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ORIGINAL ARTICLE

Vaspin as a Prognostic Marker in Patients with Acute Myocardial Infarction

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Background Our previous study showed that patients with acute myocardial infarction (AMI) had lower levels of vaspin than patients without AMI. The aim of this study was to investigate the clinical significance of vaspin in patients with AMI.

Methods A total of 80 patients with AMI were enrolled. Plasma vaspin levels, clinical parameters, lipid profile, C reactive protein (CRP) were measured. All the patients were followed-up for 24±2 months for the occurrence of major adverse major cardiac events (MACEs).

Results During the follow-up, 48 patients experienced a MACE. The plasma vaspin concentrations in the MACEs-positive group were lower than those in the MACEs-negative group (0.156 ± 0.015 vs 0.314 ± 0.229ng/mL, p<0.001). Receiver operating characteristic curves showed that circulating vaspin concentration significantly differentiated patients with MACEs (p<0.001). The optimal cutoff value for predicting MACE was 0.259ng/mL. Then the patients were divided into vaspin>0.259ng/mL group and vaspin<0.259ng/mL group according to the plasma vaspin levels. Forty-five patients (74%) in the vaspin<0.259ng/mL group and three (16%) patients in the vaspin>0.259ng/mL group experienced a MACE. Multivariate survival analyses showed that the vaspin level (hazard ratio, HR 0.423) independently predicted the occurrence of MACEs. Compared with the results of echocardiography at admission, the improvement of LVEF in the vaspin>0.259ng/mL group was significant (54.3±7.6% to 61.2±4.7%, p<0.001), but the change of LVEF in the low vaspin group was not significant (51.3±9.7% to 52.5±10.9%).

Conclusions Vaspin might be a useful predictive biomarker in patients with AMI, and patients with low vaspin levels might have a high risk of a MACE. In addition, vaspin might have protective effects on the improvement of LVEF after AMI.

Keywords Vaspin • Acute myocardial infarction • Prognosis • Cardiac remodelling • Major adverse cardiac events

Introduction

Visceral adipose tissue-derived serine protease inhibitor (vaspin) is a new adipokine indentified from visceral adipose tissue in a rat model of type 2 diabetes [1]. Although vaspin is a member of the serine protease inhibitor family, studies found it had little serine protease activity, but definite effects on metabolism, including improving insulin resistance, reducing food intakes and lowering blood glucose [2]. In human beings, accumulated data suggested that there was a close relationship between vaspin and the parameters of metabolic syndrome [3]. Moreover, recent studies revealed

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that vaspin could target vascular cells, exerting anti-inflammation and anti-apoptotic effects [4].

Clinical studies showed that there was a close relationship between plasma vaspin concentrations and atherosclerosis and vaspin might play an important role in the process of coronary artery disease (CAD) [5–7]. Experiments also showed that vaspin could inhibit inflammatory factors secretion from vascular smooth muscle cells and antagonise endothelial cells apoptosis induced by free fatty acid [8,9]. Our study in vitro found that vaspin could inhibit high glucose-induced vascular smooth muscle cells proliferation and chemokinesis by preventing ROS activation and MAPK, PI3K/Akt, and NF-κB signalling [10].

Our previous clinical study showed that circulating vaspin levels were significantly lower in patients with acute myocardial infarction (AMI) than those in patients with stable angina and unstable angina [11]. However, the role of decreased vaspin in AMI was still unknown. The aim of our study was to investigate the clinical significance of vaspin in patients with AMI.

Materials and Methods

Study Population

This study enrolled 80 patients with ST segment elevated myocardial infarction (STEMI) from the Department of Cardiology, Shanghai Tenth People's Hospital (China) from December 2010 to April 2011, consecutively. The diagnosis of STEMI was based on the guideline of ACC/AHA for the management of AMI, including: typical chest pain, ST segment elevation or new left bundle branch block and troponin T (TnT) level elevation [12]. As per inclusion criteria, the patients could fall into one of the following categories: primary percutaneous coronary intervention (PCI, STEMI at less than 12 hours after the onset of symptoms), percutaneous coronary intervention early (<24 h) after effective thrombolysis, and latecomers (STEMI at more than 12 hours after the onset of symptoms). All latecomers received coronary artery angiography and PCI before discharge. All patients received appropriate anticoagulation and other therapy according to standard hospital practice. Aspirin (loading dose 300 mg) and clopidogrel (loading dose at least 300 mg) had to be given before percutaneous coronary intervention for those patients not on chronic antiplatelet treatment. The use of glycoprotein IIb/IIIa inhibitors was left to the discretion of the investigator. Exclusion criteria included previous myocardial infarction, acute or chronic heart failure, valve heart disease, acute infection (T>38.5 °C), acute state of a chronic infectious or inflammatory diseases, severe liver (alanine transaminase>3 times upper normal limit), renal disease (creatinine>132umol/L), neoplasm and haematologic disorders (white blood cell counts $<4\times10^9$/L, platelet counts $<80\times10^9$/L, or haemoglobin <90 g/L). All study participants gave written informed consent and the study protocol was approved by the Shanghai Tenth Hospital's Ethics Committee.

Coronary Angiography

Coronary angiography was performed through radial or femoral artery approach. Significant CAD was diagnosed visually if luminal diameter stenosis ≥50% was present at a major epicardial coronary artery, and left main trunk stenosis ≥50% was considered as a two-vessel disease. Severity of coronary atherosclerosis was categorised according to the number of diseased vessels as 1-, 2- or ≥3-vessel disease [13].

Biochemical Investigation

Plasma was obtained after overnight fasting after admission. Plasma specimens were stored at -80 °C until analysis. White blood cell count (WBC), C reactive protein (CRP), serum glucose, glycosylated haemoglobin (HbA1c), creatinine (Cr), and lipid profiles were measured by colorimetric enzymatic assay systems (Roche Modular P-800, Switzerland). N-terminal Pro-brain natriuretic peptide (NT-ProBNP) was measured by the Elecsys electro-chemiluminescent immunoassay (Roche Diagnostics Ltd. Rotkreuz, Switzerland). Vaspin were measured with commercially available ELISA according to the manufacturer's instructions (Adipogen, Seoul, South Korea).

Echocardiographic Assessment

All patients underwent transthoracic echocardiography by means of an echocardiograph equipped with a broadband transducer (Vivid 7®, GE VingMed Ultrasound AS; Horten, Norway). Measurements of left ventricular and left atrium were obtained from the parasternal long-axis and apical four-chamber views, in accordance with standard criteria. Left ventricular ejection fraction (LVEF) was calculated using the modified Simpson rule in the apical two- and four-chamber views [14].

Follow-up

Follow-up started from the day of vaspin evaluation. Follow-up data were obtained through the following three ways: reviewing the patient's hospital records, interviewing the patients through telephone and examining the patients in outpatient clinics. The primary endpoints were the major adverse cardiac events (MACEs), which were defined as any of the following: cardiac death, rehospitalisation for heart failure, nonfatal myocardial infarction or severe angina for coronary revascularisation. The definition of cardiac death required the documentation of significant arrhythmia or cardiac arrest or death attributable to congestive heart failure or myocardial infarction in the absence of any other precipitating factor. Deaths caused by accidents were excluded (follow-up censored at the time of death). The mean follow-up duration was 24±2 months. At the end of the follow-up, all patients except deaths underwent transthoracic echocardiography again.

Statistical Analysis

Continuous variables were presented as mean±SD, and categorical data were summarised as frequencies or percentages. For continuous variables, normal distribution was