Interactions Between Dietary Calcium Intake and Bone Mineral Density or Bone Geometry in a Low Calcium Intake Population (KNHANES IV 2008–2010)

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Context: Little is known about the interactions between dietary calcium intake and bone strength parameters in populations or areas with low calcium intake.

Objective: The objective of the study was to investigate the relationship between dietary calcium intake and bone mineral density (BMD) or bone geometry in an Asian population with low calcium intake.

Design and Setting: This was a cross-sectional study of data from the Korea National Health and Nutrition Examination Survey, 2008–2010.

Participants: A total of 3448 men and 3812 women older than 50 years were stratified by daily dietary calcium intake: less than 400 mg/d, 400–799 mg/d, 800–1199 mg/d, and 1200 mg/d or greater.

Main Outcome Measures: BMD was measured by dual-energy X-ray absorptiometry and the geometric index was calculated.

Results: Mean daily calcium intake was 470 mg/d in this population. BMD in the lumbar spine (both sexes) and femoral neck (women) was significantly lower only when calcium intake was less than 400 mg/d. In men, femoral neck and total hip BMD was positively related to calcium intake up to 1200 mg/d. Calcium intake less than 400 mg/d was negatively related to femoral cortical thickness and buckling ratio. These interactions disappeared when the 25-hydroxyvitamin D level was 30 ng/mL or greater in men and 20 ng/mL or greater in women.

Conclusions: Low calcium intake was significantly related with low BMD and increased risk of osteoporosis. However, the association between calcium and BMD was not consistently linear, and a sufficient vitamin D level appears to compensate for the negative influences of low calcium intake on bone. (***J Clin Endocrinol Metab*** **99: 2409–2417, 2014)**

Osteoporosis is a metabolic bone disease characterized by low bone mass and decreased bone quality, which increase the risk of fracture, especially in older people (1). Osteoporotic fractures cause pain and limit mobility, thus reducing the quality of life, and increase the risk of mortality in both men and women (2). Therefore, treating osteoporosis and preventing osteoporosis-related fractures are important for maintaining health in older people.

Both genetic determination and diverse epigenetic factors can affect bone mineral density (BMD); nutritional

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Abbreviations: ANCOVA, analysis of covariance; BMD, bone mineral density; BMI, body mass index; CSA, cross-sectional area; CSMI, cross-sectional moment of inertia; FPG, fasting plasma glucose; HSA, Hip Structural Analysis; KNHANES, Korea National Health and Nutrition Examination Survey; 25(OH)D, 25-hydroxyvitamin D.

intake is an important factor related to the latter (3). Calcium is an essential nutrient for skeletal health, and the relationship between calcium intake and bone density or bone strength has been analyzed widely (4, 5). It has been well documented that maintaining adequate calcium intake is essential for adequate accrual of bone mass during childhood and adolescence (6). Several studies have also proven the beneficial effects of calcium on bone strength in the decades after the achievement of peak bone mass. For example, low dietary calcium intake is associated with low bone density, and calcium supplementation can attenuate age-related bone loss (4, 7). Therefore, calcium supplementation is generally recommended for people who might be at risk of inadequate dietary calcium intake or osteoporosis, regardless of age, particularly to prevent deterioration in bone strength in postmenopausal women (8). However, there have been inconsistent data about the effects of calcium supplementation on bone health, and several studies have failed to show the efficacy of calcium supplementation in preventing osteoporotic fractures (5, 9).

Vitamin D is another essential component for bone health (10). In addition to adequate calcium intake, maintaining an optimal vitamin D level is necessary for preventing bone loss (11). Vitamin D has been reported as an important factor in the relationship between calcium and PTH and may alter the compensatory response of PTH to hypocalcemia (12). On the other hand, detrimental effects of calcium supplementation have been suggested recently based on data from large epidemiological studies reporting the acceleration of vascular calcification (13, 14). Thus, there remain uncertainties as to whether increasing the calcium intake is beneficial or harmful for adults.

The mean dietary calcium intake is low in Korea (300–500 mg/d) and in Japan (400–500 mg/d) (15, 16). These values are much lower than those reported in Western populations (1100–1300 mg/d) (12). The dose interaction between nutrients and related health events may differ according to baseline dietary habits and/or ethnicity (17). However, most studies that investigated the effects of dietary calcium on skeletal health have been conducted in Western populations, and the evidence is lacking in Asian populations, which have lower intakes of dairy food and dietary calcium compared with Western populations (18–20).

The aim of the present study was to investigate the relationships between dietary calcium level and BMD or bone geometry in Korea, an area with low dietary calcium intake, using the data from a large nationwide survey. We also examined whether these relationships differ by gender or skeletal sites and investigated whether vitamin D status affects the relationship between dietary calcium intake and BMD.

Subjects and Methods

Study participants and data collection

The present study was performing using the data from the Korea National Health and Nutrition Examination Survey (KNHANES). The KNHANES is a nationwide, population-based, cross-sectional study in Korea designed to evaluate the health and nutritional status of Korean population. The division of Health and Nutrition Survey under the Korea Centers for Disease Control and Prevention administers this survey, and it has been conducted periodically since 1998 and annually since 2008. A stratified, multistage probability sampling design was used to select household units, and the civilian, noninstitutionalized population of Korea was included for the survey. A detailed description of the survey has been published elsewhere (21). Data were collected through health interviews, physical examinations, and medical tests. Data were acquired for this study from the results of KNHANES 2008–2010. Subjects with renal insufficiency (serum creatinine concentration >1.4 mg/dL), which is known to alter calcium and bone metabolism, were excluded from the analysis. The subjects who used antiresorptive agents such as raloxifene, bisphosphonate, or hormone replacement therapy were also excluded. Daily calcium intake was recorded for all subjects included in the study aged 20 years and older, but further analyses related to the association between dietary calcium intake and BMD or bone geometry were restricted to the subjects older than 50 years. The KNHANES was reviewed and approved by the Ethics Committee of the Korea Centers for Disease Control and Prevention (Grants 2008-04EXP-01-C, 2009-01CON-03-2C and 2010-02CON-21-C).

BMD and hip structural analysis

BMD of the lumbar spine (L_1–L_4) and femur were measured using dual X-ray absorptiometry (QDR 4500A; Hologic Inc) equipment located in mobile examination centers according to the manufacturer's protocol. All men and nonpregnant women aged 20 years and older who received a physical examination in the mobile centers were eligible for bone densitometry analysis unless they had previously fractured both hips. The left hip was scanned routinely; in the case of a left hip fracture or device, the right hip was scanned. Femoral geometric properties were then evaluated further only for subjects examined in 2008–2009 using the Hip Structural Analysis (HSA) program included in the APEX software from Hologic Inc, as described previously (22). The HSA program automatically set the region of interest, defined as the narrow neck, traversing the narrowest width of the femoral neck. The HSA program yielded data for cross-sectional area (CSA; square centimeters), cross-sectional moment of inertia (CSMI; quadruple centimeters), mean cortical thickness (centimeters), and buckling ratio at the narrow neck. The dual X-ray absorptiometry calibrations were applied as described previously (23).

Dietary assessment

Nutrient intake, including total calorie and calcium intake, was assessed using a 24-hour dietary recall questionnaire ad-

ministered by a trained dietitian. The results were calculated using the Food Composition Table developed by the National Rural Resources Development Institute (seventh revision) (24). Daily dietary calcium intake was stratified into four groups: very low, less than 400 mg/d; low, 400–799 mg/d; moderate, 800–1199 mg/d; and high, 1200 mg/d or greater.

Biochemical parameters

Blood samples were collected from each participant after an 8-hour fast and were immediately transported to the Central Testing Institute in Seoul, Korea. Biochemical measurements, including the fasting plasma glucose (FPG), total cholesterol, and high-density lipoprotein cholesterol concentrations, were assessed using enzymatic assays on an automated analyzer (Hitachi Automatic Analyzer 7600; Hitachi). The low-density lipoprotein cholesterol level was calculated by the Friedewald equation (25). Serum 25-hydroxyvitamin D [25(OH)D] concentration was measured with an RIA kit (DiaSorin Inc). Serum intact PTH was analyzed using a chemiluminescence assay (DiaSorin).

Data analysis

Differences in dietary calcium intake, BMD, and femur geometry were identified by analysis of covariance (ANCOVA) after adjusting for age and body mass index (BMI) and are expressed as estimated marginal means and SEM. Serum 25(OH)D concentration was stratified as follows: deficient, less than 20 ng/mL; insufficient, 20 ng/mL or greater, and less than 30 ng/mL; and sufficient, 30 ng/mL or greater. An ANCOVA with the covariates of age and BMI was used to assess whether the 25(OH)D level was related to BMD in each dietary calcium group. Significance was set at $P < .05$, and the Bonferroni correction was applied for multiple comparisons. All statistical analyses were performed using the Statistical Package for the Social Sciences software (version 18, IBM SPSS Statistics; IBM Corp).

Results

Daily calcium intake

Figure 1 shows the mean and distribution of daily dietary calcium intake in each decade from the age of 20 years. The average intake increased steadily from the youngest group to the group aged 50–59 years and then decreased gradually until the age of 80 years or older. The mean dietary calcium intake was 490 mg/d and lower than 800 mg/d for most age groups in both men and women (Figure 1A) older than 20 years. A daily dietary calcium intake of less than 400 mg/d was found in 37.5%–65.5% of men and in 47.5%–76.9% of women in all age groups. The highest rates of low calcium intake were observed in the oldest groups of both men and women. Almost 80% of men and 90% of women had a calcium intake of less than 800 mg/d in all age groups, and only 4.9%–16.7% of men and 5.3%–8.7% of women had a calcium intake of 800–1199 mg/d. Consequently, only fewer than 5.0% of men and women had a calcium intake of 1200 mg/d or greater in each age group.

Baseline characteristics according to dietary calcium intake

A total of 3448 men and 3812 women older than 50 years were included in further analyses of the associations between dietary calcium intake and BMD or bone geometry. The baseline characteristics of the men and women older than 50 years are presented in Table 1. After adjusting for age and BMI, the baseline serum and clinical parameters including systolic and diastolic blood pressure, lipid profile, and FPG and 25(OH)D concentrations in both men and women and PTH concentration in women did not differ between dietary calcium intake groups. Only PTH concentration in men differed significantly between calcium intake groups ($P < .001$).

BMD and femoral bone geometry according to dietary calcium intake

To examine the independent dose-response relationship between BMD or femur geometry and daily calcium intake, ANCOVA models were constructed with age and BMI added as covariates. In men, significant interactions were observed between dietary calcium intake and BMD at all sites. Lumbar spine BMD was significantly lower

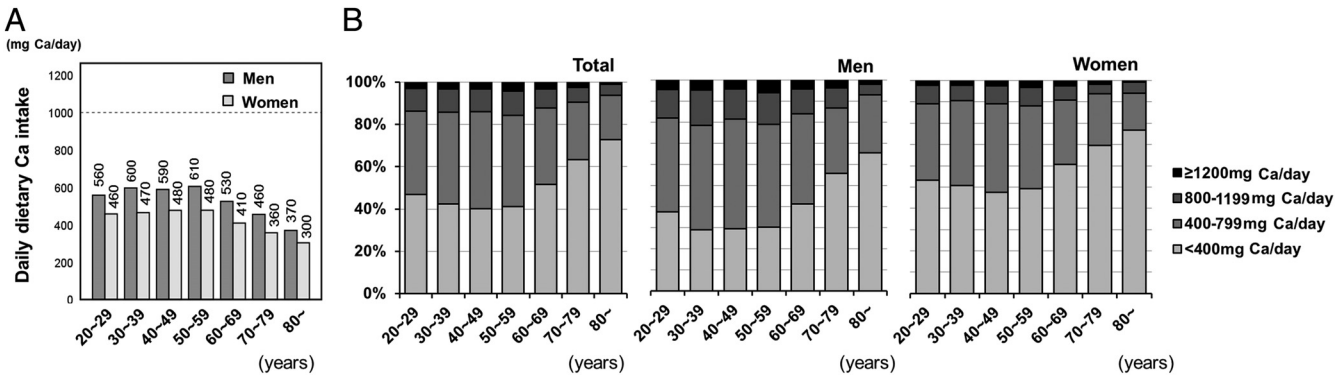

Figure 1. Mean (A) and distribution of daily dietary calcium intake (B) in each decade. A, Bars represent the mean levels. B, All study participants aged 20 years and older were stratified into four groups according to their mean dietary calcium intake: very low (<400 mg/d), low (400–799 mg/d), moderate (800–1199 mg/d), and high (≥1200 mg/d). Ca, calcium.

Table 1. Baseline Characteristics of Men and Women Older Than 50 Years

	Men (n = 3448)						Women (n = 3812)					
	Very Low, <400 mg	Low, 400–799 mg	Moderate, 800–1199 mg	High, <1200 mg	*P* Value	*P* Value[a]	Very Low, <400 mg	Low, 400–799 mg	Moderate, 800–1199 mg	High, <1200 mg	*P* Value	*P* Value[a]
N	1426	1432	428	162			2319	1140	259	94		
Age, y	66.6 ± 9.2	62.4 ± 8.5	62.1 ± 8.3	62.2 ± 8.2	<.001		66.5 ± 9.9	62.5 ± 9.5	62.3 ± 9.3	60.8 ± 8.6	<.001	
Height, cm	165.2 ± 6.1	166.7 ± 5.8	166.9 ± 6.2	166.9 ± 6.2	<.001		152.1 ± 6.2	153.8 ± 5.8	153.9 ± 5.9	154.9 ± 5.3	<.001	
Weight, kg	63.4 ± 10.1	66.7 ± 9.3	66.6 ± 10.1	67.4 ± 9.5	<.001		56.3 ± 9.0	57.4 ± 8.5	57.4 ± 7.8	57.7 ± 7.3	<.001	
BMI, kg/m^2	23.2 ± 3.1	23.9 ± 2.8	23.8 ± 2.9	24.1 ± 2.8	<.001		24.3 ± 3.3	24.2 ± 3.2	24.2 ± 2.9	24.1 ± 2.8	.856	
SBP, mm Hg	125.5 ± 17.7	124.8 ± 16.7	124.8 ± 16.8	125.1 ± 16.9	.633	.805	127.4 ± 18.3	124.4 ± 17.8	125.4 ± 19.7	124.2 ± 15.4	<.001	.205
DBP, mm Hg	75.9 ± 10.7	77.3 ± 10.2	77.2 ± 10.3	78.1 ± 10.5	.001	.727	76.3 ± 10.3	76.7 ± 100	76.1 ± 10.1	76.4 ± 9.2	.535	.762
FPG, mg/dL	104.3 ± 26.6	105.5 ± 28.2	107.1 ± 29.5	110.5 ± 42.4	.026	.098	102.0 ± 26.3	101.0 ± 25.8	101.2 ± 28.3	99.8 ± 17.8	.57	.565
TC, mg/dL	184.1 ± 37.2	186.8 ± 35.7	186.8 ± 35.7	180.4 ± 36.7	.067	.611	199.8 ± 36.8	202.4 ± 38.2	200.5 ± 34.5	205.7 ± 33.4	.096	.382
LDL-C, mg/dL	110.7 ± 35.8	113.4 ± 34.9	111.3 ± 35.4	111.9 ± 36.9	.145	.657	123.2 ± 35.2	122.9 ± 36.4	121.4 ± 33.0	123.7 ± 31.9	.84	.086
HDL-C, mg/dL	44.6 ± 10.7	44.8 ± 10.7	45.5 ± 10.5	44.1 ± 10.4	.296	.562	46.8 ± 10.5	49.0 ± 10.7	49.0 ± 10.8	50.9 ± 10.5	<.001	.141
25(OH)D, ng/dL	21.6 ± 7.6	21.6 ± 7.3	21.9 ± 7.5	22.1 ± 7.7	.707	.624	18.6 ± 7.1	18.4 ± 6.8	19.4 ± 7.1	19.8 ± 7.0	.102	.111
PTH, pg/mL	66.8 ± 25.3	63.4 ± 22.9	63.2 ± 24.9	66.2 ± 28.7	.002	.001	69.7 ± 36.1	66.3 ± 27.5	67.4 ± 27.7	60.4 ± 20.2	.002	.117

Abbreviations: DBP, diastolic blood pressure; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; TC, total cholesterol. Data are shown as mean ± SD.

[a] *P* values for ANCOVA are adjusted for age and BMI.

only in the very low calcium intake group (<400 mg/d) than in other calcium intake groups (Figure 2A). In men, femur neck and total hip BMD increased linearly with calcium intake from the low to moderate calcium intake groups (<1200 mg/d) but did not increase further in the highest calcium intake group (≥1200 mg/d) (Figure 2A). In women, significant interactions between dietary calcium and BMD were observed in the lumbar spine and femoral neck. However, only the very low calcium intake group had significantly lower BMD at both sites, and no significant interaction was observed between total hip BMD and calcium intake (Figure 2B).

A significant interaction between dietary calcium intake and femoral bone geometry was observed only in men. The lowest dietary calcium group (<400 mg/d) had significantly lower cortical thickness, CSA, and CSMI and significantly higher buckling ratio compared with the other three dietary calcium intake groups (Figure 2C). However, no significant interactions were observed between dietary calcium and these femoral bone geometric parameters in women (Figure 2D).

Differences in BMD and geometric indices between dietary calcium intake groups were also evaluated after classifying the participants according to vitamin D level. In men, significant positive relationships between dietary calcium intake and BMD of the lumbar spine, femoral neck, and total hip were observed in both groups with 25(OH)D levels less than 20 ng/mL and 20–30 ng/mL. However, there was no significant relationship between calcium intake and BMD of the lumbar spine and total hip in the group with the highest 25(OH)D level of 30 ng/mL or greater (Figure 3A). In women, a significant positive relationship was observed for all three skeletal sites only in the group with 25(OH)D less than 20 ng/mL (Figure 3B). The cortical thickness and buckling ratio differed significantly between some calcium intake groups, but there was no significant overall relationship between calcium intake and vitamin D level in the three vitamin D groups (Figure 3, C and D). CSA and CSMI showed similar results for cortical thickness in both men and women (data not shown).

Relationship between T-scores and PTH concentration and dietary calcium intake

The relationships between the T-score for each skeletal site in men and women are shown in Figure 4. The T-scores in each skeletal site were positively related to dietary calcium intake only for those with an intake of less than 800 mg/d. However, these positive trends were more apparent in the range of dietary calcium intake less than 400 mg/d and smaller in the range of 400–799 mg/d. By contrast, T-scores at each skeletal site showed a constant level for those with calcium intake of 800 mg/d or greater (Figure 4, A–C). These patterns were similar in both men and women. In the associations between dietary calcium intake and PTH, a negative association started from the level of 800 mg/d in men but from the level of less than 400 mg/d in women (Figure 4D).

Discussion

The mean daily dietary calcium intake was lower in this study than that reported for other ethnic groups and did not achieve the Korea dietary reference Intakes, and it became intensified with advancing years (14, 26, 27). Adequate calcium intake is important for bone health, and very low intake could result in reduced BMD and in-

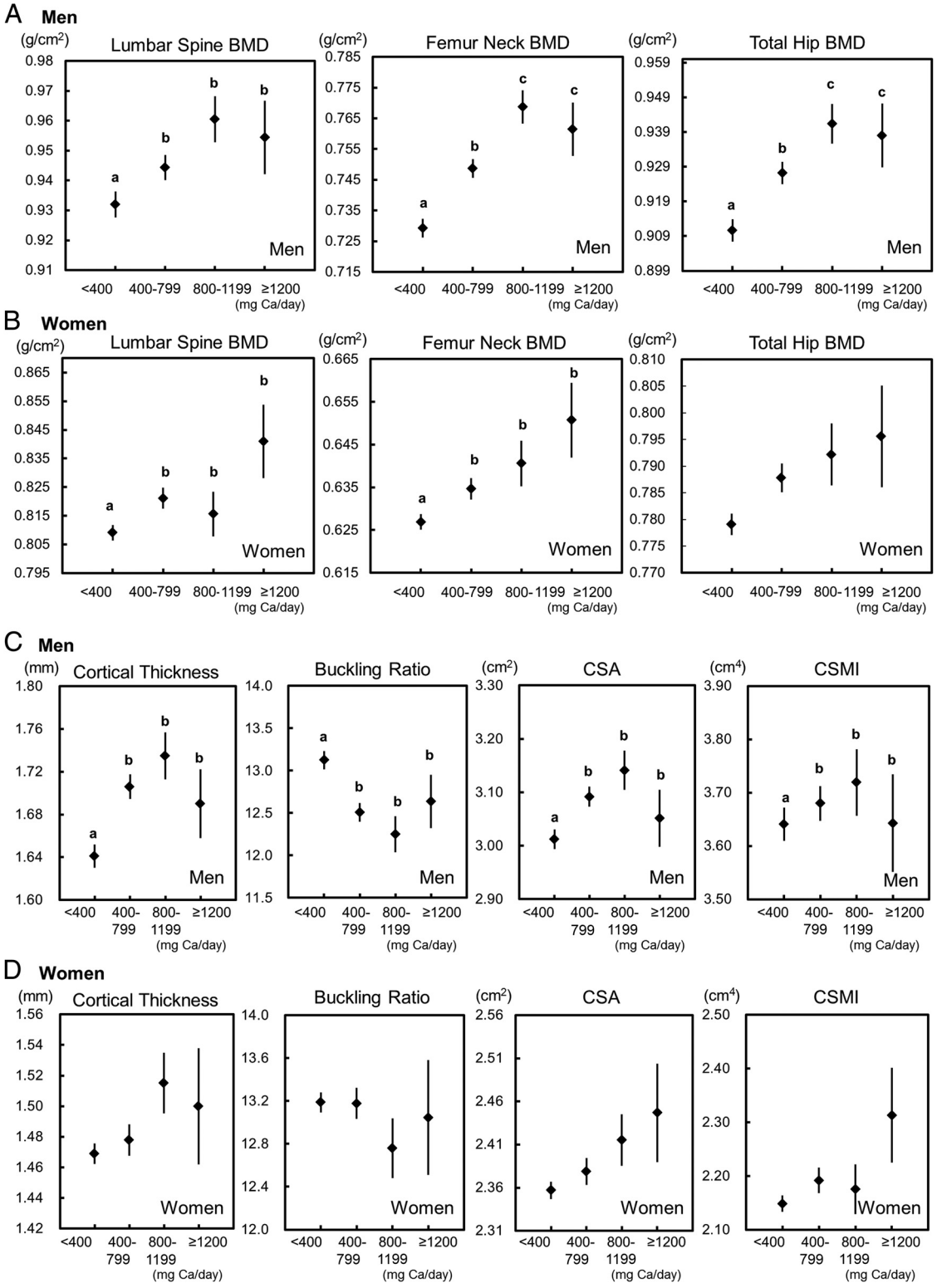

Figure 2. The effect of daily dietary calcium intake on BMD of the lumbar spine, femoral neck, and total hip (A and B), and femoral geometric profiles (C and D) in participants aged older than 50 years. A, BMD in men. B, BMD in women. C, Femoral geometry in men. D, Femoral geometry in women. Data are expressed as estimated marginal mean and SEM, with age and BMI used as covariates. Values with different superscripts are significantly different ($P < .05$ with Bonferroni correction).

creased risk of osteoporosis, but the associations between dietary calcium intake and BMD were not consistently linear in this study. Moreover, the interactions between dietary calcium intake and BMD or bone geometry seemed to differ between men and women and between skeletal sites. The associations were stronger in men than in women and in the femur than in other sites. Moreover, vitamin D status seemed to alter the negative relationships

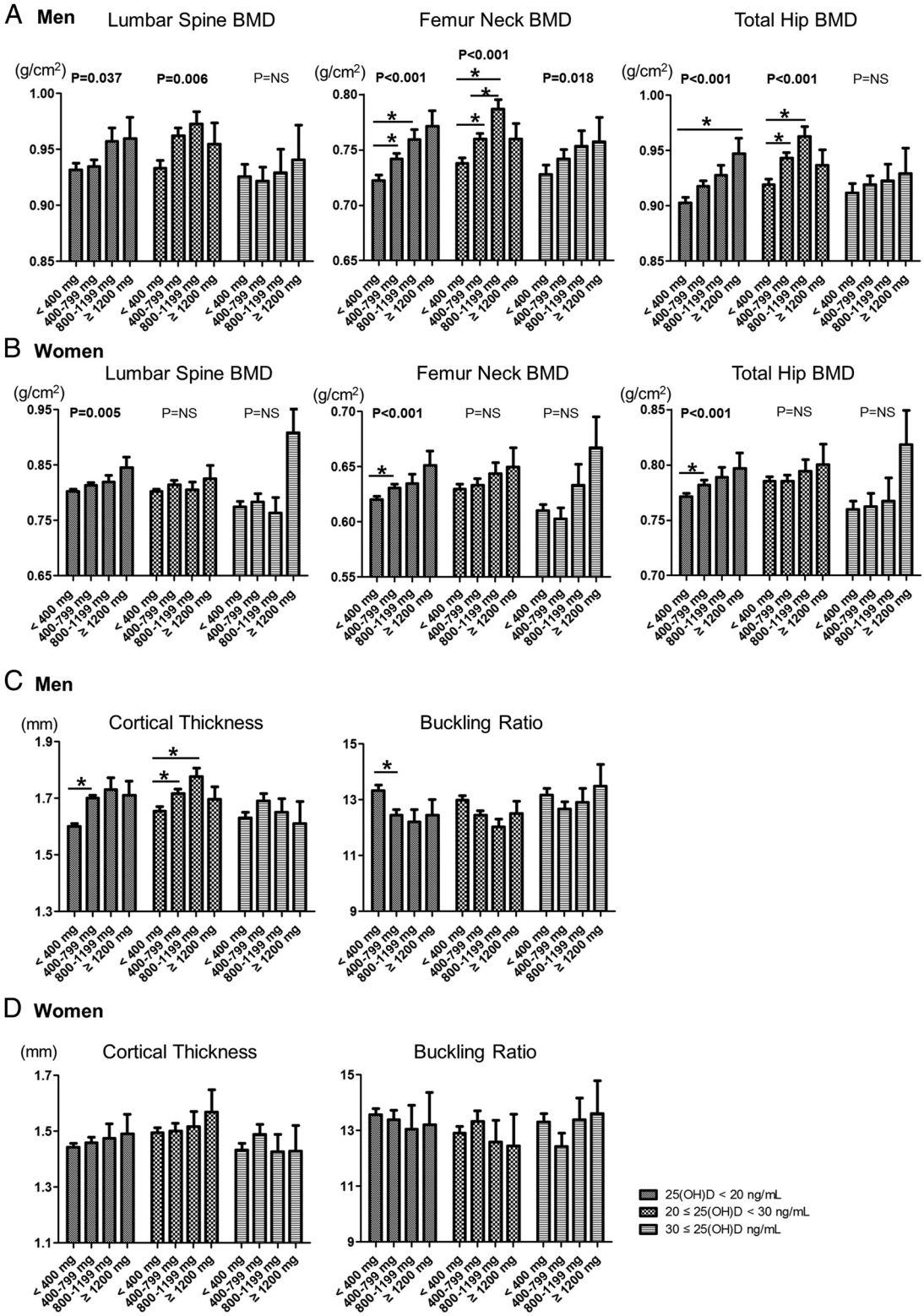

Figure 3. Adjusted mean BMD, cortical thickness, and buckling ratio in the femur according to serum 25(OH)D concentration in the different dietary calcium intake groups. A, BMD values in men. B, BMD values in women. C, Geometry values in men. D, Geometry value in women. Data were adjusted for age and BMI. The different shading patterns indicate the three groups according to 25(OH)D concentration: less than 20 ng/mL; 20 ng/mL or greater and less than 30 ng/mL; and 30 ng/mL or greater. *P* for trends were adjusted for age and BMI. *, $P < .05$ by ANCOVA after controlling for age and BMI with the Bonferroni correction.

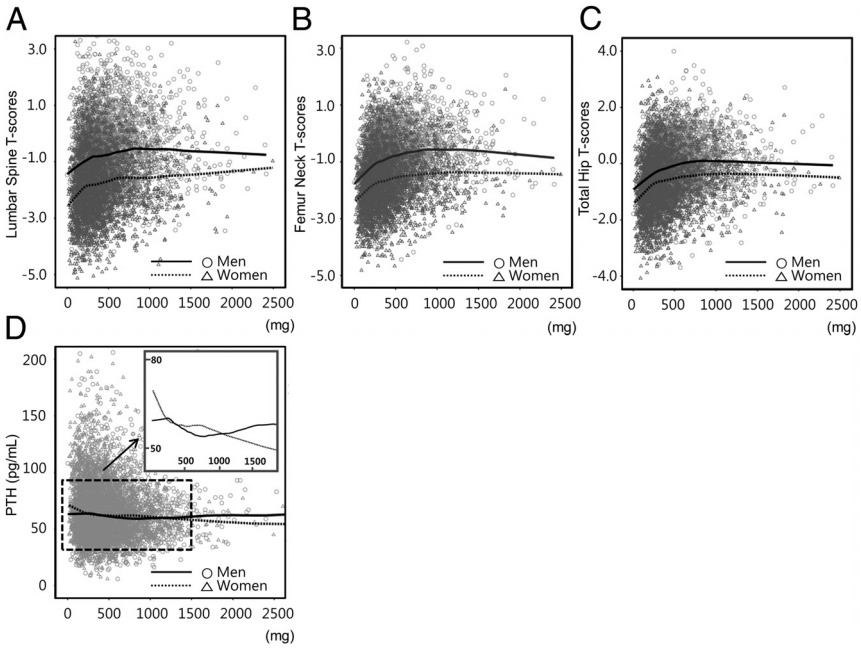

Figure 4. Relationship between dietary calcium intake and T-scores of the lumbar spine (A), femoral neck (B), and total hip (C) and PTH concentration (D) in participants aged older than 50 years. Cubic spline curves are shown. The black solid lines represent men and the black dotted lines, women.

between dietary calcium intake and BMD, and the deleterious effects of a low-calcium diet seemed to be compensated by a sufficient vitamin D level.

Calcium plays an essential role in bone health across all ages, so calcium intake is emphasized because an insufficient intake negatively affects bone metabolism (28). Asian populations tend to have low calcium intake (19, 20). In the present study, the mean dietary calcium intake was 490 mg/d in subjects older than 20 years and 470 mg/d in those older than 50 years. However, little is known about the relationship between calcium intake and bone metabolism in areas with low dietary calcium intake. In the present study, only the group with very low dietary calcium intake (<400 mg/d) had significantly lower lumbar BMD compared with the other dietary groups in both men and women, whereas calcium intake was linearly related to the femoral neck and total hip BMD in men in the low to moderate calcium intake groups. However, geometrical deterioration from the low calcium intake was observed only in the men with very low calcium intake.

A recent study from Japan, a low dietary calcium intake area, reported that low-dose calcium supplementation (500 mg elementary calcium per day) was effective in preventing postmenopausal bone loss in the lumbar spine but not in the femur (20). In another study, with a mainly Caucasian study population, low-dose calcium supplementation (500 mg elementary calcium per day) showed beneficial effects on bone only in those with a low calcium intake but not in those with a higher calcium intake (29). In a longitudinal study of a population with modest dietary calcium intake, Warensjo et al (30) reported that only the lowest quintile of calcium intake was associated with increased risk of fracture or osteoporosis. These studies suggest that the habitual or baseline dietary calcium intake can affect the relationship between calcium intake and bone health. There might be a threshold of adequate calcium intake to produce preventive effects on BMD, which might be lower in populations with a low dietary calcium intake compared with areas with moderate to high dietary intake. Moreover, calcium balance is known to be largely dependent on body size (31). The median mass of study participants was about 66 kg for men and 57 kg for women, and these values are lower than those of Caucasian populations. Therefore, the body weight dependency of the calcium requirement could partly explain these observed differences in the threshold of an adequate calcium intake between the ethnic groups. In our study, the negative association between dietary calcium intake and T-score was observed only for intake of less than 1000 mg/d in both men and women.

We observed a significant dose trend between dietary calcium intake and BMD related to hip in men but not to lumbar in men and women. In one study, a supplemental calcium dose that elicited a protective effect against loss of BMD in the lumbar spine failed to show a beneficial effect in the femur (20). In two other studies in an Asian population, low-dose calcium supplementation had a positive effect on BMD only in the lumbar spine, but a much higher dose also showed protective effects on hip BMD (19, 20). These findings correspond with previous data reporting that the effects of altering calcium metabolism are greater in cortical bone than in trabecular bone (32, 33). Conceivably, the threshold of low calcium intake associated with unfavorable effects might be higher for the femur than that for the lumbar spine, and a higher calcium intake might be needed to prevent deterioration of the hip than of the spine. Moreover, positive dose trends between calcium and BMD or geometry were more obviously observed in men than those in women. In other previous reports, supplemental calcium showed a protective effect of hip fractures only in men, not in women (34). That is, calcium

effects on bone strength seem to be much stronger in men than in women.

Vitamin D is another important nutritional component for bone health and is closely related to calcium metabolism (35). Next, we compared the relationships between dietary calcium intake and BMD in participants grouped according to their 25(OH)D level. The relationship between dietary calcium intake and BMD was strongest in the vitamin D-deficient group [25(OH)D concentration <20 ng/mL], whereas no significant interactions were observed between dietary calcium intake and BMD in the vitamin D-sufficient group [25(OH)D concentration ≥30 ng/mL]. These finding suggest that that the detrimental effects of low dietary calcium intake may be compensated by a higher 25(OH)D level.

The main pathogenesis of the deleterious effects of low dietary calcium intake on BMD occurs through the elevation of the PTH level, which accelerates bone resorption to maintain optimal serum calcium concentration (21). A sufficient vitamin D level might prevent or lessen the effect of low calcium intake on increasing PTH concentration (12). This is consistent with the observation that the relationship between dietary calcium intake and BMD was not significant in the vitamin D-sufficient group. These data suggest that a higher calcium intake may not be necessary for maintaining calcium metabolism related to bone as long as an optimal vitamin D level is achieved.

Our study has several strengths. First, we used data from the KNHANES 2008–2010, a large, representative, nationwide survey that includes subjects selected by a stratified, multistage probability sampling design. Second, we assessed bone quality with the geometric index as well as conventional BMD. Our study also has some limitations. First, this was a cross-sectional study, and prospective studies on the relationship between dietary calcium intake and bone are needed to determine whether these associations are causal. Second, the KNHANES data included self-reported dietary intake; however, a more accurate method is impractical for such a large study. Third, information about nondietary calcium intake, including supplements, was not assessed. However, the rate and dose of calcium supplementation is not high in older Koreans (36), and it is likely that the dietary calcium intake in these data reflect the total calcium intake of the participants.

In conclusion, this study suggests that calcium is an essential nutrient for preventing deteriorative changes in bone BMD and geometry associated with aging, particularly in the femur of older men. However, the relationships between dietary calcium and bone strength parameters were not consistently linear, suggesting that lower-dose calcium supplementation may be effective in preventing pathological bone loss and related fractures in populations with low calcium intake. Furthermore, vitamin D status may affect the relationship between dietary calcium intake and BMD, and the relationship between dietary calcium intake and BMD may not be significant in those with a sufficient or high vitamin D level. Habitual dietary intake seems to be important to the biological roles of each nutrient, and a prospective, longitudinal study is needed to determine the sufficient daily calcium intake and to clarify the relationship between dietary calcium intake on skeletal health particularly in Asian populations.

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Contributions of the authors include the following: K.M.K. and C.S.S. designed the study and analyzed the data. K.M.K., S.L., S.H.C., J.H.K., S.W.K., H.C.J., and C.S.S. interpreted the data, and K.M.K. and C.S.S. drafted the manuscript. C.S.S. is the study guarantor. The authors take responsibility for the integrity and accuracy of the data analysis.

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References

1. **Kanis JA.** Assessment of fracture risk and its application to screening for postmenopausal osteoporosis: synopsis of a WHO report. WHO Study Group. *Osteoporos Int*. 1994;4(6):368–381.
2. **Bliuc D, Nguyen ND, Milch VE, Nguyen TV, Eisman JA, Center JR.** Mortality risk associated with low-trauma osteoporotic fracture and subsequent fracture in men and women. *JAMA*. 2009;301(5):513–521.
3. **Krall EA, Dawson-Hughes B.** Heritable and life-style determinants of bone mineral density. *J Bone Miner Res*. 1993;8(1):1–9.
4. **Chevalley T, Rizzoli R, Nydegger V, et al.** Effects of calcium supplements on femoral bone mineral density and vertebral fracture rate in vitamin-D-replete elderly patients. *Osteoporos Int*. 1994;4(5):245–252.
5. **Shea B, Wells G, Cranney A, et al.** Meta-analyses of therapies for postmenopausal osteoporosis. VII. Meta-analysis of calcium supplementation for the prevention of postmenopausal osteoporosis. *Endocr Rev*. 2002;23(4):552–559.
6. **Lloyd T, Andon MB, Rollings N, et al.** Calcium supplementation and bone mineral density in adolescent girls. *JAMA*. 1993;270(7):841–844.
7. **Varenna M, Binelli L, Casari S, Zucchi F, Sinigaglia L.** Effects of dietary calcium intake on body weight and prevalence of osteopo-

rosis in early postmenopausal women. *Am J Clin Nutr*. 2007;86(3):639–644.
8. **Compston J, Bowring C, Cooper A, et al.** Diagnosis and management of osteoporosis in postmenopausal women and older men in the UK: National Osteoporosis Guideline Group (NOGG) update. *Maturitas*. 2013;75(4):392–396.
9. **Bischoff-Ferrari HA, Dawson-Hughes B, Baron JA, et al.** Calcium intake and hip fracture risk in men and women: a meta-analysis of prospective cohort studies and randomized controlled trials. *Am J Clin Nutr*. 2007;86(6):1780–1790.
10. **Wacker M, Holick MF.** Vitamin D— effects on skeletal and extraskeletal health and the need for supplementation. *Nutrients*. 2013;5(1):111–148.
11. **Hwang YC, Ahn HY, Jeong IK, Ahn KJ, Chung HY.** Optimal serum concentration of 25-hydroxyvitamin D for bone health in older Korean adults. *Calcif Tissue Int*. 2013;92(1):68–74.
12. **Steingrimsdottir L, Gunnarsson O, Indridason OS, Franzson L, Sigurdsson G.** Relationship between serum parathyroid hormone levels, vitamin D sufficiency, and calcium intake. *JAMA*. 2005;294(18):2336–2341.
13. **Michaelsson K, Melhus H, Warensjo Lemming E, Wolk A, Byberg L.** Long term calcium intake and rates of all cause and cardiovascular mortality: community based prospective longitudinal cohort study. *BMJ*. 2013;346:f228.
14. **Xiao Q, Murphy RA, Houston DK, Harris TB, Chow WH, Park Y.** Dietary and supplemental calcium intake and cardiovascular disease mortality: the National Institutes of Health-AARP diet and health study. *JAMA Intern Med*. 2013;173(8):639–646.
15. **Seo MH, Kim MK, Park SE, et al.** The association between daily calcium intake and sarcopenia in older, non-obese Korean adults: the fourth Korea National Health and Nutrition Examination Survey (KNHANES IV) 2009. *Endocr J*. 2013;60(5):679–686.
16. **Tanaka S, Uenishi K, Yamazaki Y, Kuroda T, Shiraki M.** Low calcium intake is associated with high plasma homocysteine levels in postmenopausal women [published online August 20, 2013]. *J Bone Miner Metab*. doi: 10.1007/s00774-013-0499-9.
17. **Larsson SC, Orsini N, Wolk A.** Dietary calcium intake and risk of stroke: a dose-response meta-analysis. *Am J Clin Nutr*. 2013;97(5):951–957.
18. **Bailey RL, Dodd KW, Goldman JA, et al.** Estimation of total usual calcium and vitamin D intakes in the United States. *J Nutr*. 2010;140(4):817–822.
19. **Lau EM, Woo J, Lam V, Hong A.** Milk supplementation of the diet of postmenopausal Chinese women on a low calcium intake retards bone loss. *J Bone Miner Res*. 2001;16(9):1704–1709.
20. **Nakamura K, Saito T, Kobayashi R, et al.** Effect of low-dose calcium supplements on bone loss in perimenopausal and postmenopausal Asian women: a randomized controlled trial. *J Bone Miner Res*. 2012;27(11):2264–2270.
21. **Choi HS, Kim KA, Lim CY, et al.** Low serum vitamin D is associated with high risk of diabetes in Korean adults. *J Nutr*. 2011;141(8):1524–1528.
22. **Beck TJ, Looker AC, Ruff CB, Sievanen H, Wahner HW.** Structural trends in the aging femoral neck and proximal shaft: analysis of the Third National Health and Nutrition Examination Survey dual-energy X-ray absorptiometry data. *J Bone Miner Res*. 2000;15(12):2297–2304.
23. **Hong S, OH HJ, Choi H, et al.** Characteristics of body fat, body fat percentage and other body composition for Koreans from KNHANES IV. *J Korean Med Sci*. 2011;26(12):1599–1605.
24. Rural Development Administration. *Food Composition Table*. 7th ed. Suwon, Korea: National Rural Resources Development Institute; 2006.
25. **Warnick GR, Knopp RH, Fitzpatrick V, Branson L.** Estimating low-density lipoprotein cholesterol by the Friedewald equation is adequate for classifying patients on the basis of nationally recommended cutpoints. *Clin Chem*. 1990;36(1):15–19.
26. **Li K, Kaaks R, Linseisen J, Rohrmann S.** Associations of dietary calcium intake and calcium supplementation with myocardial infarction and stroke risk and overall cardiovascular mortality in the Heidelberg cohort of the European Prospective Investigation into Cancer and Nutrition study (EPIC-Heidelberg). *Heart*. 2012;98(12):920–925.
27. *Dietary Reference Intakes for Koreans, 2010*. Seoul, Korea: The Korean Nutrition Society; 2010.
28. **Zhu K, Prince RL.** Calcium and bone. *Clin Biochem*. 2012;45(12):936–942.
29. **Dawson-Hughes B, Dallal GE, Krall EA, Sadowski L, Sahyoun N, Tannenbaum S.** A controlled trial of the effect of calcium supplementation on bone density in postmenopausal women. *N Engl J Med*. 1990;323(13):878–883.
30. **Warensjo E, Byberg L, Melhus H, et al.** Dietary calcium intake and risk of fracture and osteoporosis: prospective longitudinal cohort study. *BMJ*. 2011;342:d1473.
31. **Uenishi K, Ishida H, Kamei A, et al.** Calcium requirement estimated by balance study in elderly Japanese people. *Osteoporos Int*. 2001;12(10):858–863.
32. **Kuipers AL, Zmuda JM, Carr JJ, et al.** Association of volumetric bone mineral density with abdominal aortic calcification in African ancestry men. *Osteoporos Int*. 2014;25(3):1063–1069.
33. **Moosgaard B, Christensen SE, Vestergaard P, Heickendorff L, Christiansen P, Mosekilde L.** Vitamin D metabolites and skeletal consequences in primary hyperparathyroidism. *Clin Endocrinol (Oxf)*. 2008;68(5):707–715.
34. **Cooper C, Barker DJ, Wickham C.** Physical activity, muscle strength, and calcium intake in fracture of the proximal femur in Britain. *BMJ*. 1988;297(6661):1443–1446.
35. **Cline J.** Calcium and vitamin d metabolism, deficiency, and excess. *Top Companion Anim Med*. 2012;27(4):159–164.
36. **Lee JS, Kim J.** Factors affecting the use of dietary supplements by Korean adults: data from the Korean National Health and Nutrition Examination Survey III. *J Am Diet Assoc*. 2009;109(9):1599–1605.