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ORIGINAL ARTICLE

Analysis of Lipoprotein Subfractions in 920 Patients With and Without Type 2 Diabetes

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Background It has been demonstrated that diabetic dyslipidaemia is the chief bridge between diabetes and incremental risk of cardiovascular disease in patients with diabetes. However, the characteristics of lipoprotein subfractions distribution in patients with type 2 diabetes (T2D) have not been fully investigated. The aim of present study was to evaluate the distributions of lipoprotein subfractions in T2D patients.

Methods A total of 920 patients, who have not received lipid-lowering drug treatment previously, were consecutively enrolled in this study. Based on the evidence of diabetes, patients were divided into T2D group (n=204) and non-T2D group (n=716). Both low- and high-density lipoprotein cholesterol (LDL- and HDL-C) subfractions were analysed using the Quantimetrix Lipoprint System. The distributions of lipoprotein subfractions were evaluated in patients with and without T2D.

Results Compared with non-T2D individuals, the T2D group manifested significantly lower large HDL-C concentration/HDL subfraction percentage, smaller mean LDL particle size but higher small HDL-C and LDL-C concentrations as well as small HDL and LDL subfraction percentages. Moreover, the data indicated that the small HDL-C/ LDL-C concentrations, the small and large HDL subfraction percentages along with the mean LDL particle size were independently related to the existence of T2D (95% CI=1.009–1.067, p=0.009; 95% CI=0.938-0.983, p=0.001; 95% CI=1.023–1.135, p=0.005; 95% CI= 1.005–1.048, p=0.014; 95% CI=0.940-0.999, p=0.040; respectively) assessed by logistic regression analysis.

Conclusions The present study indicated that the changes of lipid profile in patients with T2D are characterised by abnormal distributions of lipoprotein subfractions apart from clinically atherogenic dyslipidaemia.

Keywords Lipoprotein subfraction • Diabetes • Chinese

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Introduction

It is well known that type 2 diabetes (T2D) is an established independent risk factor for atherosclerotic cardiovascular disease (ASCVD), particularly coronary arterial diseases (CAD). Moreover, a large number of studies have suggested that diabetic patients are prone to a higher risk of death from ASCVD, such as CAD and stroke, when compared with non-diabetes patients [1]. Until now, however, the incremental cardiovascular risk in diabetic individuals has not been explained fully by hyperglycaemia.

As we know, diabetes is always coupled with a series of metabolic abnormalities. Of them, dyslipidaemia, presented by elevated fasting and postprandial triglycerides (TG), low-density lipoprotein (LDL) cholesterol (LDL-C) and decreased high-density lipoprotein (HDL) cholesterol (HDL-C), especially predominance of small dense LDL particles, is an extremely common and remarkable one [2]. Previous studies have already demonstrated clear lipid profile and lipoproteins quantitative and qualitative changes in patients with T2D [3–5]. Although some evidence has suggested that LDL-C levels are more atherogenic in T2D than that in normal controls, changes in the details of lipoprotein subfractions have been proposed to more accurately capture the atherogenic properties than the concentrations of cholesterol contained in lipoprotein [6,7]. However, current knowledge with respect to the relation of T2D to various lipoprotein subfractions is still limited.

In this present study, therefore, we consecutively enrolled a large Chinese cohort with no lipid-lowing drugs treatment and investigated the relation of diabetes to the distribution of lipoprotein subfractions for purpose of picturing the characteristics of the changes of lipoprotein subfractions in patients with T2D.

Methods

Study Design and Population

The present study fully complied with the Declaration of Helsinki and then underwent the approval process of the Ethics Committee of FuWai Hospital and Cardiovascular Institute, Beijing, China. All included patients had provided prior written consent.

The current study recruited 920 patients consecutively who did not received lipid-lowering drugs. The exclusion criteria of patients were: 1) aged <18 years old; 2) had a treatment history of statins and/or other lipid-lowering drugs prior to entering the study; 3) had severe end-stage diseases, such as renal and/or liver dysfunction, heart failure and malignant carcinoma; 4) had systematic inflammatory disease or severe infection; 5) had a thyroid disorder; 6) were pregnant. The medical history, baseline clinical features and traditional cardiovascular risk factors were collected in all patients. Type 2 diabetes was diagnosed if repeated fasting plasma glucose (FPG)≥7.0 mmol/L and/or non-FPG ≥11.1 mmol/L or the patient was currently taking oral hypoglycaemic agents or receiving insulin therapy. Controlled T2D was defined as FPG <7.0 mmol/L and haemoglobin A1C (HbA1C)<6.5%. Moreover, the change between units of HbA1C in % or mmol/mol was according to the formula IFCC-HbA1C (mmol/mol)= [DCCT-HbA1C(%)-2.15] X10.929. The definition of dyslipidaemia was the presence of fasting total cholesterol (TC)≥ 200 mg/dl and/or TG≥150 mg/dl. Coronary artery disease was diagnosed by elective coronary angiography as at least one major epicardial coronary artery (≥2 mm) with a diameter stenosis ≥50%. Hypertension was defined as blood pressure measurements ≥140/90 mmHg in multiple determinations under a different environment or patients taking anti-hypertensive drugs although the blood pressure was normal. Patients were divided into two groups: T2D group (n=204) and non-T2D group (n=716).

Laboratory Analysis

Fasting venous blood was obtained and collected into ethylenediaminetetraacetic acid-containing -80°C for the measurement of lipoprotein subfractions. Concentrations of traditional lipid parameters (TG, TC, LDL-C, and HDL-C) and glucose were measured by automatic biochemistry analyser (Hitachi 7150, Tokyo, Japan) and HbA1C was measured using Tosoh automated glycol-haemoglobin analyser (HLC-723G8, Tokyo, Japan). Lipoprotein subfraction analysis was performed using the Lipoprint System (Quantimetrix Corporation, Redondo Beach, CA, USA) according to the manufacture's manual described previously [8]. The HDLs were divided into 10 varieties of subfractions while LDLs were classed into 7 by this analysis. For HDL, 1–3 subfractions indicated large HDL particles, 4–7 represented intermediate and 8–10 meant small [8]. Meanwhile, LDL subfraction 1 indicated large LDL particles, 2 represented intermediate and 3–7 meant small. Subsequently, each of the lipoprotein subfraction cholesterol concentrations (mg/dl) and the lipoprotein subfraction proportions (%) besides the mean LDL particle size (Å) were determined [8].

Statistical Analysis

SPSS version 19.0 (SPSS Inc., Chicago, IL, USA) was used for analysing the present data. Continuous variables are presented as mean±SD and categorical variables as number (percentage). The independent sample t-test or Mann-Whitney U test were performed to analyse the differences of clinical characteristics and lipid profiles between the two groups where appropriate. Binary logistic regression analyses were performed for assessing the independent T2D contributors from all lipoprotein subfractions. Statistically significant difference was defined as a two-tailed p-value <0.05.

Results

Clinical and Biochemical Characteristics

The characteristics of subjects enrolled are showed in Table 1, with a 62.7% male gender and a mean age of 55.90±11.19 years. Compared to the non-T2D group, the T2D group