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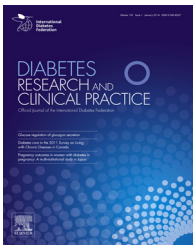

Association between vaspin level and coronary artery disease in patients with type 2 diabetes

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ABSTRACT

Aim: Adipokines contribute to the atherosclerotic process, connecting obesity and diabetes to cardiovascular disease. Vaspin is a recently discovered adipokine, so data about the relationship of vaspin to coronary artery disease in type-2 diabetes mellitus (T2DM) is limited. The current study was designed to evaluate the association of vaspin with the presence of coronary artery disease in T2DM.

Methods: We enrolled 228 patients with T2DM, with or without CAD, between March 2010 and July 2011, and 120 healthy control participants. Serum vaspin, homeostasis model assessment of insulin resistance (HOMA-IR) and other cardiovascular risk factors were assayed.

Results: Vaspin levels were significantly increased in patients with T2DM compared to healthy individuals, and were further increased in patients with both T2DM and CAD compared to those with T2DM but without CAD. Moreover, vaspin correlated positively with body mass index, fasting plasma glucose, insulin and HOMA-IR in all patients with T2DM ($P < 0.05$). Furthermore, in multivariate logistic regression analysis, vaspin level was associated with the presence of CAD in patients with T2DM.

Conclusions: Vaspin correlates with CAD in T2DM.

1. Introduction

The incidence of diabetes is increasing rapidly throughout the world. In 2011 there were 366 million people with diabetes, and this is expected to rise to 552 million by 2030 [1]. Coronary artery disease (CAD) is a major complication in diabetes and is the major cause of death for patients with diabetes [2]. Yet, the underlying mechanisms linking type-2 diabetes mellitus (T2DM) with cardiovascular disease remain far from completely elucidated.

Recent evidence has shown that increased visceral adipose tissue mass is associated with higher prevalence of insulin resistance, T2DM, and the risk of cardiovascular complications [3,4]. The realization that adipose tissue acts as an endocrine gland affecting whole-body energy homeostasis is an important breakthrough toward a better molecular understanding of T2DM and its complications [5–7]. Growing evidence indicates that adipocyte-derived factors (adipokines) associate with insulin resistance, endothelial dysfunction, pro-inflammatory state and pro-atherogenic state, resulting in significantly elevated metabolic and cardiovascular risks [3,7–9]. Vaspin,

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an adipokine discovered in 2005, has been shown in a rat model of abdominal obesity and T2DM to be predominantly secreted from visceral adipose tissue [10]. Accumulating data suggest that vaspin is related to obesity, insulin sensitivity and T2DM [11,12]. However, the association of vaspin with atherosclerosis is still obscure. Recently, several studies have focused on the influence of vaspin on vascular health, but the results are controversial [13–16]. Besides, the association of vaspin with human cardiovascular complications in patients with T2DM is still unclear. To our knowledge, no previous studies have clarified the relationship of serum vaspin with CAD prevalence in patients with T2DM. Therefore, in this study, we aimed to evaluate serum vaspin level in relation to the presence of CAD in patients with T2DM.

2. Materials and methods

2.1. Study participants

We retrospectively studied 228 patients with T2DM who underwent coronary angiography in the Department of Cardiology, First Affiliated Hospital of Harbin Medical University between March 2010 and July 2011. T2DM estimation was based on a previous history of diabetes diagnosed according to American Diabetes Association criteria [17]. The patient age ranged from 45 to 65 years. All patients were of northern Chinese origin. The study exclusion criteria included histories of acute coronary syndrome, congestive heart failure, arrhythmia, valvular heart disease, cardiomyopathy, congenital heart disease, acute or chronic inflammatory disease, liver, kidney or thyroid dysfunction, cancer, autoimmune diseases, estrogen replacement, abnormal complete blood count and alcohol or drug abuse. Patients with diabetes using insulin were also excluded because of the need to measure serum insulin levels. The control group was recruited from the medical health examination center in the hospital, and all had a normal glucose tolerance test. They had no history of any chronic disease, cardiovascular disease or overt cardiac origin symptoms, which was based on findings from a complete medical history, comprehensive physical examination, electrocardiogram, echocardiography and a treadmill exercise test. None of them were receiving any long-term medication or suffering from an acute infection. The study was approved by the Ethics Committee of the First Affiliated Hospital of Harbin Medical University and all participants gave informed consent.

2.2. Clinical and laboratory measurements

The patient information obtained from all selected participants included ethnic group, smoking status, duration of the course of diabetes, and any histories of hypertension, stroke, CAD, arterial and venous thrombosis, and drug use. Blood pressure, height and weight were also collected. Body mass index (BMI) was calculated using the formula: weight (kg)/the square of height (m^2). Diabetic retinopathy included both nonproliferative and proliferative retinopathy diagnosed by the ophthalmologist. Nephropathy status was determined based on consistent results from at least two timed urine specimens and confirmed using a 24 h urine sample. Microalbuminuria was defined as albumin-to-creatinine ratio of >30–300 μg/mg creatinine, and overt nephropathy was defined as albumin excretion rate of >300 μg/mg creatinine. Diabetic neuropathy was defined as having typical symptoms and/or evidence of reduced vibratory sensation or impairment of nerve conduction. Diagnosis of cerebrovascular disease was dependent on a history of ischemic events and/or demonstration of vascular stenosis by brain magnetic resonance imaging. An ankle-brachial index [18] ≤0.9 was used as a criterion for the diagnosis of peripheral arterial disease [19] according to the guidelines of the American College of Cardiology and the American Heart Association (ACC/AHA) [18].

All blood samples were obtained prior to the coronary angiography procedure. Samples were separated and aliquoted for storage at −80 °C until assayed. Serum glucose, total cholesterol, triglycerides, low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) were determined enzymatically using a chemical analyzer (Olympus, Japan). An automated enzyme immunoassay system was used to measure insulin level (Tosoh Corporation, Japan). Homeostatic model assessment of insulin resistance (HOMA-IR) was calculated from fasting insulin and fasting plasma glucose (FPG) by the following equation: HOMA-IR = fasting insulin (μU/ml) × FPG (mmol/l)/22.5. An automatic biochemical analyzer (BioRad, USA) was used for the determination of serum glycated hemoglobin A1c (HbA1c). C-reactive protein (CRP) was measured by an IMMAGE Immunochemistry System (Beckman Coulter, USA). Serum concentrations of vaspin and adiponectin were determined by an enzyme-linked immunosorbent assay (ELISA) kit (Cayman Chemical, USA).

2.3. Assessment of angiographic CAD

Using coronary angiography, we measured the diameter of the atherosclerotic vessel and compared the diameter to that of an adjacent normal vessel. CAD was defined as at least 50% stenosis in the left anterior descending artery, left circumflex artery, or right coronary artery [20]. According to the American Heart Association guidelines, we measured the diameter of the atherosclerotic vessel and compared to diameter to that of an adjacent normal vessel. This ratio, known as Gensini scoring [21], was used for the quantitative assessment of coronary artery stenosis. Diameters of stenosis that were reduced ≤25% were recorded as 1 point, 26–50% reduction as 2 points, 51–75% reduction as 4 points, 76–90% reduction as 8 points, 91% to 99% reduction as 16 points, and 100% reduction was recorded as a total of 32 points. These points were then multiplied by a reference value, which was determined by the location of the lesion in different vessel segments. The total score was acquired by combining points from all atherosclerotic segments.

2.4. Statistical analysis

Statistical analysis was performed using SPSS 20.0 software (IBM, USA). Data were expressed as the mean with standard deviation (SD) or median (interquartile range) for continuous variables, and frequencies for categorical variables. For continuous variables, the differences between two groups were examined by an independent samples *t*-test. More than two groups were compared by one-way ANOVA, using least significant difference