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Ability of the plasma concentration ratio of triglyceride/high-density lipoprotein cholesterol to identify increased cardio-metabolic risk in an east Asian population

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ABSTRACT

Aim: The plasma concentration ratio of triglyceride (TG)/high-density lipoprotein cholesterol (HDL-C) has identified increased cardio-metabolic risk and outcome in European populations. The goal of this study was to see if this ratio would also have clinical utility in identifying cardio-metabolic risk in an East Asian population.

Methods: Measurements of various cardio-metabolic risk factors, including coronary calcium scores, were available on 12,166 apparently healthy Korean adults. Approximately 25% of men and women with the highest TG/HDL-C ratios were classified as being at high cardiometabolic risk, and their risk factor profiles compared to the remainder of the population, as well as to individuals with the metabolic syndrome (MetS).

Results: High cardio-metabolic risk (upper 25%) was defined as a TG/HDL-C ratio \geq 3.5 (men) or \geq 2.0 (women), and all cardio-metabolic risk factors measured, including coronary calcium scores, were significantly more adverse when compared to individuals beneath these cut-points. Although cardio-metabolic risk profiles appeared reasonably comparable in subjects identified by either a high TG/HDL-C or a diagnosis of MetS, use of the TG/HDL-C increased the numbers at high risk.

Conclusion: Evidence that determination of the plasma TG/HDL-C concentration ratio provides a simple way to identify individual at increased cardio-metabolic risk has been extended to an East Asian population. The ability of an elevated TG/HDL-C ratio to accomplish this goal is comparable to that achieved using the more complicated MetS criteria.

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¹ K.-C. Sung analyzed the experimental data, performed the statistical analysis, and participated in data interpretation and manuscript preparation.

 $^{^2}$ S. Kim and G. Reaven reviewed the results as prepared by K.-C. Sung, and were actively engaged in interpretation of the data and preparation of the manuscript.

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1. Introduction

The diagnostic category of the metabolic syndrome (MetS) was introduced in effort to identify individuals at increased cardiovascular disease (CVD) risk [1,2]. Although the criteria for diagnosing the MetS permitted individuals with manifest clinical syndromes to qualify for this additional diagnosis, it could be argued that its clinical utility would be most useful if it effectively identified apparently healthy individuals before manifest disease [3]. In this context, manuscripts have recently been published [4–7] demonstrating that the plasma concentration ratio of triglyceride (TG)/high-density lipoprotein cholesterol (HDL-C) appears to accomplish this task as effectively as does a diagnosis of the MetS. In addition, these reports have pointed out that the most useful TG/HDL-C ratios vary in men and women [4], and the TG/HDL-C ratio and the MetS criteria appear to be approximately equivalent in identifying the presence of insulin resistance in apparently healthy individuals [6]. However, these studies have used criteria for diagnosing the MetS outlined in the "harmonized" version [2], in which it is emphasized that the cut-points to determine whether waist circumference (WC) is abnormal should vary with racial group. In this context, the cut-point for defining abdominal obesity (enlarged WC) is quite different in East Asians than in the populations previously studied [4–7]. Consequently, we initiated the current study in a population of apparently healthy East Asian individuals, with four goals in mind: (1) would cut-point values of the TG/ HDL-C ratio used to identify individuals at increased cardiometabolic risk in East Asians also vary in men and women; (2) would the numerical TG/HDL-C cut-points that identified the approximately 25% of the population with the highest TG/ HDL-C ratios be the same as in previously studied populations; (3) would the cut-points used effectively separate high from low risk subject; and (4) would the cardio-metabolic risk profiles, including coronary calcification score, vary in East Asians determined to be at high risk compared with individuals diagnosed with the MetS. The current report is an attempt to answer these questions based on the analysis of 12,166 apparently healthy individuals, 9962 men and 2204 women.

2. Methods

The study population consisted of individuals aged 30–60 years old who participated in a comprehensive health examination in 2010 at Kangbuk Samsung Hospital, College of Medicine, Sungkyunkwan University. Initially, 14,628 individuals were identified who met the age criterion. Individuals were excluded for the following reasons: absence of waist circumference measurements, a history of diabetes, coronary artery disease, hypertension, or drug treatment for abnormalities of carbohydrate or lipid metabolism. After exclusion, 9968 men and 2208 women were available for analysis. The study was approved by the institutional review board at Kangbuk Samsung Hospital. Informed consent requirement was waived as personal identifying information was not accessed.

The health examination included collection of full medical histories, physical examinations, and blood samples. Blood samples were collected after an overnight fast. Fasting plasma glucose, high density lipoprotein cholesterol (HDL-C), triglyceride (TG), low density lipoprotein cholesterol (LDL-C) and total cholesterol concentrations were measured using Bayer Reagent Packs on an automated chemistry analyzer (Advia 1650 Autoanalyzer; Bayer Diagnostics, Leverkusen, Germany). Insulin concentration was measured with the electrochemiluminescence immunoassay (Roche Diagnostics, Mannheim, Germany) with repeatability and precision coefficient of variation of 0.8–1.5% and 2.4–4.9%, respectively. Homeostatic model assessment of insulin resistance (HOMA-IR) index was calculated (HOMA-IR = [fasting insulin (μ U/mL) × fasting glucose (mmol/L)]/22.5.

All computed tomography scans were obtained with a Lightspeed VCT XTe-64 slice MDCT scanner (GE Healthcare, Tokyo, Japan) with the same standard scanning protocol using 40 \times 2.5-mm section collimation, 400 ms rotation time, 120 kV tube voltage, and 124 mAS (310 mA \times 0.4 s) tube current under ECG-gated dose modulation. The quantitative coronary artery calcium scores (CACS) were calculated as described by Agatston et al. [8]. Given the presumably healthy nature of the study group, and to enhance the sensitivity of the evaluation, we used two categories of scoring coronary calcium; CAC > 0 and CAC > 100.

3. Statistical analysis

The population was divided on the basis of the two indices of increased cardio-metabolic risk to be evaluated; plasma TG/ HDL-C concentration ratio and the diagnosis of the MetS. In earlier studies, 25% of the population with the highest TG/ HDL-C ratios was classified as the group of apparently healthy individuals at highest risk to develop cardio-metabolic diseases [4-6]. This arbitrary cut-point was chosen based on prospective data showing that incidence of heart disease, glucose intolerance, and hypertension was significantly increased in the 25% of individuals who were the most insulin resistant [9]. TG/HDL-C values of 3.5 (men) and 2.5 (women) served this purpose in the original studies in European individuals, as well as in persons of Mexican Mestizo ancestry [4-7]. However, in the current study of East Asian individuals the precise cut-points were identified as being 3.7 in men and 1.9 in women. In the case of the men, we felt it more useful and simple to retain a TG/HDL-C cut point of 3.5. However, in women we felt it necessary to use a TGH/HDL-C cut-point of 2.0, rather than 2.5. Criteria for the diagnosis of the MetS were those proposed by the 2009 statement of the International Diabetes Federation Task Force on Epidemiology and Prevention criteria, using waist circumference thresholds of \geq 90 cm for men and \geq 80 cm for women as specified for Asian populations [2].

Statistical analysis of the data was performed using SPSS version 15.0 (SPSS, Point Richmond, CA, USA). Continuous variables were expressed as mean \pm SD and compared using independent t-tests. Categorical variables were expressed as percentages and compared between groups using the χ^2 test. P values (two-tailed) less than 0.05 were considered to be statistically significant.

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