Association of coronary artery calcification and serum gamma-glutamyl transferase in Korean

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ABSTRACT

Background and objective: Elevated serum gamma-glutamyl transferase (GGT) has been known to be associated with the cardiovascular disease. However, there is a lack of researches on direct examination of relevance between serum GGT and coronary artery calcification (CAC). Accordingly, the aim of this study was to investigate the association between serum GGT levels and the prevalence of CAC in Korean.
Methods: The study population consisted of 14,439 male and female adults without coronary artery disease, who were conducted health examination from January 2010 to December 2010. The prevalence of CAC in relation to the quartile groups of serum GGT levels and odds ratio and 95% CI of CAC were analyzed using multiple logistic regression model.
Results: The prevalence of CAC increased with increasing GGT quartile (4.6%, 8.7%, 11.8% and 14.7% in the lowest, second, third, highest GGT quartiles, respectively; $p < 0.001$). In the logistic regression analysis adjusted for multiple variables, odds ratio (95% CI) for the prevalence of CAC comparing the 1st GGT quartile to the 4th quartile were 2.43 (1.94–3.05) for all subjects, 1.49 (1.21–1.85) for men and 1.33 (0.62–2.87) for women.
Conclusion: Elevated serum GGT levels were independently associated with the prevalence of CAC. Physicians and health care providers should be observant regarding future development of coronary artery disease among people with increasing concentration of serum GGT.

1. Introduction

In terms of the order of causes of death in Korea, cerebrovascular disorders and cardiac disorders are ranked the 2nd and the 3rd, only after malignant neoplasm, and this ranking has not changed since 2000 up to 2010. While the rate of death arising from cerebrovascular disorders has been reduced from 73.1 persons per 100,000 people in 2000 to 53.2 persons per 100,000 in 2010, the rate for cardiac disorders increased from 38.2 persons per 100,000 in 2000 to 46.9 persons per 100,000 in 2009 [1].

Atherosclerosis of coronary artery is the most common cause of ischemic cardiac disorders, and acute coronary arterial syndrome that induces unstable angina and acute myocardial infarction, etc

occurs mainly because of rapid closure of blood flow due to rupture of atherosclerotic plaque and thrombopoiesis [2]. Commonly, the screening test for ischemic cardiac disorders is made by means of exercise electrocardiogram and thallium myocardial scan, etc. which measures the blood flow and diagnoses stenosis of coronary artery indirectly. However, even if the stenosis of coronary artery is only slight, there are difficulties in early diagnosis with aforementioned method [3,4]. Coronary artery calcification (CAC) can be measured and quantified by using multiple detection computerized tomography (MDCT). Scoring system designed by Agatston et al. [5] is currently being used widely for measuring CAC, and strong correlation between the Agatston score and the atherosclerosis was confirmed [6].

Gamma-glutamyl transferase (GGT) is one of the enzymes in blood that are used frequently in assessment of liver function due to its relatively low cost and high level of sensitivity and accuracy of test. It is included as an essential item in the testing of liver function during health examination in Korea. Although serum GGT is known to be increased due to consumption of alcohol and damages to the liver tissues, interest on the role of GGT in the diseases of cardiovascular system has increased with the reports of epidemiological

and pathological reports that GGT is involved in the pathophysiologic process of atherosclerosis [7].

Although there have been numerous researches on the association between serum GGT and the diseases of cardiovascular system [7–11] in the past, there is lack of researches on direct examination of relevance between serum GGT and CAC. Although Atar et al. [12] reported that serum GGT, age, smoking and serum uric acid concentration are related to CAC in 112 subjects (97 males and 15 females), their research had limitation that the number of subjects was quite small. Therefore, the aim of this cross-sectional study was to investigate the association between serum GGT levels and the prevalence of CAC in Korean by analyzing the data from health examination, and, moreover, to examined the role of serum GGT as the index for forecasting of occurrence of coronary artery disease in the areas of health examination and clinical settings.

2. Methods

2.1. Study population

15,079 people who underwent coronary artery MDCT when they visited a university hospital for the purpose of health examination from January 2010 to December 2010 were chosen as the subjects. 14,439 people were chosen as the final subjects of the study by excluding those with past history including stroke, angina, myocardial infarction and chronic kidney disease, those for whom serum GGT test was omitted and high risk alcoholic consumer on the basis of self-report through questionnaire. High risk alcoholic consumption was defined as those who has more than 7 glasses on the average on a single sitting for male and more than 5 glasses for female, more than 2 times a week on the basis of Korea National Health & Nutrition Examination Survey (Fig. 1). This Study was approved by the Institutional Review Board of the Kangbuk Samsung Medical Center (KBC12007).

2.2. Clinical and laboratory measurements

Height (m) and weight (kg) was measured to the units of 0.1 cm and 0.1 kg, respectively, by using automatic height and weight measurement equipment while the subjects were wearing light clothing and on bare foot. Body mass index (BMI) was computed by using the measured height and weight (kg/m^2). Blood pressure (BP) was measured by experienced nurse by placing the arm at the height corresponding to the height of the heart after having taken rest for 5 min at the minimum on a chair with back support. Current smokers were defined as those who answered they are currently smoking in the questionnaire.

All blood samples were obtained in the morning after an overnight fast. Gamma-glutamyl transferase (GGT), alanine aminotransferase (ALT), aspartate aminotransferase (AST), fasting serum glucose, total cholesterol, triglyceride, low-density lipoprotein cholesterol (LDL-C), and high density lipoprotein-cholesterol (HDL-C) were measured using Bayer Reagent Packs on an automated chemistry analyzer (Advia 1650 Autoanalyzer; Bayer Diagnostics, Leverkusen, Germany). High sensitivity C-reactive protein (hsCRP) was analyzed by particle-enhanced immunonephelometry with the BNII System (Dade Behring, Marburg, Germany). The serum creatinine was measured with the alkaline picrate (Jaffe) method.

Hypertension was defined as those who are currently taking antihypertensive agents, or has measured systolic BP of more than 140 mmHg or diastolic BP of more than 90 mmHg. Diabetes was defined as those who are currently taking glucose-lowering agents or has measured fasting serum glucose of more than 126 mg/dL.

CT scans were performed with a 64-slice MDCT scanner (Lightspeed VCT XTe-64 slice, GE Healthcare), and a standard scanning protocol was 32 × 0.625-mm section collimation, 400-ms rotation time, 120-kV tube voltage, and 31-mAS (310mA30.1 s) tube current under electrocardiographic-gated dose modulation. In this study, the Agatston method was used to quantify the amount of CAC. CAC was defined to the situation in which the Agatston score is more than 0 [13].

2.3. Statistical analyses

Because there was statistically difference of all variables including serum GGT between male and female, sex-specific analyses were done. Concentration of serum GGT was divided into quartile groups in accordance with the distribution in presenting the distribution of different variables, and tendency analysis was made in accordance with the quartile groups.

The distributions of continuous variables were evaluated, and log transformations were used in the analysis as required. Logistic regression analysis was used to determine the odds ratio (OR) of presence of CAC associated with quartile groups of serum GGT levels (quartile 1 = reference). The correlation analysis and multiple linear regression analysis were also used to examine the quantitative association between serum GGT and CAC. The following variables, well-known risk factors of cardiovascular diseases, were entered into binary logistic and multiple linear regression model: age, BMI, systolic BP, ALT, fasting serum glucose, triglyceride, LDL-C, HDL-C, hsCRP, hypertension, diabetes and current status of smoking.

For statistical analysis, SPSS 18.0 for window (SPSS Inc.,Chicago, IL, USA) program was used. Statistical analysis was carried out by defining the level of statistical significance to be less than 0.05.

3. Results

Among the total of 14,439 subjects, there were 11,835 males and 2604 females, and their basic characteristics are given in Table 1. Median value (range of quartile) of serum GGT level was 32 (22–53) IU/L and 14 (11–20) IU/L, respectively in male and female. All the clinical variables except for HDL-C were higher in male than in female. Current smoking rate and prevalence of diabetes and hypertension were also higher in male than in female.

In both male and female, age, BMI, systolic and diastolic BP, AST, ALT, fasting serum glucose, total cholesterol, LDL-C, triglyceride, hsCRP and the prevalence of diabetes and hypertension increased as the serum GGT group increased, while the reverse was the case for HDL-C. However, the current smoking rate did not illustrate tendency of increasing or decreasing in either male or female (Table 2).
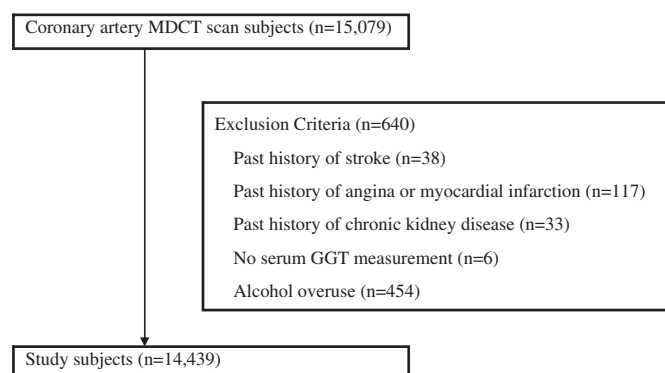

Fig. 1. Selection of study participants.