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Serum adropin levels are decreased in patients with acute myocardial infarction

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ABSTRACT

Objective: Adropin is a recently identified bioactive protein that is important for energy homeostasis and maintaining insulin sensitivity. We sought to detect serum adropin levels in acute myocardial infarction (AMI) patients.
Methods: We enrolled 138 AMI patients, 114 stable angina pectoris (SAP) patients and 75 controls. Adropin levels were measured by enzyme-linked immunosorbent assay (ELISA).
Results: Serum adropin levels were significantly lower in patients with AMI compared with SAP patients or controls ($P < 0.01$). Multivariate logistic regression demonstrated that lower adropin was the independent predictor for the presence of AMI in coronary artery disease (CAD) patients ($P < 0.01$). Serum adropin levels were negatively associated with body mass index (BMI) ($P < 0.01$) and triglyceride levels ($P < 0.05$) in AMI patients.
Conclusion: Decreased serum adropin levels are associated with the presence of AMI in CAD patients. These results revealed that adropin might represent as a novel biomarker for predicting AMI onset in CAD patients.

1. Introduction

Critical cardiovascular events such as acute myocardial infarction (AMI) remain the leading cause of morbidity and mortality worldwide. Accurate diagnosis of AMI improve prognosis through appropriate treatment without delay. In addition, biomarkers have increasingly emerged as important alternatives to traditional methods for rapid diagnosis and risk stratification of high-risk individuals [1–3].

Many blood-based protein biomarkers such as cardiac troponin (cTn) I or T, B-type natriuretic peptide (BNP) and high-sensitivity C-reactive protein (hs-CRP) has an established role in providing crucial diagnostic or prognostic value in the field of coronary artery disease (CAD). Adropin is a recently identified bioactive protein encoded by the energy homeostasis associated gene (Enho) that is expressed in the liver and the brain [4]. Adropin appears to participate in the maintenance of energy homeostasis and insulin response, which is closely related to the development and progression of atherogenesis [4]. Besides, a recent study found that adropin is also expressed in coronary artery endothelial cells and plays a potential endothelial protective role in mice [5]. It is well known that endothelial dysfunction is a key early event in atherogenesis and is integral in the onset of CAD and acute coronary syndromes (ACS) [6]. More recently, Wu et al. [7] demonstrated that decreased serum adropin was an independent predictor of clinically relevant coronary atherosclerosis. Based on these findings, we hypothesized that adropin deficiency might be involved in the pathogenesis of AMI. However, the relationship between adropin concentrations and AMI has never been fully elucidated. Therefore, we aimed to detect serum adropin levels in AMI patients, and to investigate their correlation with AMI.

2. Patients and methods

2.1. Patients

From August 2012 to June 2013, a total of 297 subjects admitted to Xijing hospital for coronary angiography owing to AMI (AMI group, $n = 108$), stable angina pectoris (SAP group, $n = 114$) or a clinical suspicion of CAD in subjects with multiple coronary risk factors but without lesions on angiography (controls group, $n = 75$) were recruited. AMI was defined by an increase in serum troponin I ($2 \times$ upper limit of the hospital normal range) associated symptoms of ischemia and/or characteristic ECG signs (ST segment-T wave changes, left bundle branch block or development of pathological Q waves) [8]. SAP was defined as no change in frequency, duration or intensity of symptoms more than 3 months before the admission. Patients were excluded on the basis of having peripheral artery disease, active inflammatory disease, autoimmune disorders, suspected myocarditis or pericarditis,

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malignant disease, diabetes, severe heart failure and advanced renal and hepatic disease. Written informed consent was individually obtained regarding participation in this study. The study protocol was approved by the ethics committee of Xijing hospital.

2.2. Blood chemistry measurement

Peripheral venous blood samples were drawn from the antecubital vein of all participants before the angiographic procedure. After clotting, the samples were immediately centrifuged and stored at −80 °C until analysis. All participants underwent conventional laboratory analyses, including determination of total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-c) and density lipoprotein cholesterol (HDL-c) using an autoanalyzer(Hitachi 7170, Hitachi Co., Japan). Hs-CRP levels were measured on an Olympus AU5400 Automatic Biochemical Analyzer (Olympus Co., Japan). N-terminal pro BNP (NT-proBNP) and cTnT levels were detected in Siemens Immulite 1000 Immunoassay System (Siemens, Germany). Serum adropin levels were measured using a commercially available enzyme-linked immunosorbent assay (ELISA) kit (Cusabio Biotech Co, Wuhan, CN). The assay recognizes recombinant and natural human adropin. No significant cross-reactivity or interference was observed [9]. Test range was 0.32–20 ng/mL [9]. The sensitivity of the assay was 0.08 ng/mL, and inter-assay and intra-assay coefficients of variation (CV) were less than 14% and 5%, respectively [9]. All the serum samples were analyzed by ELISA in duplicate, and the results were averaged. Preliminary study demonstrated that adropin levels in serum are closely correlated with those in paired plasma samples.

2.3. Statistical analysis

All statistical analyses were performed using SPSS 17.0 for Windows version (SPSS Inc., Chicago, USA). The Kolmogorov–Smirnov test was used to analyze data normality results of normally distributed continuous variables are expressed as the mean value ± SD, and those for continuous variables with skewed distribution are expressed as the median value (interquartile range) and categorical variables as frequencies or percentages. Differences among the three groups were analyzed by one-way analysis of variance (ANOVA), followed by Tukey post hoc analysis or Kruskal–Wallis test as indicated. Multivariate logistic analysis was performed to determine the independent predictors of AMI in CAD patients. The correlation between serum adropin levels and other clinical characteristics in AMI patients was assessed by Pearson or Spearman correlation coefficient when appropriate. Probability values (two-tailed) were considered significant at $P < 0.05$.

3. Results

3.1. Baseline clinical characteristics

The baseline characteristics of the three groups were shown in Table 1. Compared with controls, SAP patients had significantly higher diastolic blood pressure (SBP), LDL-c, hs-CRP and NT-proBNP levels. Compared with SAP patients, AMI patients had significantly higher hs-CRP levels as well as significantly lower HDL-c levels and left ventricular ejection fraction (LVEF). Besides, AMI patients were older than controls.

3.2. Serum adropin levels

As shown in Fig. 1, our study demonstrated that SAP patients had significantly lower serum adropin levels compared to controls (3.81 ± 1.78 vs 5.12 ± 1.44 ng/ml, $P < 0.01$). In CAD patients, AMI patients had significantly lower serum adropin levels compared to SAP patients (2.19 ± 1.61 vs 3.81 ± 1.78 ng/ml, $P < 0.01$).

3.3. The independent predictors of AMI

We perform multivariate logistic regression including all variables to assess the independent predictors of AMI in CAD patients. Our results revealed that lower serum levels of adropin was the significant and independent predictor of AMI in CAD patients (OR = 0.555, 95% CI = 0.438–0.704, $P < 0.01$; Table 2).

3.4. Correlations between adropin and other clinical characteristics in AMI patients

As demonstrated in Table 3, serum adropin levels were negatively correlated with body mass index (BMI) ($\rho = -0.252$, $P = 0.008$) and TG levels in AMI patients ($\rho = -0.202$, $P = 0.036$). However, serum adropin levels were neither correlated with cTnT levels ($\rho = -0.161$, $P = 0.095$) nor correlated with Creatine Kinase (CK)-MB levels ($\rho = 0.045$, $P = 0.646$). There was also no correlation between serum adropin levels with other conventional cardiovascular biomarkers such as hs-CRP ($\rho = -0.101$, $P = 0.297$) and NT-proBNP ($\rho = -0.008$, $P = 0.936$).

Table 1
Baseline clinical and laboratory characteristics.

Variables	AMI ($n = 108$)	SAP patients ($n = 114$)	Controls ($n = 75$)
Age (years)	64.50 ± 10.53*	63.67 ± 11.18	60.40 ± 9.58
Male, *n* (%)	62 (57.41%)	67 (58.77%)	39 (52.00%)
BMI	25.07 (23.18–26.49)	25.12 (23.79–25.92)	24.74 (23.29–25.94)
SBP (mm Hg)	131.76 ± 18.88	135.60 ± 14.26	130.04 ± 16.00
DBP (mm Hg)	81.06 ± 10.95	83.72 ± 11.92*	79.42 ± 12.43
TC (mmol/L)	4.62 ± 1.09*	4.36 ± 1.06	4.16 ± 1.04
TG (mmol/L)	1.77 (1.30–2.67) *	1.61 (1.13–2.19)	1.50 (1.02–2.17)
LDL-c (mmol/L)	2.80 ± 0.80**	2.67 ± 0.95*	2.32 ± 0.88
HDL-c (mmol/L)	0.92 (0.75–1.17) **††	1.03 (0.86–1.21)	1.04 (0.86–1.26)
FBG (mmol/L)	5.64 (5.04–6.26)	5.62 (4.96–6.13)	5.65 (5.12–6.16)
hs-CRP (mg/L)	1.68 (1.24–3.64) **††	0.88 (0.67–1.43) **	0.61 (0.34–0.96)
NT-proBNP (ng/L)	277 (220–324) **	282 (83–334) *	164 (58–313)
LVEF	53.94 ± 11.40**††	63.49 ± 8.93	65.09 ± 7.34
Smoking, *n* (%)	40 (37.04%)	40 (35.09%)	22 (29.33%)
On statins, *n* (%)	21 (19.44%)	32 (28.07%)	14 (18.67%)
On ACEI/ARB, *n* (%)	29 (26.85%)	33 (28.95%)	26 (34.67%)

All values are presented as mean ± SD, median value (interquartile range) or *n* (%). AMI = acute myocardial infarction, SAP = stable angina pectoris, BMI = body mass index, SBP = systolic blood pressure, DBP = diastolic blood pressure, TC = total cholesterol, TG = triglycerides, LDL-c = low-density lipoprotein cholesterol, HDL-c = high density lipoprotein cholesterol, FBG = fasting glucose, hs-CRP = high-sensitivity C-reactive protein, NT-proBNP = N-terminal pro B-type natriuretic peptide, LVEF = left ventricular ejection fraction and ACEI/ARB = (on the use of) angiotensin converting enzyme inhibitor/angiotensin receptor blocker.
*$P < 0.05$ compared with healthy controls, **$P < 0.01$ compared with controls; †$P < 0.05$ compared with SAP patients, ††$P < 0.01$ compared with SAP patients.