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Association of pooled cohort risk scores with vascular inflammation and coronary artery calcification in Korean adults☆

Hye Jin Yoo[a,1], Hwan Seok Yong[b,1], Soon Young Hwang[c], Jae Seon Eo[d], Ho Cheol Hong[a], Ji A. Seo[a], Sin Gon Kim[a], Nan Hee Kim[a], Dong Seop Choi[a], Sei Hyun Baik[a], Kyung Mook Choi[a,*]

[a] Division of Endocrinology and Metabolism, Department of Internal Medicine, College of Medicine, Korea University, Seoul, Republic of Korea
[b] Department of Radiology, Korea University Guro Hospital, Korea University College of Medicine, Seoul, Republic of Korea
[c] Department of Biostatistics, College of Medicine, Korea University, Seoul, Republic of Korea
[d] Department of Nuclear Medicine, Korea University College of Medicine, Seoul, Republic of Korea

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ABSTRACT

Objectives. A new pooled cohort risk equation to estimate atherosclerotic cardiovascular disease (CVD) risk was recently published, but the equation is based primarily on data from Caucasian populations. The relationship of this new risk scoring system with vascular inflammation and calcification has yet to be examined.

Methods. A total of 74 participants were retrospectively selected based on inclusion and exclusion criteria. All participants underwent ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography (PET) and multi-detector computed tomography (MDCT) examination in the Korea University Guro Hospital between June 2009 and May 2013. Vascular inflammation of the carotid artery was measured as target-to-background ratio (TBR) using ^{18}F-FDG-PET/CT and coronary artery calcification was quantified as Agatston score by MDCT.

Results. Agatston scores were not significantly associated with any metabolic risk factors, but maximum TBR values exhibited a significant positive correlation with body mass index ($r = 0.31$, $P = 0.01$), waist circumference ($r = 0.42$, $P < 0.01$), waist-to-hip ratio ($r = 0.49$, $P < 0.01$), and systolic ($r = 0.35$, $P < 0.01$) and diastolic blood pressure ($r = 0.39$, $P < 0.01$). Furthermore, maximum TBR values were significantly correlated with serum high-sensitivity C-reactive protein (hsCRP) levels ($r = 0.26$, $P = 0.03$), whereas Agatston scores had no correlation. When pooled cohort risk equation scores were divided into incremental tertiles, age, waist circumference, waist-to-hip ratio and systolic blood pressure showed significant incremental trends. In particular, pooled cohort risk scores

Abbreviations: CVD, cardiovascular disease; FDG, ^{18}F-fluorodeoxyglucose; PET, positron emission tomography; MDCT, multi-detector computed tomography; TBR, target-to-background ratio; FRS, Framingham risk score; CACS, coronary artery calcium scores; hsCRP, high-sensitivity C-reactive protein; BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment for insulin resistance; SUV, standardized uptake value.

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* *Corresponding author at:* Division of Endocrinology and Metabolism, Department of Internal Medicine, Korea University Guro Hospital, 80 Guro-Dong, Guro-Gu, Seoul, 152-050, Republic of Korea. Tel.: +82 2 2626 3043; fax: +82 2 2626 1096.
E-mail address: medica7@gmail.com (K.M. Choi).

[1] The first two authors contributed equally to this article.

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exhibited a significant positive correlation with maximum TBR values ($r = 0.35$, $P < 0.01$), but not with Agatston scores ($r = 0.11$, $P = 0.34$).

Conclusions. The pooled cohort risk equation exhibited significant positive correlations with vascular inflammation but not with calcification in Asian subjects without CVD, suggesting that this novel risk equation may detect early inflammatory changes preceding the structural modification of vessel walls.

1. Introduction

Cardiovascular disease (CVD) is the leading cause of death worldwide. Optimization of risk prediction is an important clinical concern for a more tailored management of lipids and blood pressure, as well as the prescription of antiplatelet agents. The 2013 Guidelines for the Assessment of Cardiovascular Risk published a new equation for predicting 10-year atherosclerotic CVD risk, the pooled cohort risk equation [1]. Previously, the Framingham risk score (FRS) was widely used [2], but the FRS can only predict 60–65% of acute cardiovascular events, resulting in the occurrence of many preventable cardiovascular events [3]. Therefore, direct visualization of subclinical atherosclerosis using non-invasive imaging techniques is recommended as a part of risk assessment.

Calcification of the coronary arteries is a crucial part of atherosclerotic plaque formation and can be easily quantified by computed tomography (CT) [4]. The Agatston score, defined as the sum of the area of calcification per coronary segment, was developed to quantify the extent of coronary calcium [5]. Coronary artery calcium scores (CACS) have been shown to predict the risk for cardiovascular events in large prospective studies [6,7]. Furthermore, previous studies have demonstrated that addition of CACS to a traditional risk scoring system significantly improves the prediction rate for CVD [8,9]. Therefore, the American Heart Association (AHA) has supported the use of the CACS in individuals with intermediate risk scores (10% < FRS < 20%) to improve risk stratification [10]. However, CACS assessment does not provide information about plaque characteristics [4]. Most forms of calcification present as stable plaque [11], but some features are closely related to plaque rupture, directly leading to acute coronary events.

Recently, ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography (PET) has been established as a useful imaging technique to identify vascular inflammation that may reflect vulnerability to atherosclerotic plaque [12]. ^{18}F-FDG-PET can visualize inflamed vessels and ^{18}F-FDG uptake is strongly correlated with macrophage infiltration in vessel walls [13]. Previously, we observed that, in the intermediate FRS risk group, vascular inflammation as measured by FDG-PET increased in individuals with higher high-sensitivity C-reactive protein (hsCRP) levels compared to those with lower hsCRP [14], suggesting the potential of FDG-PET as an adjuvant tool for CVD risk stratification. Furthermore, Figueroa et al. demonstrated that arterial FDG uptake measured using FDG-PET substantially improved incident CVD prediction beyond FRS in individuals without prior CVD [15].

To clarify the clinical meaning of these various CVD risk assessment tools, the present study for the first time examined the relationship of the novel pooled cohort risk equation with coronary calcification and vascular inflammation using multi-detector computed tomography (MDCT) and FDG-PET in Korean men and women without CVD.

2. Methods

2.1. Study Design and Participants

We retrospectively recruited subjects between the age of 40 and 75 years-old from the Korea University Guro Hospital, who had undertaken both ^{18}F-FDG-PET and MDCT for the evaluation of cancer and coronary heart disease within six months during the period of June 2009 and May 2013. Subjects were excluded from this study if they met any of the following criteria: history of CVD (myocardial infarction, unstable angina, stroke, or cardiovascular revascularization); diabetes (defined as a fasting plasma glucose value ≥7.0 mmol/L or a previous diagnosis of type 1 or type 2 diabetes); stage 2 hypertension (resting blood pressure ≥160/100 mm Hg); any lipid-lowering therapies; history of inflammatory conditions that would affect the study results; taking medications that might affect inflammatory status, including steroid and non-steroidal anti-inflammatory drugs; or malignancy or severe renal or hepatic diseases (serum creatinine or alanine aminotransferase or aspartate aminotransferase levels greater than twice the upper limit of the laboratory reference range). The Korea University Institutional Review Board approved this study protocol in accordance with the Declaration of Helsinki of the World Medical Association.

2.2. Anthropometric and Laboratory Measurements

Body mass index (BMI) was calculated as weight/height squared (kg/m^2), and waist circumference was measured at the midpoint between the lower border of the rib cage and the iliac crest. All blood samples were obtained the morning after a 12-hour overnight fast including medication and were immediately stored at −80 °C for subsequent assays. Serum triglyceride and high-density lipoprotein cholesterol (HDL-C) levels were determined enzymatically using a model 747 chemistry analyzer (Hitachi, Tokyo, Japan). The glucose oxidase method was used to measure plasma glucose levels, and an electrochemiluminescence immunoassay (Roche Diagnostics, Indianapolis, IN) was used to measure insulin levels. Insulin resistance was calculated using the homeostasis model assessment for insulin resistance (HOMA-IR). A latex-enhanced turbidimetric immunoassay (HiSens hsCRP LTIA; HBI, Anyang, Korea) was used for measurement of high