Magnesium Intake and Incidence of Metabolic Syndrome Among Young Adults

Ka He, MD, ScD; Kiang Liu, PhD; Martha L. Daviglus, MD, PhD; Steven J. Morris, PhD; Catherine M. Loria, PhD; Linda Van Horn, PhD; David R. Jacobs, Jr, PhD; Peter J. Savage, MD

Background—Studies suggest that magnesium intake may be inversely related to risk of hypertension and type 2 diabetes mellitus and that higher intake of magnesium may decrease blood triglycerides and increase high-density lipoprotein (HDL) cholesterol levels. However, the longitudinal association of magnesium intake and incidence of metabolic syndrome has not been investigated.

Methods and Results—We prospectively examined the relations between magnesium intake and incident metabolic syndrome and its components among 4637 Americans, aged 18 to 30 years, who were free from metabolic syndrome and diabetes at baseline. Metabolic syndrome was diagnosed according to the National Cholesterol Education Program/Adult Treatment Panel III definition. Diet was assessed by an interviewer-administered quantitative food frequency questionnaire, and magnesium intake was derived from the nutrient database developed by the Minnesota Nutrition Coordinating Center. During the 15 years of follow-up, 608 incident cases of the metabolic syndrome were identified. Magnesium intake was inversely associated with incidence of metabolic syndrome after adjustment for major lifestyle and dietary variables and baseline status of each component of the metabolic syndrome. Compared with those in the lowest quartile of magnesium intake, multivariable-adjusted hazard ratio of metabolic syndrome for participants in the highest quartile was 0.69 (95% confidence interval [CI], 0.52 to 0.91; P for trend <0.01). The inverse associations were not materially modified by gender and race. Magnesium intake was also inversely related to individual component of the metabolic syndrome and fasting insulin levels.

Conclusions—Our findings suggest that young adults with higher magnesium intake have lower risk of development of metabolic syndrome. (Circulation. 2006;113:1675-1682.)

Key Words follow-up studies ■ magnesium ■ nutrition ■ risk factors ■ syndrome X

People with metabolic syndrome, characterized by a group of metabolic risk factors, have been widely found to be at elevated risk of coronary heart disease and type 2 diabetes mellitus. The metabolic syndrome has become increasingly common in the United States, and it is estimated that approximately a quarter of American adults suffer from this problem.

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Magnesium, a mineral needed by living cells of human body, is a cofactor in a number of key enzymatic reactions in the body and appears to play an important role in glucose metabolism and insulin homeostasis. Epidemiological studies indicate that deficient magnesium intake may be an independent risk factor for the development of type 2 diabetes mellitus. Previous studies also suggest an inverse association between magnesium and blood pressure and support a role for magnesium in the pathogenesis of hypertension. Although the mechanisms are poorly understood, studies demonstrate that increased intake of dietary magnesium may lower blood triglyceride level and increase high-density lipoprotein (HDL) cholesterol level.

One cross-sectional study reported an inverse correlation of serum magnesium levels and metabolic syndrome, and another found an inverse association between dietary magnesium intake and the prevalence of metabolic syndrome. To our knowledge, data are not available on the longitudinal relation of magnesium intake and the development of metabolic syndrome. In addition, most of the current knowledge on the influence of magnesium on the risk of cardiovascular diseases or diabetes comes from studies of middle-aged and older adults or diabetes patients. However, middle-aged or older men and women are more likely to have already had onset of diseases. Their lifestyle choice and health conditions...
may be affected by perceived ill health or treatment for existing disease that is related to individual components of the metabolic syndrome. Therefore, we prospectively examined the relation between magnesium intake and incidence of metabolic syndrome in a cohort of 4637 young adults, aged 18 to 30 years, who were free from metabolic syndrome and diabetes at baseline.

Methods

Study Population

The Coronary Artery Risk Development in Young Adults (CARDIA) Study is an ongoing, multicenter, longitudinal study designed to examine the role of physiological, psychological, and lifestyle factors in the evolution of cardiovascular disease risk among young adults. The details of this study cohort and design have been described elsewhere. Briefly, 5115 black and white men and women, aged 18 to 30 years, were enrolled in 1985–1986. Race and gender were roughly balanced by the sample design. To date, 5 follow-up examinations have been completed. The average follow-up rate was >90%, and 74% of participants in the original cohort returned for the year 15 examination (2000–2001).

At baseline, we excluded participants who had metabolic syndrome (n = 106) or diabetes (n = 10). We further excluded participants who had missing data on magnesium intake (n = 4), baseline body mass index (n = 3), or any component of the metabolic syndrome (n = 120) or participants who reported implausible total energy intake (n = 122; <800 and >8000 kcal/d for men; <600 and >6000 kcal/d for women). Pregnant women at any examination (n = 111) and 2 trans-sex participants were also excluded. After these exclusions, a total of 4637 participants (91%) remained in the analyses. All participants gave written informed consent, and the study design, data collection, and analyses were approved by the institutional review boards of the centers involved.

Dietary Assessment

Dietary information was collected at baseline and year 7 with the use of a dietary history obtained with an interviewer-administered quantitative food frequency questionnaire. Participants were asked about their consumption of foods in the past month along with portion sizes. Provisions were made for reported foods not found in the questionnaire. Nutrients were derived from the food and nutrient content databases (version 10 at baseline and version 20 at year 7) developed by the Minnesota Nutrition Coordinating Center. Data on the supplemental intake of magnesium through multivitamin or other preparations were taken into account to assess intake of supplemental magnesium. Total magnesium represents the sum of magnesium intake from both dietary and supplemental sources. The validity of the dietary history questionnaire has been evaluated in 128 participants by comparison with seven 24-hour dietary recalls, and the correlations of mean daily intakes from both methods were >0.50 for most nutrients. In particular, the correlations of energy-adjusted potassium and calcium intakes across race and gender groups ranged from 0.56 to 0.73 and 0.56 to 0.69, respectively. After correction for within-person variability, the correlations ranged from 0.65 to 0.83 and 0.66 to 0.80, respectively. The correlation for magnesium intake was not reported in the evaluation study. However, it is likely to be similar to the correlations for potassium and calcium because the intakes of these elements are correlated. In addition, toenail samples were collected at the year 2 examination in CARDIA. To further validate the magnesium intake, 99 toenail samples were randomly selected from the Chicago Field Center. Toenail magnesium concentrations were measured with the use of inductively coupled plasma mass spectrometry at the University of Missouri–Columbia Research Reactor Center. The correlation coefficient was 0.37 between toenail magnesium and the average magnesium intake of year 0 and year 7.

Other Measurements

All participants underwent a clinical examination at baseline and were required to complete a set of questionnaires including sociodemographic, medical, and psychosocial questionnaires. The major lifestyle variables and clinical measurements were reexamined in the follow-up period. Details of the manuals of operations and the procedures for clinic measurements have been previously reported. In brief, waist circumference was measured at the maximum abdominal girth, and all anthropometric measures were taken in duplicate and averaged. The resting blood pressure was measured on the right arm with a random-zero sphygmomanometer with the participant seated and after 5 minutes of rest. Systolic and diastolic pressures were recorded as phase I and phase V Korotkoff sounds.

Three measurements were taken at 1-minute intervals. The average of the second and third measurements was taken as the blood pressure value. Participants were asked to fast for at least 12 hours and to avoid smoking and heavy physical activity for at least 2 hours before examination. Fasting glucose and insulin levels were measured by the hexokinase method and radioimmunoassay, respectively. Triglyceride measurements were made with the use of enzymatic methods, and HDL cholesterol levels were quantified by dextran sulfate–magnesium precipitation.

Metabolic Syndrome Ascertainment

Metabolic syndrome was determined according to the National Cholesterol Education Program/Adult Treatment Panel III (ATP-III) definition. An incident case was identified if participants developed ≥3 of the following: fasting glucose level ≥6.1 mmol/L; systolic blood pressure ≥130 or diastolic blood pressure ≥85 mm Hg; waist circumference >88 cm for women or >102 cm for men; triglyceride level ≥1.70 mmol/L; HDL cholesterol level <1.30 mmol/L in women or <1.04 mmol/L in men. Participants who reported using diabetes or hypertension control medications were classified as having high glucose or hypertension. Positive fasting glucose level and triglyceride level were considered missing if participants had fasting time <8 hours before the examination.

Statistical Analysis

Each participant contributed follow-up time from the date of the baseline examination to the date of metabolic syndrome determined or end of the year 15 examination or until censored. Participants were divided into quartiles according to their total magnesium intake standardized by total energy intake (mg/1000 kcal). We used Cox proportional hazards models to estimate the hazard ratios (HRs) and 95% confidence intervals (CIs) of incident metabolic syndrome for the second through fourth quartiles of magnesium intake with the first quartile as the reference. The follow-up time was calculated from baseline to the date of the first event or end of the follow-up. A number of lifestyle and dietary variables were considered potential confounders on the basis of the existing literature and statistical tests. Because obesity may cause insulin resistance and hyperinsulinemia, baseline body mass index was included in the multivariable models. We also adjusted for the potential effects of baseline status of individual components of the metabolic syndrome in the multivariable analyses. In addition, we examined magnesium intake in relation to each component of the metabolic syndrome. For example, we considered participants to have incident abnormal blood pressure if their systolic blood pressure was ≥130 mm Hg or if they were using antihypertensive medications in the follow-up examinations. Prevalent events at baseline were excluded in the analyses for each component. We also considered the cross-sectional association between baseline magnesium intake and fasting plasma insulin level. Simple correlation of magnesium and insulin level in the original cohort has been reported. We examined the underlying correlations with appropriate multivariable adjustment among those participants who met our enrollment criteria. Multivariable-adjusted geometric means of insulin level and 95% CIs were calculated with general linear models according to quartiles of magnesium intake.
TABLE 1. Baseline Characteristics According to Quartiles of Total Magnesium Intake

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Black Men and Women (n=2363)</th>
<th>White Men and Women (n=2274)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Quartile 1</td>
<td>Quartile 2</td>
</tr>
<tr>
<td>Total magnesium intake, mg/1000 kcal</td>
<td>97.9 (10.1)</td>
<td>108.5 (4.7)</td>
</tr>
<tr>
<td>Age, y</td>
<td>23.6 (3.8)</td>
<td>23.9 (3.8)</td>
</tr>
<tr>
<td>Female, %</td>
<td>58.0</td>
<td>53.5</td>
</tr>
<tr>
<td>Education, %</td>
<td>12.7 (1.7)</td>
<td>12.9 (1.7)</td>
</tr>
<tr>
<td>Physical activity score, U</td>
<td>344.8 (289.1)</td>
<td>367.4 (290.9)</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>25.1 (5.8)</td>
<td>25.0 (5.6)</td>
</tr>
<tr>
<td>Smoking status, %</td>
<td>56.3</td>
<td>57.3</td>
</tr>
<tr>
<td>Use of supplement including magnesium, %</td>
<td>4.8</td>
<td>11.6</td>
</tr>
<tr>
<td>Alcohol intake, g/d</td>
<td>6.9 (15.0)</td>
<td>10.3 (18.5)</td>
</tr>
<tr>
<td>Total energy, kcal</td>
<td>3174 (1546)</td>
<td>3169 (1481)</td>
</tr>
<tr>
<td>Polyunsaturated fat, % of energy</td>
<td>6.8 (1.9)</td>
<td>6.8 (2.1)</td>
</tr>
<tr>
<td>Saturated fat, % of energy</td>
<td>14.2 (3.0)</td>
<td>14.4 (2.7)</td>
</tr>
<tr>
<td>Total carbohydrates, % of energy</td>
<td>48.0 (8.1)</td>
<td>46.4 (6.8)</td>
</tr>
<tr>
<td>Fiber, g/1000 kcal</td>
<td>1.4 (0.5)</td>
<td>1.7 (0.6)</td>
</tr>
<tr>
<td>Folic acid, mcg/1000 kcal</td>
<td>93.5 (82.4)</td>
<td>116.6 (77.6)</td>
</tr>
<tr>
<td>Calcium, mg/1000 kcal</td>
<td>303.0 (83.7)</td>
<td>377.0 (128.1)</td>
</tr>
<tr>
<td>Potassium, mg/1000 kcal</td>
<td>958 (179)</td>
<td>1125 (177)</td>
</tr>
</tbody>
</table>

Data are mean (SD), unless otherwise specified. BMI indicates body mass index. P values are for test of difference across all quartiles of magnesium intake.

We used multivariable nutrient density method26 in all analyses because total energy intake varied greatly among participants. To determine the long-term effects of diet on the outcomes, we used baseline dietary intake in the analyses. In the secondary analyses, we used the accumulative average of year 0 and 7 dietary intakes.26,27 In addition, we analyzed the data using total magnesium and dietary magnesium intake, respectively. To explore the possible effect modifications, we stratified data according to gender and race. All analyses were performed with the use of SAS software (SAS Institute, Cary, NC). Reported probability values are 2-sided.

The authors had full access to the data and take responsibility for its integrity. All authors have read and agree to the manuscript as written.

Results
At baseline, the participants (n=4637, 53.8% female) included 2363 blacks (1321 women) and 2274 whites (1174 women). A total of 608 incident metabolic syndrome cases were identified during the 15 years of follow-up. For the 5 components, the identified incident events numbered 932 for meeting the blood pressure criterion, 226 for glucose, 1286 for HDL cholesterol, 807 for triglycerides, and 1010 for waist circumference. Sixteen percent of participants were taking supplements that contain magnesium. Compared with persons in the lowest quartile of magnesium intake, those in the highest quartile group were older and were more likely to be female, to have more years of education, to have more physical activity, and to take supplements and less likely to be current smokers among both blacks and whites (Table 1).

Magnesium intake was associated inversely, in a dose-response manner, with the risk of incident metabolic syndrome. Those in the 2 highest quartiles of magnesium intake had significantly lower risk of metabolic syndrome. The risk was reduced by 31% (HR, 0.69; 95% CI, 0.52 to 0.91; P for trend <0.01) for participants in the highest quartile compared with the lowest after adjustment for potential dietary and nondietary confounders as well as each component of the metabolic syndrome at baseline (Table 2). In addition, mag-
Magnesium intake was inversely related to individual components of the metabolic syndrome (Table 3). Particularly, significant inverse relations were found between magnesium intake and fasting glucose level, waist circumference, and HDL cholesterol. For blood pressure and triglycerides, the inverse associations were attenuated after adjustment for major lifestyle and dietary factors. A few participants used statins during the follow-up primarily to lower low-density lipoprotein (LDL) cholesterol. In the sensitivity analyses, we excluded those who used statins. The associations between magnesium intake and triglyceride as well as HDL cholesterol levels were essentially identical. In this cohort, magnesium intake was correlated with intakes of potassium (Spearman correlation, \( r = 0.80 \), and folic acid (\( r = 0.71 \)). To determine the influence of these nutrient intakes on the association of magnesium and metabolic syndrome, we additionally adjusted for these nutrients in secondary analyses based on the multivariable analysis model 3. The HR for the highest quartile versus the lowest quartile of magnesium intake was 0.65 (95% CI, 0.47 to 0.90; \( P \) for trend <0.01) with additional adjustment for calcium, 0.75 (95% CI, 0.53 to 1.06; \( P \) for trend=0.07) for potassium, and 0.75 (95% CI, 0.52 to 1.07; \( P \) for trend=0.08) with additional adjustment for both calcium and potassium. In addition, the HR for the highest quartile versus the lowest quartile of magnesium intake was 0.72 (95% CI, 0.53 to 0.98; \( P \) for trend=0.02) with additional adjustment for folate acid based on multivariable analysis model 3.

We also examined whole grain consumption, a major source of dietary magnesium intake, in relation to metabolic syndrome. The multivariable HRs across quartiles of whole grain consumption were 1.0, 0.71 (95% CI, 0.56 to 0.88), 0.77 (95% CI, 0.61 to 0.96), and 0.80 (95% CI, 0.63 to 1.01) (\( P \) for trend=0.22).

We stratified data according to gender and race and found that gender and race did not appreciably modify the inverse associations of magnesium and metabolic syndrome (Figure). We also conducted tests for interactions between gender and/or race and magnesium intake on incidence of metabolic syndrome. They were not statistically significant.

To eliminate the possible confounding by supplement use, we analyzed data using dietary magnesium intake alone with adjustment for supplement use and in supplement nonusers only. The inverse associations of magnesium intake with metabolic syndrome and its components remained (data not shown).

In addition, we investigated the cross-sectional associations between magnesium intake and fasting insulin levels among 4622 participants who had fasting insulin data available. A consistent inverse correlation between magnesium intake and fasting insulin level was observed in crude and multivariable-adjusted analyses in the entire study cohort as well as in supplement users and nonusers (Table 4).

**Discussion**

In this prospective study, magnesium intake was associated in a dose-response manner with reduced risk of incident metabolic syndrome and its components among young adults after adjustment for major lifestyle and dietary factors as well as baseline status of individual components of the metabolic syndrome. These inverse associations were not appreciably modified by gender and race.

To our knowledge, no longitudinal study or clinical trial on magnesium and metabolic syndrome has been reported. One cross-sectional study, based on 576 middle-aged men and women, found that the risk of metabolic syndrome was significantly increased among participants in the lowest quartile of serum magnesium (odds ratio, 6.8; 95% CI, 4.2 to 10.9).\(^{13}\) Notably, the definition used for metabolic syndrome was slightly different from that of the ATP-III. Another cross-sectional survey conducted in 11 686 women, aged 20 to 24 years, also reported an inverse correlation of magnesium intake and the prevalence of metabolic syndrome.\(^{14}\) However, fasting glucose levels were not available in this study.

Our findings are biologically plausible. Although data are not entirely consistent, accumulating evidence generated from both experimental and observational studies suggests

### Table 2. HRs (95% CIs) of Metabolic Syndrome According to Quartiles of Total Magnesium Intake Among Young Adults

<table>
<thead>
<tr>
<th>Magnesium Intake</th>
<th>Quartile 1</th>
<th>Quartile 2</th>
<th>Quartile 3</th>
<th>Quartile 4</th>
<th>( P ) for Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of events</td>
<td>188</td>
<td>172</td>
<td>131</td>
<td>117</td>
<td>( \ldots )</td>
</tr>
<tr>
<td>Model 1</td>
<td>1.00</td>
<td>0.85 (0.69–1.05)</td>
<td>0.59 (0.47–0.74)</td>
<td>0.49 (0.38–0.63)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Model 2</td>
<td>1.00</td>
<td>0.87 (0.70–1.07)</td>
<td>0.63 (0.50–0.80)</td>
<td>0.59 (0.45–0.76)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Model 3</td>
<td>1.00</td>
<td>0.91 (0.73–1.13)</td>
<td>0.67 (0.52–0.85)</td>
<td>0.63 (0.47–0.84)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Model 4</td>
<td>1.00</td>
<td>0.98 (0.79–1.21)</td>
<td>0.75 (0.59–0.96)</td>
<td>0.69 (0.52–0.91)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

*All events are incident and defined based on the ATP-III definition (see Methods for details).
that magnesium intake may have beneficial effects on individual components of the metabolic syndrome.

Experimental data suggest that magnesium may directly regulate cellular glucose metabolism through its role as a cofactor for a number of relevant enzymes\(^28,29\) and may influence insulin secretion by interacting with cellular calcium homeostasis.\(^6\) In addition, epidemiological studies and clinical trials indicate that magnesium intake may improve insulin sensitivity,\(^29–31\) and an inverse correlation between dietary magnesium and fasting insulin level was observed in various populations.\(^9,25,32,33\)

Evidence that magnesium is directly involved in body weight regulation is lacking. The mechanisms for an inverse association between magnesium intake and abdominal obesity are unclear. It was hypothesized that magnesium may have an antiobesity effect because of its capability of forming

<table>
<thead>
<tr>
<th>TABLE 3. HRs (95% CIs) of Each Component of the Metabolic Syndrome According to Total Magnesium Intake*</th>
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<tbody>
<tr>
<td></td>
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<tr>
<td>Blood pressure</td>
</tr>
<tr>
<td>No. of events</td>
</tr>
<tr>
<td>Model 1</td>
</tr>
<tr>
<td>Model 2</td>
</tr>
<tr>
<td>Model 3</td>
</tr>
<tr>
<td>Glucose</td>
</tr>
<tr>
<td>No. of events</td>
</tr>
<tr>
<td>Model 1</td>
</tr>
<tr>
<td>Model 2</td>
</tr>
<tr>
<td>Model 3</td>
</tr>
<tr>
<td>HDL cholesterol</td>
</tr>
<tr>
<td>No. of events</td>
</tr>
<tr>
<td>Model 1</td>
</tr>
<tr>
<td>Model 2</td>
</tr>
<tr>
<td>Model 3</td>
</tr>
<tr>
<td>Triglycerides</td>
</tr>
<tr>
<td>No. of events</td>
</tr>
<tr>
<td>Model 1</td>
</tr>
<tr>
<td>Model 2</td>
</tr>
<tr>
<td>Model 3</td>
</tr>
<tr>
<td>Waist circumference</td>
</tr>
<tr>
<td>No. of events</td>
</tr>
<tr>
<td>Model 1</td>
</tr>
<tr>
<td>Model 2</td>
</tr>
<tr>
<td>Model 3</td>
</tr>
</tbody>
</table>

*All events are incident and defined on the basis of the ATP-III definition (see Methods for details); adjusted for covariates cited in Table 2.
soaps with fatty acids in the intestine and thus reducing the
digestible energy content of the diet.34,35 Nevertheless, in-
takes of whole grain,36 nuts,37 and fruits and vegetables,38
which are the major foods contributing to magnesium intake,
have been shown to be inversely related to body weight.
The relation between magnesium and blood pressure has
been studied for decades. Experimental and observational
studies demonstrate an inverse association between magne-
sium and blood pressure.39 Some evidence supports the
concept that cardiac excitability and vascular tone can be
modified in decreasing blood pressure by minor changes in
magnesium levels.40 Neither epidemiological nor clinical trial
data are consistent. However, a meta-analysis including 20
randomized clinical trials and 1220 individuals detected
significant dose-dependent blood pressure reductions from
magnesium supplementation.11

In addition, animal studies found that serum triglycerides
were significantly higher and HDL cholesterol levels were
significantly lower with magnesium deficiency.41,42 Observa-
tional data13,32 and a clinical trial43 provide further evidence
to support these potential beneficial effects. One possible
explanation is that magnesium intake may increase lipopro-
tein lipase activity, which is involved in the conversion of
triglycerides to HDL cholesterol.44

Our study has a number of strengths that support the validity
of the findings. The prospective design reduced the possibility of
selection and recall biases. In addition, the inverse associations
are observed between magnesium intake and metabolic syn-
drome as well as its components. The strength of these associa-
tions makes it unlikely that the findings are due to chance.
These associations held even after adjustment for a number of
dietary and nondietary factors including baseline body mass
index as well as the baseline status of individual components of
the metabolic syndrome that could potentially confound the
observed HRs. In addition, the inverse correlation between
magnesium intake and fasting insulin level provides further
rationale to support our findings. Moreover, an inverse relation
was also observed between whole grain consumption, one of the
major sources of dietary magnesium intake, and metabolic
syndrome. Furthermore, it is unlikely that our results were
biased by misdiagnosis of end points because all clinical mea-
surements were performed by certified technicians who were
blinded to participants’ dietary habits, and the cutoff points for
event identification are straightforward.

One concern of the study is the accuracy of the measure-
ment for magnesium intake. However, the diet history ques-
tionnaire has been evaluated and found to reasonably capture
habitual diet intake.19 In addition, the correlation of toenail
magnesium concentration and dietary magnesium intake is
reasonable even though the toenail specimens and diet infor-
mation were not collected in the same year. In addition,
because of the prospective nature, any misclassification of
nutrient assessment is likely to be nondifferential and would
tend to attenuate our findings and make the observed associa-
tions conservative. Moreover, the dietary history is designed
to measure usual dietary intake. In the primary analyses, we

<table>
<thead>
<tr>
<th>TABLE 4. Fasting Insulin Levels by Quartiles of Magnesium Intake</th>
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</thead>
<tbody>
<tr>
<td>Magnesium Intake</td>
</tr>
<tr>
<td>Quartz 1           Quartz 2           Quartz 3           Quartz 4          P for Trend</td>
</tr>
<tr>
<td>--------------------</td>
</tr>
<tr>
<td>Both supplement users* and nonusers (n = 4622)</td>
</tr>
<tr>
<td>Magnesium intake, median, mg/1000 kcal</td>
</tr>
<tr>
<td>Crude insulin level, median (interquartile range)</td>
</tr>
<tr>
<td>Multivariable-adjusted insulin level, geometric mean (95% CI)†</td>
</tr>
<tr>
<td>Supplement nonusers (n = 3870)</td>
</tr>
<tr>
<td>Magnesium intake, median, mg/1000 kcal</td>
</tr>
<tr>
<td>Crude insulin level, median (interquartile range)</td>
</tr>
<tr>
<td>Multivariable-adjusted insulin level, geometric mean (95% CI)†</td>
</tr>
<tr>
<td>Supplement users (n = 752)*</td>
</tr>
<tr>
<td>Magnesium intake, median, mg/1000 kcal</td>
</tr>
<tr>
<td>Crude insulin level, median (interquartile range)</td>
</tr>
<tr>
<td>Multivariable-adjusted insulin level, geometric mean (95% CI)†</td>
</tr>
</tbody>
</table>

Insulin levels are expressed as microunits per milliliter.
*Supplement users are those who use any supplement contain magnesium.
†Adjusted for covariates cited in model 3 in Table 2.
used baseline dietary intake. However, the results were consistent when we used the accumulative average dietary intakes measured at baseline and examination year 7 (data not shown).

Another concern of the study is whether the observed beneficial effect of magnesium intake on metabolic syndrome is independent of other minerals such as calcium and potassium. In secondary analyses, we found that the inverse associations were only slightly attenuated with additional adjustment for calcium. When we further adjusted for potassium intake, the associations were attenuated and become statistically nonsignificant. Presumably, the significant attenuation was due to the colinearity. In addition, our findings are less likely to be confounded by multivitamin supplement use because the results are similar among supplement nonusers. Nevertheless, our study was observational; thus, the possibility of residual confounding and confounding from other unmeasured factors cannot be ruled out. The effects of magnesium intake per se cannot be completely isolated from the effects of other factors without experimental data.

In conclusion, our results provide prospective evidence that magnesium intake is inversely associated with incident metabolic syndrome and its components in healthy young adults independent of their baseline body mass index. Our study also raises a further question: Will higher magnesium intake prevent people from developing metabolic syndrome, which leads to diabetes and coronary heart disease? Further studies, particularly well-designed randomized trials, are warranted.

Acknowledgments

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Disclosures

None.

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**CLINICAL PERSPECTIVE**

Some studies suggest that magnesium intake may be inversely related to the risk of hypertension and type 2 diabetes mellitus and that higher intake of magnesium may decrease blood triglycerides and increase high-density lipoprotein (HDL) cholesterol levels. In this analysis of data from the Coronary Artery Risk Development in Young Adults (CARDIA) Study, a prospective cohort study with 15 years of follow-up, He and colleagues found that magnesium intake from diet and supplements was inversely associated with incidence of metabolic syndrome after adjustment for major lifestyle and dietary variables as well as baseline status of each component of the metabolic syndrome. The inverse associations were not modified appreciably by gender and race. Magnesium intake was also inversely related to individual components of the metabolic syndrome and fasting insulin levels. This study suggests that young adults with higher magnesium intake have lower risk of development of metabolic syndrome.
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