Serum magnesium rather than calcium was inversely associated with abnormal glycated hemoglobin concentrations in adults with coronary artery disease

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ABSTRACT

Background and Objectives: Mechanism studies have indicated that magnesium (Mg) and calcium (Ca) had important biological functions in glucose regulation, but epidemiological data on their associations with glycosylated hemoglobin (HbA1c) are sparse. We aimed to explore the associations of Mg and Ca with abnormal HbA1c, and examined the mediating effects of inflammation in coronary artery disease (CAD) Chinese adults. **Methods and Study Design:** A hospital–based cross–sectional study of 11934 patients with CAD was conducted. Serum Mg and Ca concentrations were measured. **Results:** In multivariable analyses, Mg and Mg/Ca ratio were inversely associated with abnormal HbA1c (Q4 vs Q1: OR_{Mg}: 0.61, 95% CI_{Mg}: 0.53, 0.71; $OR_{Mg/Ca\ ratio}$: 0.67, 95% $CI_{Mg/Ca\ ratio}$: 0.54, 0.84). However, null association of Ca with abnormal HbA1c was shown (Q4 vs Q1: OR: 1.15, 95% CI: 0.92, 1.44). Serum Mg and Mg/Ca ratio were inversely associated with abnormal fasting blood glucose (FBG). In contrast, serum Ca was positively associated with abnormal FBG. Path analysis indicated that there were no mediating effects of hypersensitivity C reactive protein (hsCRP) on Mg and Mg/Ca-abnormal HbA1c associations. **Conclusions:** Our study suggested that serum Mg and Mg/Ca ratio were inversely associated with abnormal HbA1c in Chinese adults with CAD. The Mg-abnormal HbA1c relationship might not be mediated by hsCRP.

Key Words: magnesium, calcium, abnormal glycosylated hemoglobin, coronary artery disease, cross–sectional study

INTRODUCTION

Glycated hemoglobin (HbA1c), an index of average blood glucose concentrations in the past 3-4 months,[1] plays an important role in the development of coronary artery disease (CAD).[2] Elevated HbA1c level has been proven to be an independent risk factor for mortality in populations with CAD patients.[3] Previous studies indicated that magnesium (Mg) and calcium (Ca) were obvious established in the risk of CAD [4, 5] and might modulate circulating HbA1c concentration in body.[6-9] Thus, it is possible that Mg and Ca might improve the risk and prognosis of CAD by regulating HbA1c concentration. However, the effects of Mg and Ca on HbA1c are less well known.

Ca and Mg have important biological functions in glucose regulation.[10, 11] *In vitro* and animal experiments have revealed the potential role of Ca and Mg in modulating glucose concentrations.[12-14] However, sparse data aimed at examining the associations between blood

Ca and HbA1c were inconsistent, with inverse,[15] and positive associations.[16, 17] Additionally, some epidemiological studies reported inverse associations of Mg with HbA1c.[17-27] But a recent meta-analysis found that Mg supplementation could not improve HbA1c concentrations.[28] Other studies found null correlation between Mg and HbA1c.[20, 22, 29] Liu et al. even reported a positive association between serum Mg and HbA1c in persons with diabetes or central obesity.[30] Therefore, the associations of Ca and Mg with HbA1c remained to be speculative. Moreover, CAD patients were more likely to have some degree of lipid and glucose metabolism than general populations. However, it is not clear whether the previous research results can be generalized to CAD patients.

Additionally, previous evidence revealed that Mg and Ca could modulate inflammation status,[31, 32] which was considered as an important regulatory factor of glucose metabolism. However, no study had yet examined whether the associations of Mg and Ca with HbA1c concentrations might be mediated by inflammation.

This study aimed to examine the associations of Mg and Ca with abnormal HbA1c and the mediating role of inflammation on the Mg and Ca-abnormal HbA1c association in Chinese adults with CAD.

MATERIALS AND METHODS

Study participants

A hospital–based cross–sectional study was conducted between November 2016 and December 2019 from Wuhan Asia Heart Hospital. 11934 patients (The age range was 29 - 89 years, mean age 61.7 years) with CAD were included in this study. CAD was defined as meeting one of the following criteria: a). history of angina pectoris, myocardial infarction or coronary intervention; b). coronary angiography implied vascular stenosis >50%; c). significant myocardial infarction was presented from electrocardiogram. The present study was conducted based on the Declaration of Helsinki and approved by the ethics committee of Wuhan Asia Heart Hospital (No. 2016–B008). Informed consents were obtained from all the participants.

Data collection

The information collected from all CAD patients included height, weight, smoking, alcohol intake, age, sex, antihypertensive and hypoglycemic agent use based on medical records. Body mass index (BMI) was calculated as weight (kg)/height (m^2).

Serum Mg and Ca concentrations were measured by a NexION 350X (PerkinElmer, USA). The pressurizing collision cell was used to eliminate polyatomic interferences in the kinetic energy discrimination mode.33 HbA1c concentrations in the red blood cells was measured using a Bole glycated hemoglobin D-10 kit by a Bole glycated hemoglobin analyzer D-10. Fasting blood glucose (FBG) was measured by a commercial kit (Roche Diagnostics GmbH, China). High-sensitivity C-reactive protein (hsCRP) was measured by a Cardiac CRP (Latex) High Sensitive kit. Abnormal HbA1c and abnormal FBG was defined as: HbA1c $\geq$ 6.5% and FBG $\geq$ 5.6 mmol/L.34

Statistical analysis

Continuous variables were presented as the mean (standard deviation). Discrete variables were presented as frequencies (percent). Comparisons of differences between groups were tested using the analysis of variance. All subjects were divided into sex-specific quartile groups according to the rank of serum Mg and Ca concentrations and Mg/Ca ratio. The higher the quartile levels, the higher the corresponding exposure levels. Quartile 1 (Q1) was the lowest concentrations group and Q4 was the highest concentrations group. Logistic regression models were performed to assess the associations of Mg and Ca with abnormal HbA1c. Multivariable adjusted models were performed as follows: Model 1 adjusted for age and sex; Model 2 further adjusted for smoking status, alcohol consumption, BMI, hypoglycemic and antihypertensive agent use. The mediating effects of hsCRP on the associations of serum Mg, Ca and Mg/Ca ratio with abnormal HbA1c and abnormal FBG were examined by path analyses[35] using SPSS AMOS v.24 (IBM, Armonk, NY). Two-tailed $p \leq 0.05$ was statistical significance.

RESULTS

Characteristics of subjects

As shown in Table 1, all participants were divided into quartiles of the serum Mg (n = 11934) and Ca (n = 4606) levels. A higher age and lower proportion of hypoglycemic drugs intake were observed in subjects with higher serum Mg concentrations. A lower age and hsCRP were observed in subjects with higher serum Ca concentrations. No significant correlations were found between serum Mg, Ca and other indices (e.g., BMI, alcohol drinker, smoking status, and hypotensor agent using, all p trend > 0.05).

Associations of Mg, Ca and the ratio with abnormal HbA1c

In general, serum Mg and Mg/Ca ratio showed inverse associations with abnormal HbA1c, while Ca exhibited null association with abnormal HbA1c (Table 2). With adjustment for sex and age in Model 1, inverse associations for serum Mg and Mg/Ca ratio were found with odd raitos (ORs) 95% confidence interval (95% CI) of 0.53 (0.47, 0.60) and 0.64 (0.53, 0.77) in the fourth quartile compared with the first quartile. But Ca was not associated with abnormal HbA1c (OR: 1.06, 95% CI: 0.88, 1.28). After further adjusting for the other potential covariates in Model 2, Mg and Mg/Ca ratio were inversely associated with abnormal HbA1c (Q4 vs Q1: ORMg: 0.61, 95% CIMg: 0.53, 0.71; ORMg/Ca ratio: 0.67, 95% CIMg/Ca ratio: 0.54, 0.84). However, null association of Ca concentrations with abnormal HbA1c were showed (Q4 vs Q1: OR: 1.15, 95% CI: 0.92, 1.44).

Table 3 showed the stratified analyses by sex. In multivariable analysis, serum Mg and Mg/Ca ratio were inversely associated with abnormal HbA1c (OR_{Mg}: 0.67, 95% CI_{Mg}: 0.56, 0.80; $OR_{Mg/Ca\ ratio}$: 0.69, 95% $CI_{Mg/Ca\ ratio}$: 0.52, 0.91) in the fourth quartile compared with the first quartile in men. Inverse associations between serum Mg and Mg/Ca ratio and abnormal HbA1c were also observed in women (OR_{Mg}: 0.51, 95% CI_{Mg}: 0.40, 0.64; $OR_{Mg/Ca\ ratio}$: 0.65, 95% $CI_{Mg/Ca\ ratio}$: 0.45, 0.94). There was no significant association between Ca and abnormal HbA1c in both men and women. Additionally, multivariable analysis found that Mg and Ca were still inversely associated with abnormal HbA1c in subjects without using hypoglycemic medications. The corresponding OR (95% CI) were 0.66 (0.56, 0.78) for Mg and 0.71 (0.56, 0.92) for Ca in the fourth quartile compared with the first quartile (Supplemental Table 1).

Associations of Mg, Ca and its ratios with abnormal FBG

As shown in Supplemental Table 2, serum Mg and Mg/Ca ratio were inversely associated with abnormal FBG in both Models 1 and 2. In contrast, serum Ca was positively associated with abnormal FBG.

Path analysis

Path analysis was conducted to evaluate whether hsCRP had effects on the Mg and Mg/Ca-abnormal HbA1c associations. Figure 1 indicated that serum Mg and Mg/Ca ratio did not have direct effect on hsCRP. Mediating effects of hsCRP on serum Mg and Mg/Ca-abnormal HbA1c associations were not found. Similarly, no mediating effects of hsCRP on serum Mg and Mg/Ca-abnormal FBG associations were also observed (Supplemental Figure 1).

DISCUSSION

In this hospital–based cross–sectional study of patients with CAD, we observed graded and inverse associations of serum Mg and Mg/Ca ratio with abnormal HbA1c. These associations might not be mediated by hsCRP. Additionally, there was no significant association between serum Ca and abnormal HbA1c. As we all know, our study was the first to examine the associations of serum Mg, Ca and Mg/Ca ratio with abnormal HbA1c in Chinese adults with CAD. Our results indicated that serum Mg might influence HbA1c concentrations.

Emerging evidence focused on the health benefits of Mg in patients with cardiovascular diseases. Previous studies demonstrated that higher circulating Mg concentrations were associated with lower risk of cardiovascular diseases.[36] Mg appears to play an important role in protecting against cardiovascular diseases[37] by regulating glycometabolism.[10] Some studies had evaluated the associations between Mg and HbA1c.[17-30] However, these findings were contradictory. Bertinato et al. pointed out that serum Mg was negatively correlated with HbA1c ($r = - 0.02$).[26] Ozcaliskan et al. observed a negative relationship between serum Mg and HbA1c values in patients with diabetes mellitus ($r = - 0.309$).[20] Other studies also found the negative association in patients with diabetes mellitus[17-19, 23-25, 27] or in pre-diabetes.[21] Animal study also demonstrated that Mg might improve HbA1C concentrations via regulating lipid profiles, energy metabolism, oxidative state and activation of glucose transporter-4 in skeletal muscle.[6] Consistent with these previous studies, we found an inverse association between Mg and abnormal HbA1c in patients with CAD. Nevertheless, a recent meta-analysis of randomized controlled trials revealed no significant effect of Mg supplementation on plasma concentrations of HbA1c.[28] It is possible that HbA1c could not reflect the effect on glucose concentrations of short-term clinical trials due to HbA1c is an index of overall glycemia in the past 3-4 months.[1] Other studies also found null association between Mg and HbA1c in patients with diabetes mellitus.[20, 22, 29] Even a positive association between serum Mg and HbA1c was observed in persons with diabetes or central obesity (HbA1c: 5.7% in high Mg $\geq$ 0.95 mmol/L group vs 5.3% in low Mg $\leq$ 0.65 mmol/L).30 Small sample (n=57) and the presence of long-duration diabetes might attenuate the relationship between serum Mg concentrations and HbA1c.[20]

The targeting of Ca modulation is emerging as a crucial area for innovative heart failure treatments, which could significantly enhance cardiac function and improve disease outcomes.[38] Previous studies also demonstrated that Ca played an important role in CAD.[5] However, scarce data examined the association between Ca and HbA1c.[15-17] A cross-sectional study observed that serum Ca had a good negative correlation with HbA1c concentrations in

patients with diabetes mellitus (r = - 0.56).[15] Nevertheless, Akter et al. found that serum Ca was positively associated with HbA1c in health populations (HbA1cQ4 vs Q1: 5.29% vs 5.24%).[16] Wang et al. observed that serum Ca concentrations were positively correlated with HbA1c (Standardization β = 0.17) in patients with diabetes mellitus.[17] Our study found null association between serum Ca and HbA1c. The lower Ca concentrations in patients with CAD (2.27 mmol/L [this study]) than in patients with diabetes mellitus (2.29 mmol/dL[15] and 2.34 mmol/L[17]) might provide a potential explanation for the null results of our study. Different statistical method (person correlation,[15] analyses of covariance[16] [this study], linear regression analysis[17]), and subjects (patients with diabetes mellitus,[15, 17] health populations,[16] patients with CAD [this study]) might also explain the inconsistent results among studies.

Strengths and limitations

This study has several strengths. As we all know, this was the first study that investigated the associations of Mg and Ca with abnormal HbA1C concentrations and examined the mediating effects of hsCRP in these relationships in Chinese adults with CAD. Moreover, both abnormal HbA1c and abnormal FBG were used as glycaemic indicators for correlation analysis, which strengthens the stability and reliability of our results. Additionally, the relative large sample size and adjustment of potential confounders in our study provided good insights into the associations of Mg and Ca with abnormal HbA1C. Nevertheless, this study also had several limitations. First, no causal associations of Mg and Ca with abnormal HbA1C were established due to the cross-sectional design of the study. Second, subjects were adults with CAD in this study, thus the generalization of the results is limited. Third, although hypotensor and hypoglycemic agents were considered in multivariable analysis, the use of other cardiovascular drugs was not considered. The associations of Mg and Ca with abnormal HbA1C might be overestimated in our study. Further prospective studies will be needed to validate our findings. Finally, although some potential confounding factors were adjusted in our study, the possibility of bias was not ruled out because of residual confounding.

Conclusion

Generally, our study suggested that serum Mg and Mg/Ca ratio were inversely associated with abnormal HbA1c in Chinese adults with CAD. The glucose regulation of Mg and Mg/Ca ratio reported here might lead to new intervention approaches in abnormal glucose metabolism related diseases among patients with CAD such as diabetes, hypertension and dyslipidemia. Replication of these findings is warranted in experimental settings and in different population.

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CONFLICT OF INTEREST AND FUNDING DISCLOSURE

The authors declare no conflict of interest.

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Table 1. Baseline characteristics of the study participants with coronary artery disease by quartiles of serum Mg and Ca[†]

Variables	Quartiles by Mg and Ca				*p*-trend
	Q1	Q2	Q3	Q4	
Mg, n	2829	3312	2729	3064	
Age, years	61.1 ± 9.81	61.6 ± 10.01	61.7 ± 10.00	62.4 ± 10.04	<0.001
Sex					0.196
Male, n (%)	1777 (62.8)	2083 (62.9)	1594 (58.4)	2023 (66.0)	
Female, n (%)	1052 (37.2)	1229 (37.1)	1135 (41.6)	1041 (34.0)	
BMI, kg/m^2	25.66 ± 16.04	25.94 ± 17.33	25.37 ± 13.01	25.89 ± 19.11	0.923
Alcohol drinker, n (%)	253 (8.9)	308 (9.3)	237 (8.7)	279 (9.1)	0.969
Smoker, n (%)	424 (15.0)	452 (13.6)	367 (13.4)	442 (14.4)	0.511
Hypotensor agents user, n (%)	1357 (48.0)	1576 (47.6)	1307 (47.9)	1518 (49.5)	0.204
Hypoglycemic agents user, n (%)	676 (23.9)	573 (17.3)	404 (14.8)	461 (15.0)	<0.001
hsCRP, mg/L (n=5208)	6.20 ± 0.35	5.14 ± 0.37	5.05 ± 0.35	5.71 ± 0.39	0.327
Ca, n	1146	1183	1171	1106	
Age, years	64.2 ± 9.92	62.1 ± 9.73	61.0 ± 9.97	59.5 ± 10.70	<0.001
Sex					0.461
Male, n (%)	730 (63.7)	788 (66.6)	757 (64.6)	729 (65.9)	
Female, n (%)	416 (36.3)	395 (33.4)	414 (35.4)	377 (34.1)	
BMI, kg/m^2	25.30 ± 21.02	25.03 ± 12.23	26.09 ± 18.46	25.54 ± 13.18	0.432
Alcohol drinker, n (%)	87 (7.6)	107 (9.0)	109 (9.3)	94 (8.5)	0.415
Smoker, n (%)	150 (13.1)	179 (15.1)	149 (12.7)	153 (13.8)	0.985
Hypotensor agents user, n (%)	547 (47.7)	536 (45.3)	551 (47.1)	516 (46.7)	0.858
Hypoglycemic agents user, n (%)	236 (20.6)	207 (17.5)	203 (17.3)	206 (18.6)	0.249
hsCRP, mg/L (n=1911)	12.75 ± 0.78	7.34 ± 0.78	6.55 ± 0.84	7.29 ± 0.78	<0.001

BMI, body mass index. Ca, calcium; hsCRP, hypersensitivity C reactive protein; Mg, Magnesium; Q, quartile.
[†]Values were means ± standard deviations or n (%).
p values were calculated using analyses of covariance.

Table 2. Associations of Mg and Ca concentrations with abnormal HbA1c for all participants

Variables	Quartiles by Mg and Ca			
	Q1	Q2	Q3	Q4
Mg				
Mean (SD)	0.77 ± 0.04	0.83 ± 0.01	0.88 ± 0.01	0.97 ± 0.12
Case/N	911/2829	776/3312	570/2729	632/3064
OR (95%CI)				
Model 1†	1	0.64 (0.57, 0.71)**	0.55 (0.48, 0.62)**	0.53 (0.47, 0.60)**
Model 2‡	1	0.70 (0.61, 0.81)**	0.65 (0.56, 0.75)**	0.61 (0.53, 0.71)**
Ca				
Mean (SD)	2.13 ± 0.08	2.24 ± 0.02	2.31 ± 0.02	2.41 ± 0.07
Case/N	325/1146	288/1183	286/1171	312/1106
OR (95%CI)				
Model 1†	1	0.84 (0.70, 1.01)	0.85 (0.71, 1.03)	1.06 (0.88, 1.28)
Model 2‡	1	0.88 (0.70, 1.10)	0.90 (0.72, 1.13)	1.15 (0.92, 1.44)
Mg/Ca ratio				
Mean (SD)	0.33 ± 0.02	0.37 ± 0.01	0.39 ± 0.01	0.44 ± 0.07
Case/N	378/1150	281/1152	264/1152	288/1152
OR (95%CI)				
Model 1†	1	0.64 (0.53, 0.77)**	0.59 (0.49, 0.71)**	0.64 (0.53, 0.77)**
Model 2‡	1	0.71 (0.57, 0.89)*	0.63 (0.50, 0.78)**	0.67 (0.54, 0.84)**

Ca, calcium; Mg, Magnesium; OR, odd ratio; 95% CI, 95% confidence interval; Q, quartile; SD, standard deviation; HbA1c, glycosylated hemoglobin.
†Model 1 adjusted for age and sex.
‡Model 2 further adjusted for smoking status, BMI, alcohol consumption, hypotensor and hypoglycemic drug use.
* $p < 0.05$, ** $p < 0.001$.

Table 3. Associations of Mg and Ca concentrations with abnormal HbA1c by sex (OR 95% CI)

Variables	Quartiles by Mg and Ca			
	Q1	Q2	Q3	Q4
Mg				
Men				
Model 1†	1	0.71 (0.61, 0.82)**	0.70 (0.60, 0.82)**	0.63 (0.54, 0.73)**
Model 2‡	1	0.73 (0.62, 0.87)**	0.77 (0.64, 0.93)*	0.67 (0.56, 0.80)**
Women				
Model 1†	1	0.53 (0.44, 0.63)**	0.37 (0.30, 0.45)**	0.39 (0.32, 0.48)**
Model 2‡	1	0.64 (0.52, 0.80)**	0.48 (0.38, 0.61)**	0.51 (0.40, 0.64)**
Ca				
Men				
Model 1†	1	0.86 (0.68, 1.09)	0.95 (0.75, 1.20)	1.18 (0.93, 1.50)
Model 2‡	1	0.89 (0.67, 1.18)	0.93 (0.70, 1.24)	1.22 (0.92, 1.62)
Women				
Model 1†	1	0.82 (0.61, 1.11)	0.72 (0.53, 0.97)*	0.88 (0.65, 1.19)
Model 2‡	1	0.87 (0.60, 1.27)	0.83 (0.57, 1.20)	0.97 (0.66, 1.41)
Mg/Ca ratio				
Men				
Model 1†	1	0.74 (0.59, 0.94)*	0.74 (0.59, 0.94)*	0.69 (0.55, 0.87)*
Model 2‡	1	0.74 (0.56, 0.98)*	0.75 (0.57, 0.99)*	0.69 (0.52, 0.91)*
Women				
Model 1†	1	0.49 (0.36, 0.67)**	0.38 (0.28, 0.52)**	0.55 (0.41, 0.75)**
Model 2‡	1	0.67 (0.46, 0.97)*	0.44 (0.30, 0.65)**	0.65 (0.45, 0.94)*

Ca, calcium; Mg, Magnesium; OR, odd ratio; 95% CI, 95% confidence interval; Q, quartile; HbA1c, glycosylated hemoglobin.
†Model 1 adjusted for age.
‡Model 2 further adjusted for smoking status, BMI, alcohol consumption, hypotensor and hypoglycemic drug use.
* $p< 0.05$, ** $p< 0.001$.

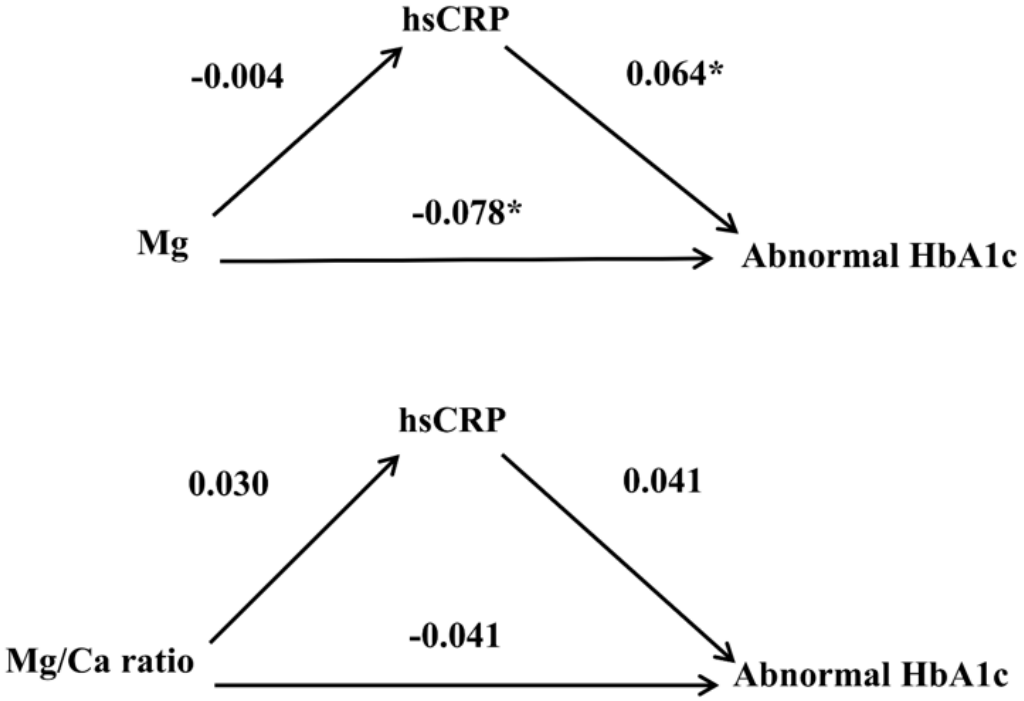


Figure 1. The mediating effects of hsCRP on the Mg and Mg/Ca-abnormal HbA1c associations among subjects with CAD in path analyses. CAD, coronary artery disease; Ca, calcium; hsCRP, hypersensitivity C reactive protein; Mg, magnesium; HbA1c, glycosylated hemoglobin.

Supplementary Figure and Tables

Supplementary Table 1. Multivariable analysis of the associations of Mg and Ca concentrations with abnormal HbA1c in subjects without using hypoglycemic medications[†]

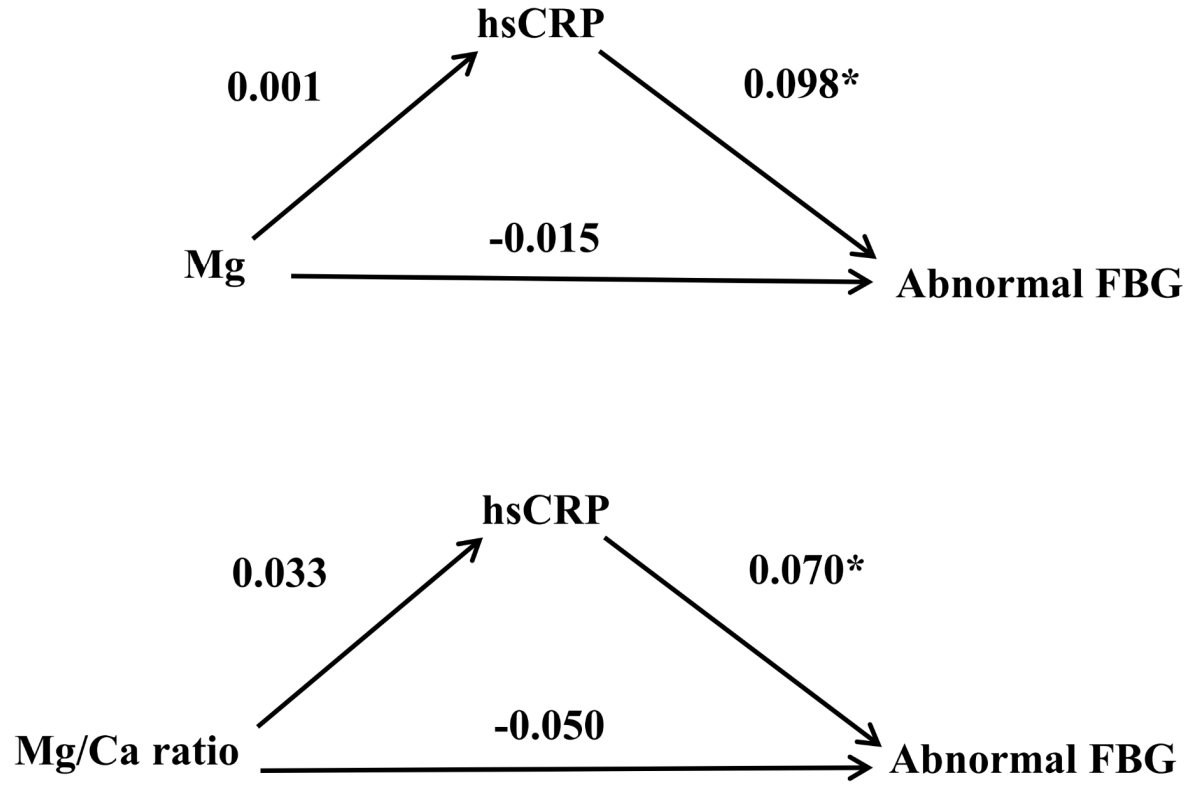
Variables	Quartiles by Mg and Ca			
	Q1	Q2	Q3	Q4
Mg				
Mean (SD)	0.77 ± 0.04	0.84 ± 0.01	0.88 ± 0.01	0.97 ± 0.10
Case/N	389/2324	327/2568	301/2605	278/2323
OR (95%CI)	1	0.72 (0.61, 0.85)**	0.64 (0.55, 0.76)**	0.66 (0.56, 0.78)**
Ca				
Mean (SD)	2.13 ± 0.09	2.24 ± 0.02	2.31 ± 0.02	2.41 ± 0.07
Case/N	139/910	123/976	132/968	155/900
OR (95%CI)	1	0.82 (0.63, 1.07)	0.91 (0.70, 1.18)	1.23 (0.96, 1.59)
Mg/Ca ratio				
Mean (SD)	0.33 ± 0.02	0.37 ± 0.01	0.39 ± 0.01	0.44 ± 0.05
Case/N	172/939	118/936	123/939	136/940
OR (95%CI)	1	0.63 (0.49, 0.81)**	0.65 (0.51, 0.84)**	0.71 (0.56, 0.92)*

Ca, calcium; Mg, Magnesium; OR, odd ratio; 95% CI, 95% confidence interval; Q, quartile; SD, standard deviation; HbA1c, glycosylated hemoglobin.
[†]Sex, age, smoking status, BMI, alcohol consumption, and hypotensor drug use were adjusted.
* $p< 0.05$, ** $p< 0.001$.

Supplementary Table 2. Associations of Mg and Ca concentrations with abnormal FBG for all participants

Variables	Quartiles by Mg and Ca			
	Q1	Q2	Q3	Q4
Mg				
Mean (SD)	0.77 ± 0.04	0.83 ± 0.01	0.88 ± 0.01	0.96 ± 0.12
Case/N	1394/2539	1490/3029	1129/2477	1346/2758
OR (95%CI)				
Model 1[†]	1	0.79 (0.71, 0.88)**	0.69 (0.61, 0.77)**	0.77 (0.69, 0.86)**
Model 2[‡]	1	0.87 (0.78, 0.97)*	0.79 (0.70, 0.88)**	0.88 (0.79, 0.99)*
Ca				
Mean (SD)	2.13 ± 0.08	2.24 ± 0.02	2.31 ± 0.02	2.41 ± 0.07
Case/N	571/981	553/1041	601/1052	638/985
OR (95%CI)				
Model 1[†]	1	0.83 (0.70, 1.00)	0.99 (0.83, 1.19)	1.40 (1.17, 1.69)*
Model 2[‡]	1	0.86 (0.72, 1.04)	1.03 (0.86, 1.24)	1.48 (1.22, 1.79)**
Mg/Ca ratio				
Mean (SD)	0.33 ± 0.02	0.37 ± 0.01	0.39 ± 0.01	0.44 ± 0.07
Case/N	654/1014	567/1016	558/1014	584/1015
OR (95%CI)				
Model 1[†]	1	0.67 (0.56, 0.81)**	0.66 (0.55, 0.79)**	0.71 (0.59, 0.85)**
Model 2[‡]	1	0.72 (0.60, 0.87)**	0.70 (0.58, 0.84)**	0.77 (0.64, 0.93)*

Ca, calcium; Mg, Magnesium; OR, odd ratio; 95% CI, 95% confidence interval; Q, quartile; SD, standard deviation; FBG, fasting blood glucose.
[†]Model 1 adjusted for age.
[‡]Model 2 further adjusted for smoking status, BMI, alcohol consumption, hypotensor and hypoglycemic drug use.
* $p< 0.05$, ** $p< 0.001$.



Supplementary Figure 1. The mediating effects of hsCRP on the Mg and Mg/Ca-abnormal FBG associations among subjects with CAD in path analyses. CAD, coronary artery disease; Ca, calcium; FBG, fasting blood glucose; Mg, magnesium.