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Association between serum albumin, carotid atherosclerosis, and metabolic syndrome in Japanese individuals

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Abstract

Serum albumin is a maker of nutritional status and possesses antioxidative properties. Here, we have sought to investigate the mode of association between serum albumin levels, metabolic syndrome, and carotid atherosclerosis by analyzing the data of the cross-sectional data from 8143 individuals who underwent general health screening test. After adjusting for age, total cholesterol, and smoking status, the highest quartile of serum albumin (≥4.7 g/dL) was associated with increased prevalence of metabolic syndrome with an odds ratio of 1.80 (95% CI 1.41–2.23, $P < 0.0001$) in women, and 1.60 (95% CI 1.44–1.78, $P < 0.0001$) in men, when compared to the lowest serum albumin quartile (<4.3 g/dL). By contrast, when compared with the lowest quartile, the highest quartile of serum albumin was associated with reduced prevalence of carotid plaque with an odds ratio of 0.62 (95% CI 0.42–0.91, $P < 0.001$) in women, and 0.76 (95% CI 0.62–0.93, $P < 0.01$) in men, and for carotid intima-media thickening with an odds ratio of 0.57 (95% CI 0.35–0.94, $P < 0.05$) in women, and 0.71 (95% CI 0.55–0.92, $P < 0.01$) in men. Our data showed that higher serum albumin was inversely associated with the prevalence of early carotid atherosclerosis, although it was positively associated with the prevalence of metabolic syndrome. Whether these observations are in part explained by the antioxidative properties of albumin requires further investigation.

Keywords: Metabolic syndrome; Carotid atherosclerosis; Ultrasonography; Albumin; Antioxidants

1. Introduction

Serum albumin level is known to be reduced in various diseased conditions, such as malnutrition, inflammatory states, and liver diseases [1]. It has been shown that lower levels of serum albumin are associated with increased risk of cardiovascular mortality [2,3] and carotid atherosclerosis [4,5]. On the other hand, serum albumin levels show positive association with some of the coronary risk factors, such as body mass index (BMI), blood pressure, and lipid profiles [6–9], although these associations cannot distort the association between low serum albumin levels and cardiovascular disease.

It has recently been suggested that there may be an inverse association between circulating antioxidants, such as Vitamin C and carotenoids, and metabolic syndrome [10]. In the serum, albumin as well as bilirubin and uric acid represent major plasma antioxidant components. In the previous study, we reported negative association between serum bilirubin and metabolic syndrome and positive association between serum uric acid and metabolic syndrome [11]. Serum albumin may be associated positively with several atherogenic risk factors [6]; however, little has been known about the mode of association between serum albumin and metabolic syndrome. Thus, in the present study, we have investigated the mode of association between serum albumin, carotid

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atherosclerosis, and metabolic syndrome by analyzing the cross-sectional data from individuals undergoing general heath screening.

2. Methods

2.1. Study subjects

The study was approved by The Ethical Committee of Mitsui Memorial Hospital. Between September 1994 and December 2003, 49,331 (16,868 women, 32,463 men) subjects aged 20 years old or older underwent a general health screen. Of the 49,331 subjects, 8143 subjects (2671 women, 5472 men) underwent health screening course including carotid ultrasonography, and were enrolled in the present study. In Japan, regular health check-ups for employees are legally mandated, and all or most of the costs of the screening are usually paid by the company to which they belong or by each subject. There are several courses, with different costs, in our health screening. Some courses include carotid ultrasonography, but some do not. Therefore, the study subjects were not considered to be a random selection from the whole subjects who underwent general health screening during the study period; however, which course to be chosen was not recommended by the physicians or health care participants. The interquartile cut off points of serum albumin, 4.3, 4.5, and 4.7 g/dL, were used in both genders. Cigarette smoking outcome data were collected in a structured questionnaire.

2.2. Laboratory data

Blood samples were taken from our subjects after an overnight fast. Serum albumin was measured by Bromcresol Green (BCG) dye-binding method and inter-assay coefficient of variation was 0.6%. Serum levels of total cholesterol (TC), HDL-cholesterol (HDL-C), and triglycerides were determined enzymatically. Serum uric acid was measured by the uricase-peroxidase method, haemoglobin A_{1C} was determined using the latex agglutination immunoassay, and bilirubin was determined by the vanadium oxide method. Plasma glucose was measured by hexokinase method and serum insulin was measured by enzyme immunoassay.

The data of basal insulin levels were available in 6338 subjects (2026 women, 4312 men), and homeostasis model assessment insulin resistance (HOMA-IR) was calculated in these individuals according to the following formula: HOMA-IR = [fasting immunoreactive insulin (IRI; μU/mL) × FPG (mg/dL)]/405.

When converting from mg/dL to mmol/L or mg/dL to μmol/L, following conversion factors would be used: uric acid, 59.48 (mg/dL to μmol/L); bilirubin, 17.10 (mg/dL to μmol/L); TC, 0.0259 (mg/dL to mmol/L); HDL-C, 0.0259 (mg/dL to mmol/L); triglycerides, 0.0113 (mg/dL to mmol/L); and glucose, 0.0555 (mg/dL to mmol/L).

2.3. Carotid ultrasonography

Carotid artery status was studied and analyzed as described previously [11]. In brief, this was examined by high resolution B-mode ultrasonography, using a machine (Sonolayer SSA270A, Toshiba, Japan) equipped with a 7.5 MHz transducer (PLF-703ST, Toshiba). The carotid arteries were examined bilaterally at the levels of the common carotid, the bifurcation, and the internal carotid arteries from transverse and longitudinal orientations by trained sonographers. The intima-media thickness was measured using a computer-assisted method by experienced sonographers who were unaware of the subjects' clinical and laboratory findings. Plaque was defined as a clearly isolated focal thickening of the intima-media layer with thickness of ≥1.3 mm at the common or internal carotid artery or the carotid bulb. Carotid intima-media wall thickening was said to occur when the intima-media thickness which was measured at the far wall of the distal 10 mm of the common carotid artery was ≥1.0mm.

2.4. Criteria for metabolic syndrome

Diagnosis of metabolic syndrome was made according to the criteria of the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP-III) [12] with BMI used as a surrogate for waist circumference as has been done in previous other studies, because waist circumference was not available in this study sample. The five thresholds used were: (1) triglyceride levels ≥150 mg/dL (1.69 mmol/L), (2) HDL-C levels <40 mg/dL (1.04 mmol/L) in men or <50 mg/dL (1.29 mmol/L) in women, (3) fasting plasma glucose levels ≥110 mg/dL (6.1 mmol/L), or taking an antidiabetic medication, (4) systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg or taking an antihypertensive medication, and (5) body mass index (BMI) ≥25 kg/m^2. These five parameters were designated 'metabolic syndrome risk factor components' in the current study. Metabolic syndrome was diagnosed when three or more of these components were present.

2.5. Statistical analysis

The data in this study were analyzed by the χ^2-test, ANOVA with a Bonferroni post hoc test, and multivariate logistic regression analysis using computer software, StatView ver. 5.0 (SAS Institute, NC, USA). A value of $P < 0.05$ was taken to be statistically significant. Results are expressed as the mean ± S.D. unless stated otherwise.

3. Results

3.1. Baseline characteristics

The baseline characteristics of the study subjects are given in Table 1. The age of the enrolled subjects ranged from 22