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Magnesium Intake Is Inversely Associated With Coronary Artery Calcification

The Framingham Heart Study

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OBJECTIVES The aim of this study was to examine whether magnesium intake is associated with coronary artery calcification (CAC) and abdominal aortic calcification (AAC).

BACKGROUND Animal and cell studies suggest that magnesium may prevent calcification within atherosclerotic plaques underlying cardiovascular disease. Little is known about the association of magnesium intake and atherosclerotic calcification in humans.

METHODS We examined cross-sectional associations of self-reported total (dietary and supplemental) magnesium intake estimated by food frequency questionnaire with CAC and AAC in participants of the Framingham Heart Study who were free of cardiovascular disease and underwent Multi-Detector Computed Tomography (MDCT) of the heart and abdomen (n = 2,695; age: 53 ± 11 years), using multivariate-adjusted Tobit regression. CAC and AAC were quantified using modified Agatston scores (AS). Models were adjusted for age, sex, body mass index, smoking status, systolic blood pressure, fasting insulin, total-to-high-density lipoprotein cholesterol ratio, use of hormone replacement therapy (women only), menopausal status (women only), treatment for hyperlipidemia, hypertension, cardiovascular disease prevention, or diabetes, as well as self-reported intake of calcium, vitamins D and K, saturated fat, fiber, alcohol, and energy. Secondary analyses included logistic regressions of CAC and AAC outcomes as cut-points (AS >0 and AS ≥90th percentile for age and sex), as well as sex-stratified analyses.

RESULTS In fully adjusted models, a 50-mg/day increment in self-reported total magnesium intake was associated with 22% lower CAC ($p < 0.001$) and 12% lower AAC ($p = 0.07$). Consistent with these observations, the odds of having any CAC were 58% lower (p trend: <0.001) and any AAC were 34% lower (p trend: 0.01), in those with the highest compared to those with the lowest magnesium intake. Stronger inverse associations were observed in women than in men.

CONCLUSIONS In community-dwelling participants free of cardiovascular disease, self-reported magnesium intake was inversely associated with arterial calcification, which may play a contributing role in magnesium's protective associations in stroke and fatal coronary heart disease. (J Am Coll Cardiol Img 2014;7:59–69) © 2014 by the American College of Cardiology Foundation

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Coronary artery calcification (CAC) (1–3) and abdominal aortic calcification (AAC) (3–5) are measures of advanced atherosclerosis that predict cardiovascular disease (CVD) morbidity and mortality independently of traditional CVD risk factors. CAC in particular has been shown to discriminate and reclassify future risk for clinical coronary events (6). Dietary magnesium, found in a broad range of foods including whole grains, green leafy vegetables, almonds, coffee, and dark chocolate, has been linked to many aspects of cardiovascular health (7–9), and this mineral may play a key role in vascular calcification. A protective role of magnesium in calcification may underlie previous observations of higher magnesium intake and lower risk of stroke (10,11), nonfatal myocardial infarction (MI), sudden cardiac death, and fatal coronary heart disease (CHD) (12–14).

ABBREVIATIONS AND ACRONYMS

AAC = abdominal aortic calcification

AS = Agatston score

CAC = coronary artery calcification

CKD = chronic kidney disease

CT = computed tomography

ESRD = end-stage renal disease

GFR = glomerular filtration rate

IMT = intima-medial thickness

MDCT = Framingham Heart Study Multi-Detector Computed Tomography Sub-study

PWV = pulse-wave velocity

In vitro (15–19) and animal (19–23) studies suggest biological mechanisms through which magnesium may prevent or reverse plaque formation and calcification. Magnesium may be acting as a calcium antagonist (24), and it may directly inhibit hydroxyapatite and crystal precipitation (25–27). In individuals with chronic kidney disease (CKD), end-stage renal disease (ESRD), or on hemodialysis—known to exhibit accelerated calcification—inverse associations have been reported between serum magnesium and calcification in various vascular beds (27) and with related measures of atherosclerosis or arteriosclerosis, such as carotid intima-medial thickness (IMT) and pulse-wave velocity (PWV) (17). In healthy populations, observational studies have also found serum magnesium to be inversely associated with IMT, presence of atherosclerotic plaque, and progression of atherosclerosis (28,29).

However, serum magnesium is a poorly correlated biomarker of magnesium intake (30,31). Only one observational study has examined dietary magnesium in association with CAC in a generally healthy population, observing no association (32). No study has examined the association between magnesium intake and AAC. Therefore, we tested the hypothesis that higher magnesium intake is associated with lower levels of calcification of the coronary arteries and abdominal aorta in a generally healthy population, by assessing the cross-sectional association between self-reported total (dietary and supplemental) magnesium intake with CAC and AAC in community-dwelling participants free of clinically apparent CVD.

METHODS

Study population. The National Heart, Lung, and Blood Institute's Framingham Heart Study is a longitudinal, community-based, observational study that began in 1948 in Framingham, Massachusetts. The children, and their spouses ("Offspring," enrolled 1971–1975), of the original cohort participants have returned for follow-up examination following standardized protocols approximately every four years (33). The third-generation cohort (enrolled 2002 to 2005) includes 4,095 children of the Offspring (34). The present study includes dietary and risk factor data collected from participants who attended Offspring exam 7 (1998 to 2001; n = 3,539) or Third Generation exam 1 (2002 to 2005; n = 4,095), and who participated in exam 1 (2002 to 2005) of the ongoing Multi-Detector Computed Tomography (MDCT) substudy. Although previously described (35), in brief, 3,529 Offspring or Third Generation participants located in the greater New England area underwent MDCT scanning. Men were ≥35 years of age, women were ≥40 years of age and not pregnant, and all participants weighed ≤350 lbs (35).

We excluded participants from this analysis if they had missing or uninterpretable CT scans (n = 278); had clinically apparent CVD (n = 136), defined as CABG, valve replacement, percutaneous coronary stent placement, pacemaker, stroke, CHF, MI, or coronary insufficiency identified or occurring prior to the date of the clinic exam (35); had missing or invalid dietary information (n = 172, reporting <600 or ≥4,000 kcal/day for women, <600 or ≥4,200 kcal/day for men, or with ≥12 blank items); self-reported extreme values of magnesium or calcium intake (n = 48, with intake values in the 0.5th or 99.5th percentile); or were missing complete covariate information (n = 200, as defined subsequently). After exclusions, 2,695 participants remained in the present analyses.

The original data collection protocols were approved by the institutional review boards at Boston University and Massachusetts General Hospital,

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