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ORIGINAL ARTICLE

Analysis of Lipoprotein Subfractions in Chinese Han Patients with Stable Coronary Artery Disease

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Background The relation of lipoprotein subfractions with stable coronary artery disease (CAD) has not been fully investigated in the Chinese Han population.

Methods Four-hundred-and-thirteen consecutive patients without any lipid-lowering drug treatment were investigated. Patients were classified into two groups according to the angiographic results: CAD group (n=293) and non-CAD group (n=120). The high-density lipoprotein (HDL) and low-density lipoprotein (LDL) subfractions were analysed using the Quantimetrix Lipoprint system.

Results The data showed that the large HDL-cholesterol (HDL-C) level, large HDL subfraction percentage, and mean LDL particle size were significantly lower, while the small HDL-C level and HDL subfraction percentage, intermediate and small LDL-cholesterol (LDL-C) levels, and LDL subfraction percentages were higher in the CAD group compared with those in the non-CAD group. Interestingly, our results suggested that the small HDL-C level and HDL subfraction percentage as well as mean LDL particle size were independently associated with the presence of CAD assessed by logistic regression analysis (OR=1.136, 95%CI=1.018-1.268, p=0.022; OR=1.076, 95%CI=1.021-1.134, p=0.007; OR=0.946, 95%CI=0.898-0.997, p=0.040; respectively).

Conclusions Similar to previous Western population studies, our data suggested a clear association between the lipoprotein subfractions and stable CAD presented as higher small HDL subfraction and smaller mean LDL particle size in Chinese Han patients.

Keywords High-density lipoprotein subfraction • Low-density lipoprotein subfraction • Chinese • Coronary angiography • Coronary artery disease

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Introduction

Coronary artery disease (CAD) is a life-threatening disease associated with severe morbidity and mortality [1]. Dyslipidaemia such as increased low-density lipoprotein (LDL)-cholesterol (LDL-C) and decreased high-density lipoprotein (HDL)-cholesterol (HDL-C) concentration is an important factor that has been implicated in the development of CAD [2,3]. However, previous clinical trials showed that elevated HDL-C concentration alone or in combination with intensive statin therapy for further reducing LDL-C did not retard atherosclerosis progression or reduce the incidence of cardiovascular events [4–6]. More recently, there has been a great interest regarding the lipoprotein subfractions besides lowering serum LDL-C and/or raising HDL-C levels in cardiovascular field [7]. The reason for this interest may be associated with the fact that lipoprotein particles consist of a heterogeneous group of subfractions differing not only in size and density but also in chemical composition and physiological function [8,9]. Therefore, the measurement of HDL-C, the cholesterol carried by HDL particles, may not fully capture the HDL-related risk [10]. Moreover, the atherogenic potential of LDL particles is not only related to their concentration, but also to their heterogeneity with regard to particle size, density, and lipid composition [11]. Previous data indicated that the improvement in coronary stenosis was significantly associated with the decrease of cholesterol in the small dense LDL particles but not with the buoyant LDL fractions [12]. However, the features of HDL and LDL subfractions in patients with stable CAD have not been well assessed, especially in the Chinese Han population who have not received any lipid-lowering drugs.

Thus, the aim of the present study was to investigate the association of lipoprotein subfractions including HDL and LDL with angiography-proven CAD, Chinese Han patients with no lipid-lowering drug treatment.

Material and Methods

Ethical Approval

The study complied with the Declaration of Helsinki and was approved by the Ethics Committee of FuWai Hospital and Cardiovascular Institute, Beijing, China. Informed written consent was obtained from all patients enrolled in this study.

Study Design and Population

In the current study, we consecutively recruited 413 patients who were referred for elective coronary angiography due to angina-like chest pain and/or positive treadmill exercise test or coronary computed tomography (CT) angiography. Patients with acute coronary syndrome (ACS), heart failure (left ventricular ejection fraction < 45%), infectious or systematic inflammatory disease, thyroid dysfunction, severe liver and/or renal insufficiency and malignant disease were excluded from the current study. Inclusion criteria of patients were as follows: 1) with definite clinical evidence of atherosclerotic lesions associated with the diagnosis criteria of CAD; 2) without treatment history of statins and/or other lipid-lowering drugs at least three months prior to entering the study; 3) with assessment for clinical history, anthropometric characteristics and standard cardiovascular risk factors. The definition of hypertension was repeated blood pressure measurements $\geq$ 140/90 mmHg or currently taking anti-hypertensive drugs. Diabetes mellitus (DM) was diagnosed if the fasting blood glucose $\geq$ 7.0 mmol/L in multiple determinations or patients were receiving an active treatment with insulin or oral hypoglycaemic agents. Dyslipidaemia was defined as the presence of fasting total cholesterol (TC) $\geq$ 200 mg/dl and/or triglyceride (TG) $\geq$ 150 mg/dl.

The enrolled patients were classified into two groups: CAD group (n=293, patients who had significant CAD, which was defined as one or more diseased epicardial vessels with a diameter of more than 2 mm that had at least a 50% diameter stenosis) and non-CAD group (n=120, patients who had a normal coronary artery or minimal disease <50% diameter stenosis assessed by coronary angiography).

Laboratory Examinations

Blood samples were obtained in all patients from the cubital vein after a 12-hour overnight fasting and collected into EDTA-containing tubes. All samples were subsequently stored at -80^{0}C and analysed immediately after thawing. Concentrations of plasma TC, TG, HDL-C, LDL-C, apolipoprotein AI (apo AI) and apolipoprotein B (apo B) were measured using an automatic biochemistry analyzer (Hitachi 7150, Tokyo, Japan). Of which, TC, TG, HDL-C and LDL-C levels were measured by enzymatic assay. The apoA-I and apoB levels were measured by turbidimetric immunoassay.

HDL Subfraction Analysis

Blood samples were also used for HDL subfraction analysis. The HDL subfraction analysis was performed electrophoretically by the use of high-resolution 3% polyacrylamide gel tubes and the Lipoprint HDL System (Lipoprint^{TM} HDL System; Quantimetrix Corporation, Redondo Beach, CA, USA) according to the manufacturer's instructions as previously described [13]. By this analysis, HDL was divided into 10 subfractions. Subfractions 1-3 represent large HDL particles; subfractions 4-7 indicate intermediate HDL particles, and subfractions 8-10 mean small HDL particles [14]. The cholesterol concentration (mg/dl) of each HDL subfraction and the proportion (%) of the cholesterol concentration of HDL subfractions over the HDL-C concentration were subsequently determined. A typical electrophoretogram of HDL subfractions analysed by the Lipoprint HDL system is shown in Figure 1A.

LDL Subfraction Analysis

Blood samples were also used for LDL subfraction analysis. The LDL subclass analysis was performed electrophoretically by the use of high-resolution 3% polyacrylamide gel tubes and the Lipoprint LDL System (Quantimetrix Corporation, Redondo Beach, CA, USA) according to the