

Serum calcium levels are not associated with coronary heart disease

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Background: Numerous studies have reported that low calcium intake is related to a higher prevalence of cardiovascular disease. However, the relationship between serum calcium and coronary heart disease is unclear. The purpose of this study was to compare serum calcium levels in patients with coronary heart disease and those in healthy individuals.

Methods: This retrospective, case-control study conducted in the People's Republic of China comprised 380 cases and 379 controls. Serum calcium levels, blood lipids, and anthropometric measurements were measured in both groups. The Student's unpaired *t*-test or Chi-square test was used to compare differences between cases and controls. Pearson's partial correlation coefficient was used to determine the association between serum calcium, blood lipids, and blood pressure in both groups.

Results: Our results indicate that the average level of serum calcium in cases was higher than in controls. Serum calcium levels showed no correlation with any parameter except for triglycerides in either group.

Conclusion: Overall, these data suggest that serum calcium has no influence on coronary heart disease or triglyceride levels in the general population.

Keywords: serum calcium, hypertension, blood lipids

Introduction

Cardiovascular disease is the leading source of global disease burden.¹⁻³ Numerous epidemiologic studies have reported that the prevalence of cardiovascular disease is high in the People's Republic of China.^{4,5} Also, a Markov computer simulation model showed that future risk of cardiovascular disease would increase by more than 50% between 2010 and 2030.⁶ A recent study demonstrated a weak causal relationship between the hardness of drinking water and mortality from cardiovascular disease in males.⁷ Another study documented that individuals who consume hard water rich in calcium and magnesium have a lower mortality rate from circulatory disease than those who consume soft water. However, some researchers have drawn the opposite conclusion, ie, that there is no association between changes in the hardness or calcium content of drinking water and cardiovascular mortality.⁸ Also, individual calcium intake was not unrelated to cardiovascular endpoints.⁹ One possible reason for this is that calcium ions cannot be completely absorbed after ingestion. More recent studies have shown that serum calcium may influence the level of high-density lipoprotein (HDL) cholesterol and decrease the level of low-density lipoprotein (LDL) cholesterol.^{10,11} Given that dyslipidemia is a major risk factor for coronary heart disease, the relationship between serum calcium levels and coronary heart disease should be investigated. Therefore, this

study was carried out to evaluate the relationship between serum calcium levels in patients with coronary heart disease and healthy individuals and to investigate the correlation between serum calcium levels, blood lipid parameters, and blood pressure in both groups.

Subjects and methods

Participants

Initially, routine health screening was performed in a total of 2,746 subjects who attended the Anhui Normal University in the east of the People's Republic of China from August 2006 to September 2006. All subjects were subjected to full history-taking and clinical examination. All those with the diagnosis of angina pectoris and whom the existence of coronary artery disease had been proved upon angiography, according to the diagnostic criteria of angina pectoris in coronary heart disease prepared by World Health Organization in 1979, 380 subjects met the above criteria of angina pectoris, and 379 healthy individuals matched with cases in age and sex were designated as the controls. All subjects agreed to provide their personal information, were informed regarding the purpose and procedures of our study, and gave their written informed consent. The study was approved by the ethics committee at Wannan Medical College.

Blood pressure and anthropometric measurements

Blood pressure was measured three times in the seated position using a mercury sphygmomanometer, and the three measurements were averaged for systolic and diastolic pressure. Height and weight were measured at least three times for each subject. Height was measured using a standard stadiometer following the study protocol, and weight in kilograms was measured on an electronic scale. Body mass index was calculated as weight (kg)/height (m²).

Collection of blood samples and analysis of biochemical indices

During health screening, 10 mL of venous blood was collected into an evacuated blood collection tube. Serum was separated by centrifugation at 600g for 10 minutes. Serum triglycerides and total cholesterol were measured using a commercial kit based on enzymatic principles, and the HDL cholesterol content was determined by the colorimetric method after separating LDL and very LDL using dextran sulfate-Mg²⁺ sedimentation.¹² Serum LDL cholesterol was calculated by the Friedewald formula¹³ using triglycerides, total cholesterol, and HDL cholesterol values. The total

serum calcium level was measured using the ADVIA 2400 (Siemens Healthcare Diagnostics, Malvern, PA, USA) with colorimetry.

Statistical analysis

Data analyses were performed using the R software programming language.¹⁴ The Student's unpaired *t*-test was used for comparison of quantitative data. The Chi-square test was used to compare the sex distribution between cases and controls. Pearson's partial correlation coefficient was used to investigate the relationship between serum calcium, blood lipids, and blood pressure after adjustment for age, sex, body mass index, height, and weight. All statistical tests were two-sided, and a value of *P* < 0.05 was considered to be statistically significant.

Results

General characteristics

Among the total 759 subjects identified, 379 subjects served as controls and 380 subjects as cases with coronary heart disease. The baseline characteristics of the controls and cases are shown in Table 1. The mean age of the controls and cases was 67.48 ± 8.16 years and 67.71 ± 8.47 years, respectively. No significant differences were found in age, height, sex distribution, diastolic blood pressure, blood lipid levels (total cholesterol, HDL cholesterol,

Table 1 General characteristics of controls and cases with coronary heart disease

Parameter	Controls (n = 379)		Cases (n = 380)		P-value
	Mean or %	SD	Mean or %	SD	
Age (years)	67.48	8.16	67.71	8.47	0.697
Sex (%)					
Male	63.1		62.6		0.604 ^a
Female	36.9		37.2		
Height (m)	1.63	0.08	1.63	0.08	0.630
Weight (kg)	60.99	9.91	64.25	10.42	0.000
Body mass index (kg/m ²)	22.94	3.01	24.08	3.22	0.000
SBP (mmHg)	130.26	18.81	134.88	18.88	0.002
DBP (mmHg)	77.65	10.27	78.14	10.01	0.536
Serum calcium (mmol/L)	2.54	0.15	2.57	0.14	0.038
Total cholesterol (mg/dL)	5.56	0.89	5.47	0.90	0.12
HDL cholesterol (mg/dL)	1.34	0.32	1.28	0.31	0.60
LDL cholesterol (mg/dL)	3.46	0.79	3.39	0.82	0.249
Triglycerides (mg/dL)	1.66	1.07	1.74	1.23	0.366

Note: ^aP-value show from Chi-square test comparing sex in the coronary heart disease group with controls.

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; CHD, coronary heart disease; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SD, standard deviation.

LDL cholesterol, and triglycerides) between controls and cases. However, average weight, body mass index, systolic blood pressure, and serum calcium were higher in cases than in controls.

Correlation between serum calcium levels, blood lipids, and blood pressure

Table 2 shows the relationship between serum calcium, blood pressure, and blood lipids in both groups after adjustment for age, sex, body mass index, height, and weight. The results show that the serum calcium level was positively correlated with triglycerides in both groups ($P < 0.05$) but not with any other parameters ($P > 0.05$).

Discussion

The present study examined serum calcium levels, blood lipids, and blood pressure in subjects with and without coronary heart disease. Our results show that serum calcium was higher in cases than in controls. Sabanayagam and Shankar¹⁵ reported that higher serum calcium levels were positively correlated with hypertension in a representative sample of US adults, which is consistent with our findings. Further, Cook et al have shown that myeloperoxidase-mediated modulation of intracellular calcium ion levels may exacerbate endothelial dysfunction, a key early event in hypertension.¹⁶ A possible explanation is that higher serum calcium levels may influence the risk of coronary heart disease via blood pressure. However, a recent short-term study showed that supplementation with 2.25% CaCO₃ can reduce LDL cholesterol.¹⁷

In our study, the serum calcium level did not correlate with any parameter except for triglycerides in either group after adjusting for age, sex, body mass index, height, and weight. Other findings were that triglyceride levels had a significant positive correlation with serum calcium in the normotensive group and that LDL cholesterol had

a negative correlation with serum calcium in males but not in females. However, a positive relationship between serum calcium and LDL cholesterol has been observed in premenopausal women.¹⁸ The relationship between serum calcium and blood lipids may be influenced by sex and racial differences. Torres et al¹⁹ reported that a higher dietary calcium intake could be associated with less global adiposity. Other researchers have reached a conclusion similar to ours, ie, that calcium consumption is related to lipoprotein metabolism and affects the blood lipid profile.^{20,21} Calcium absorption according to age and physiologic status and the role of daily calcium intake in the prevalence of coronary heart and other cardiovascular disease should be further investigated.

Serum calcium may be involved in regulating blood pressure by controlling vascular smooth muscle cell contractility and thus modulating peripheral vascular resistance.^{21,22} In addition, extracellular ionized calcium inhibits renin secretion by interacting with the calcium-sensing receptor.^{23,24} However, a study of two cohorts that included whites and blacks did not suggest that molecular variations in the calcium-sensing receptor influence either sodium balance or blood pressure. The mechanisms by which calcium lowers blood lipid levels need further research. This study has several limitations, in particular its small sample size. Moreover, it was based on data derived from routine health screening and lacks detailed information on relevant factors such as diet and lifestyle. In conclusion, serum calcium levels were higher in patients with coronary heart disease than in controls. These data suggest the serum calcium does not influence the risk of coronary heart disease.

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Disclosure

The authors report no conflicts of interest in this work.

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Table 2 Correlation between serum calcium levels, blood lipids, and blood pressure

Parameter	Control group (n = 379)		CHD group (n = 380)	
	r	P-value	r	P-value
Total cholesterol	-0.033	0.583	0.028	0.0635
HDL cholesterol	-0.021	0.725	-0.002	0.968
LDL cholesterol	-0.110	0.064	-0.090	0.122
Triglycerides	0.134	0.024	0.168	0.004
SBP	-0.027	0.649	-0.028	0.625
DBP	-0.026	0.664	-0.056	0.335

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; CHD, coronary heart disease; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

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