving size was small, medium, or large. The caffeine values assigned to a medium serving size of the foods are as follows: regular coffee (137 mg/8 oz), decaffeinated coffee (2 mg/8 oz), regular tea, (36 mg/8 oz), caffeinated cola (40 mg/12 oz), hot chocolate (5 mg/8 oz), and chocolate (5 mg/oz) [30]. To characterize caffeine consumption from medications, participants were asked to report how frequently during the previous year they had consumed the following medications: pills for pain relief, diet pills, and pills to stay awake (e.g., NoDoz); they were also asked the number of pills consumed and the brand name of the medication. Caffeine values were assigned using information from the 1998 Physicians Desk Reference.

To determine total caffeine consumption, the product of the frequency, quantity, and caffeine content of each source were calculated. These values were then summed across all sources, and average caffeine consumption (in milligrams) per day was calculated. Consumption of coffee was the primary contributor to caffeine consumption in this population, accounting for 88% of the total caffeine consumed.

Measurements of Potential Confounders

Covariates were chosen for this analysis because of their previous documented associations with BMD. We defined total calcium intake (milligrams/day) as the sum of the average daily intake from foods and the average daily intake from other sources. Calcium intake from foods was obtained from the National Cancer Institute's Health Habits and History Questionnaire [31], and intake from nondietary sources was obtained by querying participants about their consumption of multivitamins, calcium supplements, and antacids. Alcohol intake (grams/day) and protein intake (grams/day) were also estimated using the NCI Health Habits and History Questionnaire [31]. Height was measured in duplicate to the nearest 0.1 cm with the use of an anthropometric plane and scale. Current weight (in light clothing and without shoes) was measured to the

nearest 0.1 kg with the use of a balance-beam scale. Body mass index (BMI) was calculated as kilograms per square meter. Age, age at menarche, and smoking status were obtained using a standardized questionnaire during the clinic interview. Smokers were defined as those who had smoked more than 10 cigarettes per week during the previous year. The activity metabolic index (AMI), as measured by the Minnesota Leisure Time Activity Questionnaire [32,33], was used to characterize levels of leisure-time physical activity during the previous 12 months. AMI is an indirect measure of the average daily energy expended in approximately 70 leisure-time physical activities.

Statistical Analysis

All analyses were done using SAS for Windows (Version 6.12). We used simple and multiple variable linear regression, with caffeine consumption as a continuous variable, to evaluate the associations between caffeine intake and BMD. We examined a model in which the sources of caffeine (coffee, tea, cola, other) were included separately to determine whether the direction and magnitude of the association between caffeine and BMD was independent of the caffeine source. Since previous studies [14,16] reported that adequate calcium intake may offset the negative effect of caffeine on BMD, we evaluated the interaction among caffeine, BMD, and calcium consumption, where calcium consumption was stratified at the median level for the population (836 mg/day). Ninety-five percent confidence intervals were calculated around the beta coefficients; variables whose intervals did not include zero were considered significant at $P = 0.05$. We used regression diagnostics, including examination of residuals and influential points, to test model assumptions. For the ease of reading, caffeine consumption is reported in units of 100 mg/day in the tables.

RESULTS

Population Description and Covariate Analysis

In the study population, caffeine intake ranged from 0.0 to 678.4 mg/day with an average of 99.9 mg/day (1.59 ± 1.85 mg/kg/day). This caffeine intake is comparable to that observed in other studies of women of similar ages [23,26,27,34]. The study population had a mean age of 21 years, mean body mass index of 22.7 kg/m², and mean height of 165.4 cm (Table 1). Participants consumed an average of 930 mg calcium per day with an average of 873 mg per day provided by the diet. Although only 12% of the population smoked, 89% reported drinking alcohol at least once a month. Participants spent an average of 83 minutes in physical activity per day (including walking for transportation), expending approximately 400 kcal. Larger body mass

TABLE 1

Mean, Standard Deviation, and Correlation between Selected Characteristics and Caffeine in 177 Caucasian Women, Aged 19–26, Enrolled in a Midwestern University

	Mean or %	SD	Correlation with caffeine intake ^a
Caffeine intake (mg/day)	99.9	114.7	—
Physical characteristics			
Femoral neck BMD (g/cm ²)	1.0208	0.1157	-0.01
Lumber spine BMD (g/cm ²)	1.1987	0.1220	-0.03
Age (years)	21	2	0.03
Height (cm)	165.4	6.8	0.03
Body mass index (kg/m ²)	22.7	2.8	0.16*
Age at menarche (years)	13	1	-0.06
Dietary characteristics			
Total calcium intake (mg/day)	930	447	0.12
Dietary calcium (mg/day)	873	413	0.13
Protein intake (g/day)	60.8	23.6	0.11
Lifestyle characteristics			
Alcohol intake (g/day)	1.6	2.9	0.12
Ever smoke (%)	12	—	0.20 ^{a,b}
Activity metabolic index (AMI)	414	296	0.03

^a Pearson correlation unless otherwise specified.

^b Spearman correlation.

* P value < 0.05.

index ($r = 0.16$) and smoking ($r = 0.20$) were significantly correlated with increased caffeine intake.

BMD at the femoral neck was significantly associated with height ($r = 0.23$) and body mass index ($r = 0.29$). At the lumbar spine BMD was significantly associated with height ($r = 0.21$), body mass index ($r = 0.27$), and age at menarche ($r = -0.25$). Although age, total calcium intake, protein intake, alcohol intake, smoking, and physical activity were not significantly associated with BMD in this population, other studies have reported these associations. Therefore, we chose to include these variables as covariates in our models.

Is Caffeine Intake Associated with Bone Mineral Density?

Caffeine consumption was not a significant predictor of BMD (Table 2). For every 100 mg/day increase in caffeine consumption (approximately 6 oz of coffee), BMD decreased by 0.0069 and by 0.0119 g/cm² in the femoral neck and in the lumbar spine, respectively. We found no evidence for a nonlinear relationship between caffeine consumption and BMD when we classified caffeine consumption as either a second-order polynomial or a categorical variable with caffeine intake grouped into quartiles (data not shown). When the individual contributors to caffeine intake were analyzed separately, we observed a consistent inverse association between caffeine and BMD for all sources. However, no single source was significantly associated with BMD.

TABLE 2

Regression Analysis between Caffeine and Bone Density Evaluated at the Femoral Neck and Lumbar Spine in 177 Caucasian Women, Aged 19–26, Enrolled in a Midwestern University

		Femoral neck			
		Crude		Adjusted	
		β	95% CI	β	95% CI
		Caffeine (100 mg/day)		Caffeine (100 mg/day)	
Model 1	All sources	-0.0006	(-0.0156, 0.0143)	-0.0069	(-0.0215, 0.0076)
Model 2	Coffee	-0.0043	(-0.0210, 0.0125)	-0.0039	(-0.0200, 0.0122)
	Tea	0.0272	(-0.0399, 0.0943)	-0.0069	(-0.0709, 0.0571)
	Caffeinated cola	0.0153	(-0.0298, 0.0604)	-0.0264	(-0.0726, 0.0198)
		Lumbar spine			
		Crude		Adjusted	
		β	95% CI	β	95% CI
		Caffeine (100 mg/day)		Caffeine (100 mg/day)	
Model 1	All sources	-0.0037	(-0.0194, 0.0121)	-0.0119	(-0.0271, 0.0033)
Model 2	Coffee	-0.0060	(-0.0237, 0.0116)	-0.0086	(-0.0255, 0.0083)
	Tea	0.0215	(-0.0493, 0.0923)	-0.0182	(-0.0855, 0.0491)
	Caffeinated cola	0.0027	(-0.0449, 0.0502)	-0.0300	(-0.0785, 0.0185)

Note. Model 1 (adjusted): BMD (femoral neck or lumbar spine) (g/cm^2) = caffeine (mg/day) + total calcium (mg/day) + age (years) + height (cm) + BMI (kg/m^2) + age at menarche (years) + protein (g/day) + alcohol (g/day) + ever smoke (Y/N) + activity metabolic index. Model 2 (adjusted): BMD (femoral neck and lumbar spine) (g/cm^2) = coffee (mg/day) + tea (mg/day) + caffeinated cola (mg/day) + all other caffeine sources (mg/day) + total calcium (mg/day) + age (years) + height (cm) + BMI (kg/m^2) + age at menarche (years) + protein (g/day) + alcohol (g/day) + ever smoke (Y/N) + activity metabolic index.

Is the Association between Caffeine and Bone Mineral Density Modified by Calcium Consumption?

No significant interaction was found among caffeine intake, calcium consumption, and BMD at either the femoral neck (test for interaction, $P = 0.79$) or the lumbar spine (test for interaction, $P = 0.37$) (Fig. 1). Although not significant, caffeine did have a stronger negative association with BMD at the lumbar spine among persons who consumed calcium levels below the population median, compared to those who consumed calcium above the median intake.

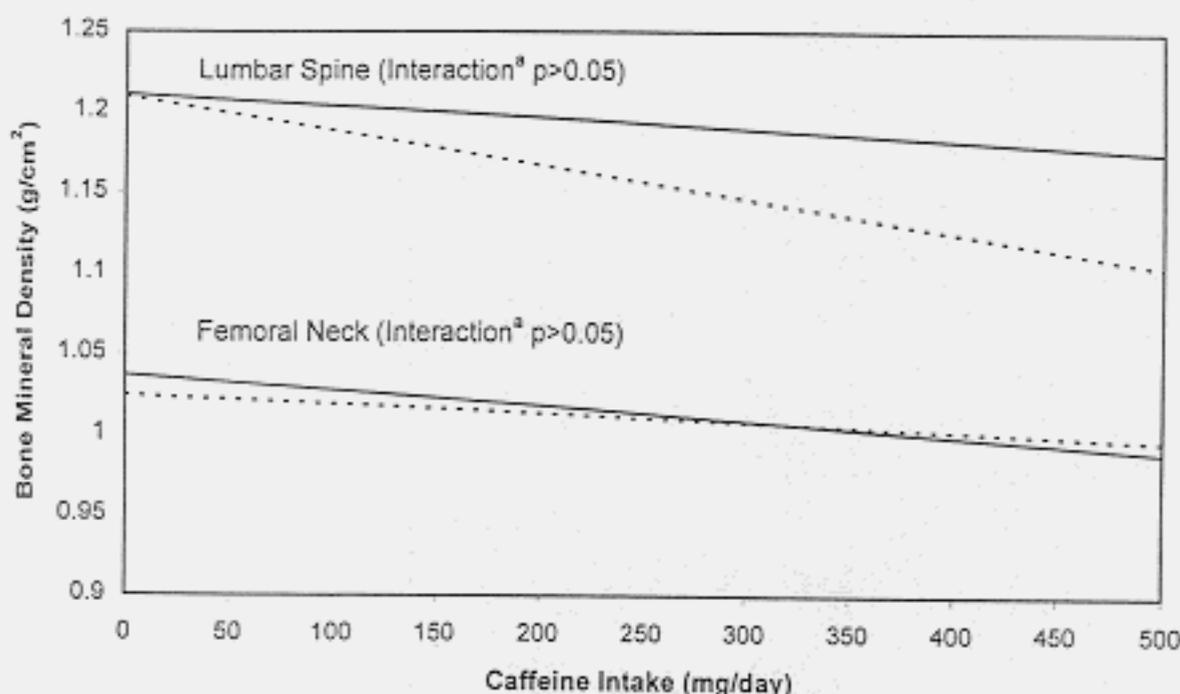
DISCUSSION

In this cross-sectional study of young premenopausal women, caffeine was not a significant predictor of BMD at either the femoral neck or the lumbar spine after controlling for covariates. Furthermore, the association between caffeine and BMD was not significantly modified by level of calcium consumption.

Previous epidemiologic studies evaluated the effect of caffeine on bone status by assessing either bone fracture or BMD. In bone fracture studies, four cohort studies of postmenopausal women found a small but significant increase in fracture risk with increased caffeine consumption [10–13], while one cohort [18] and two case-control [19,22] studies reported no association between caffeine consumption and bone fracture.

Because bone fractures are a function of both trauma and bone fragility, caffeine could increase the propensity for injury without directly affecting bone through its short-term effects, such as tremors, decreased sleep, anxiety symptoms, and increased muscle contraction at lower frequencies of stimulation [35]. Metabolic evidence, however, indicates that caffeine may be directly detrimental to bone by increasing urinary [7–9] and fecal calcium [7,8] excretion. Calcium loss may then lead to a negative calcium balance that is restored by increased bone resorption. Chronic bone resorption can decrease BMD and thus increase the risk for osteoporosis and bone fracture [36].

Like the fracture studies, some [14–16] but not all studies [20,21] of postmenopausal women that specifically investigate the effect of caffeine on BMD report negative associations. Two of the three studies found an effect in low calcium user only. Harris and Dawson-Hughes [14] found increased caffeine consumption to be associated with a significant decrease in both the lumbar spine and total body BMD but only among women with calcium intakes of less than 744 mg/day. Barrett-Connor et al. [16] reported a similar negative association at the femoral neck and lumbar spine of women over age 50; like the findings of Harris and Dawson-Hughes [14], this association was significant only for low calcium consumers, defined as women who



^a Interaction Model: BMD (femoral neck or lumbar spine) (g/cm²) = caffeine (mg/day) + calcium category (0 = below 836 mg/day, 1 = above 836 mg/day) + caffeine*calcium category + age (years) + height (cm) + BMI (kg/m²) + age at menarche (yr) + protein (g/day) + alcohol (g/day) + ever smoke (Y/N) + Activity Metabolic Index

FIG. 1. Predicted bone mineral density for the average nonsmoking participant with increasing daily caffeine intake stratified by the median calcium intake (836 mg/day). Solid lines represent calcium intakes above the median. Dotted lines represent calcium intakes below the median.

did not drink at least one glass of milk a day from age 20 to 50.

Although these studies of postmenopausal women demonstrate some evidence for a negative relationship between caffeine and bone status, the results may not be applicable to premenopausal women. Calcium absorption efficiency declines with age [37], and metabolic studies of the effects of caffeine on calcium balance in pre- [7] and postmenopausal [8] women suggest that premenopausal women may be able to compensate through increased calcium absorption for a negative calcium balance caused by caffeine consumption. However, whether this compensation occurs even at low levels of calcium consumption is not known.

Differences in the levels of endogenous estrogens may also limit the generalizability of results from postmenopausal women to premenopausal women. The loss of estrogen at the menopause results in a rapid decline in BMD. The benefits of estrogen in maintaining BMD may outweigh the negative effects of caffeine for premenopausal women.

Previous epidemiologic studies provide some evidence that the effect of caffeine on bone status differs between post- and premenopausal women since studies of premenopausal women report no association between caffeine consumption and bone mineral gain [26,27] or BMD [23-25,28]. In 183 French-Canadian women age

40 through 50 years, Picard et al. [25] found no association between caffeine consumption and BMD in the distal forearm and lumbar spine. Lloyd et al. [23] also found no association between caffeine intake and BMD at the lumbar spine in his evaluation of vegetarian and omnivore women age 28 through 45 years. Similarly, in four studies of adult women less than 35 years of age, no significant associations were found between coffee consumption and BMD at the os calcis [24], cups of caffeine containing beverages and BMD at either the lumbar spine or femoral neck [28], and caffeine intake and gains in either total body bone mineral [26] or lumbar spine BMD [27]. In addition, calcium intake did not modify the association between caffeine consumption and gain in lumbar spine BMD [27]. Three observations about these studies should be noted, however. First, the Picard et al. [25] and Lloyd et al. [23] studies may include perimenopausal women. Therefore, the rapid bone mineral loss that occurs at menopause may have masked an effect of caffeine. Second, several studies did not account for the effects of body size [23,24,26,27] or calcium intake [23,24,26]. In our study, body size was positively associated with both caffeine intake and BMD. Other studies found calcium intake to be positively associated with caffeine consumption [14] and BMD [25]. Failure to control for these potential

confounding variables may have masked a negative association between caffeine and BMD. Third, none of the studies evaluated whether calcium consumption modified the effect of caffeine consumption on BMD at the femoral neck. Caffeine may affect bone sites differently [15]. Thus, the lack of effect at the lumbar spine [27] cannot be generalized to the femoral neck.

Similar to these studies of premenopausal women, we found no relationship between caffeine and BMD in young adult women. However, we extend the findings of previous studies by demonstrating that this lack of association remains after controlling for potential confounders and that the association between caffeine consumption and BMD at both the lumbar spine and the femoral neck is not different for women who consume low levels of calcium than for those who do not.

Although our study extends the findings of previous studies of premenopausal women, several limitations should be noted. First, selective participation cannot be excluded as a bias because not all eligible women were contacted and less than half of the eligible population interviewed actually participated. Second, nondifferential misclassification of caffeine consumption may have biased our results to the null. Third, because this is a cross-sectional study, a causal link among caffeine consumption, calcium intake, and BMD cannot be established.

In conclusion, caffeine consumption was not an important risk factor for low BMD in this population of premenopausal young women, even among those who consume low levels of calcium. Further investigation, however, may be warranted for premenopausal women with abnormal menstrual cycles, such as amenorrhea, since they may be similar to postmenopausal women with regard to estrogen status and may be susceptible to the effects of caffeine.

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