Correlations of soluble osteoclast-associated receptor (sOSCAR) with acute coronary syndrome

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Background: An osteoclast-associated receptor (OSCAR) is an immunoglobulin receptor expressed in an osteoclast, and takes part in the formation of an osteoclast. While the soluble OSCAR (sOSCAR) component is reported to be involved in the pathogenesis of arteriosclerosis, the aim of this present study is to investigate the relationship between sOSCAR and acute coronary syndrome (ACS).

Methods: This study enrolled 41 patients with ACS and 33 patients without ACS as a control, from March 2017 to June 2017. The baseline clinical parameters and serum levels of sOSCAR were collected in the participants. The univariate and multivariate logistic regressions were applied to explore the independent association of sOSCAR with ACS. A receiver operating characteristic (ROC) curve was applied to explore the ability of sOSCAR to indicate ACS.

Results: The results showed that the levels of sOSCAR in the patients with ACS was lower than the patients without ACS (P=0.005). The multivariate logistic regression tests demonstrated that a decreased sOSCAR level was independently associated with the presence of ACS (OR: 0.174, 95% CI: 0.047–0.638, P=0.008). ROC analysis showed that the optimal sOSCAR cut-off value for the indication of ACS was <110.87 pg/mL, the corresponding sensitivity was 65.85%, and the specificity was 69.70%.

Conclusions: The decreased levels of sOSCAR are independently associated with the presence of ACS. sOSCAR could then be considered as a potential biomarker for the prediction of ACS.

Keywords: Immunoglobulin receptor; osteoclast-associated receptor; acute coronary syndrome

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Introduction

As a novel osteogenic protein, the osteoclast-associated receptor (OSCAR) plays an important role in the process of osteoclastogenesis (1). OSCAR can be divided into soluble and membranous forms (2). Previous studies have found there to be a correlation between OSCAR and osteoarticular disease or osteoporosis (3-5). In recent years, it was found that OSCAR was involved in the inflammatory response and the cell activation in the process of arteriosclerosis, acting as an immunological mediator and a regulator of the osteoclast differentiation (6). Moreover, OSCAR was also identified as playing an important role for both vascular inflammation and/or plaque vulnerability during atherosclerosis (7). However, the correlations between sOSCAR and ACS are largely unknown. The aim of this work is to evaluate the

association between sOSCAR and ACS.

Methods

Study population

A total of 41 ACS patients, of which 23 were male and 18 were female, admitted to the Second Affiliated Hospital of Nantong University from the dates of March 2017 to June 2017, were enrolled in this study. The clinical features of all the patients were confirmed using the diagnostic criteria set for ACS (8,9). Additionally the other 33 non-ACS patients were enrolled as a control, which included patients with stable angina and normal coronary angiography result. The age, gender, hypertension status, hyperlipemia status, diabetes status and smoking history of the patients were recorded after admission. Moreover, fasting venous blood samples were collected on the next morning after their admission, and the levels of hypersensitive C-reactive protein (hs-CRP), cholesterol, triglyceride, high-density lipoprotein (HDL), low-density lipoprotein (LDL), and N-terminal pro-brain natriuretic peptide (NT-proBNP) were measured. Patients were excluded from the study if they had any of the following: acute infectious disease, acute infection, connective tissue disease, malignant tumor, hepatorenal dysfunction, history of hematopathy, skeletal and joint disorders, major surgery, congenital heart disease, valvular heart disease and/or cardiomyopathy.

sOSCAR detection

Four ml of fasting peripheral whole blood was fetched and put into a centrifuge, and set to 2,500 rpm for 10 min. The supernatant was taken and preserved in a –80 ℃ refrigerator until its application. The human soluble OSCAR ELISA kit was purchased from BioTSZ (HG30932, 96 Tests, CITY, STATE) with a detection range of 6–650 pg/mL.

Statistical analysis

The measurement data were presented as means ± the standard deviation, while those conforming to a skewed distribution were expressed as M (P25–P75). Afterwards, the enumeration data were then presented as a percentage or frequency. Measurement data between the two groups were then compared using an independent-sample *t*-test or the Mann-Whitney U test. While the enumeration data were compared using the chi-square test. Multivariable logistic regression analyses were used to identify the independent risk factors for the presence of ACS. Data were analyzed using the SPSS 17.0 (SPSS Inc., Chicago, Illinois) and the Med-Calc (version 11.2.1; MedCalc, Mariakerke, Belgium) software. P<0.05 was deemed statistically significant.

Results

The comparative results of the baseline data from the two groups were as follows: sOSCAR level and LVEF in ACS group were lower than those in the non-ACS group (P<0.05), whereas hs-CRP and NT-proBNP levels in the ACS group were higher than those in the non-ACS group (P<0.05) (*Table 1*).

The area under the receiver–operating characteristic curve for sOSCAR was 0.691 for predicting ACS, with the cut-off value of 110.87 pg/mL, a 95% confidence interval of 0.573–0.793, a sensitivity of 65.85% and a specificity of 69.70% (P<0.05) (*Figure 1*).

Moreover, a multivariate regression analysis indicated that sOSCAR (OR: 0.174, 95% CI: 0.047–0.638, P=0.008) and NT-proBNP (OR: 6.636, 95% CI: 1.821–25.193, P=0.004) were independently associated with the presence of ACS (*Table 2*).

Discussion

Atherosclerosis (AS) is a common vascular disease with plaque formation being one of its pathological features. An unstable plaque rupture within the coronary artery will lead to thrombosis, which accounts for the foundation of ACS incidence. Meanwhile, the osteoclast-associated receptor (OSCAR) is a type of immunoglobulin receptor expressed in an osteoclast, which is one of the members encoded by the lymphocyte receptor complexes (LRC) family. OSCAR can be markedly expressed in an osteoclast, and it can also be found in monocytes; a discovery which has laid down a molecular basis for understanding the differentiation of a monocyte into an osteoclast. In humans, OSCAR can be expressed as a macrophage, a monocyte and a monocyte-derived dendritic cell (10). Moreover, clinical investigations have suggested that OSCAR may participate in the pathogenesis of rheumatoid arthritis and osteoporosis (5,11,12).

OSCAR can be divided into two types: soluble and membranous. As shown in this study, the sOSCAR in the ACS group is remarkably lower than in the non-ACS

Table 1 Comparison of the general clinical information between the 2 groups

Clinical information	ACS group (n=41)	Non-ACS group (n=33)	P
Age (year)	68.61±12.21	64.93±9.99	0.168
Female (%)	18 (43.9%)	17 (51.5%)	0.514
Hypertension (%)	27 (65.9%)	18 (54.5%)	0.322
Diabetes (%)	11 (26.8%)	11 (33.3%)	0.543
Hyperlipidemia (%)	8 (19.5%)	10 (30.3%)	0.282
Smoking (%)	12 (31.0%)	7 (21.2%)	0.43
sOSCAR (pg/mL)	68.57 (33.05–167.15)	195.65 (55.50–371.36)	0.005
hs-CRP (mg/L)	6.62 (1.84–17.28)	1.37 (0.66–4.91)	0.017
Triglyceride (mmol/mL)	1.91±1.09	2.17±1.09	0.414
Total cholesterol (mmol/mL)	4.57±0.88	4.70±1.03	0.56
HDL (mmol/mL)	0.99±0.29	1.09±0.25	0.108
LDL (mmol/mL)	2.39±0.61	2.41±0.78	0.897
NT-proBNP (pg/mL)	526.95 (115.22–1539.75)	78.10 (32.75–202.57)	0
LVEF (%)	61.54±5.26	64.41±4.63	0.025

LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro brain natriuretic peptide; hs-CRP, hypersensitivity C reactive protein; HDL, high density lipoprotein; LDL, low density lipoprotein.

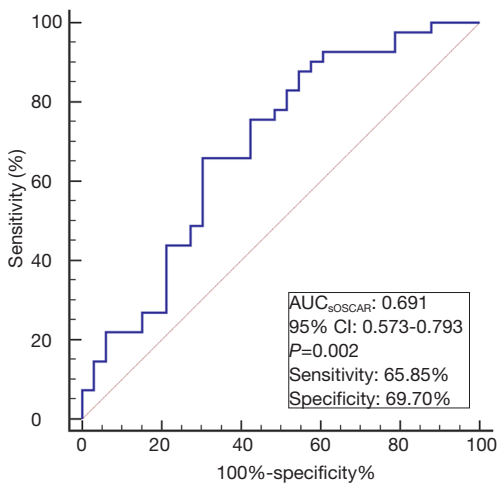

Figure 1 The ROC area under the curve (AUC) in predicting ACS. ROC, receiver operating characteristic; ACS, acute coronary syndrome.

group (P=0.005). Multivariate regression analysis indicated that the decreased level of sOSCAR is independently-associated with the presence of ACS. For predicting ACS, the area under the receiver–operating characteristic curve of sOSCAR was 0.691 (0.573–0.793, P=0.002). However, this is an observational study which may not demonstrate the cause-effect relationship between decreased OSCAR levels and ACS; therefore, a prospective follow-up study is needed to clarify the associations between sOSCAR levels and ACS.

Oxidized low density lipoproteins (oxLDL) are formed through the oxidation of low density lipoproteins (LDL) *in vivo*. This is an important factor that leads to the genesis and the development of AS, and unstable plaque formation (13). Ehara *et al.* discovered that an elevated oxLDL level was positively correlated with ACS severity (14). Circulating oxLDL-specific markers strongly reflect the presence of ACS. Furthermore, OSCAR has been identified in endothelial cells, responding to the proatherogenic factor of oxLDL (6,7,15). Therefore, we speculate that this association between sOSCAR and oxLDL may explain the correlation between sOSCAR and ACS.

Conclusions

The decreased levels of sOSCAR are independently-associated with ACS, and might be considered as a potential biomarker for the prediction of ACS.

Table 2 Results of multiple logistic regression analysis for ACS

Variables	OR, 95% CI	P
sOSCAR	0.174 (0.047–0.638)	0.008
NT-proBNP	6.636 (1.821–25.193)	0.004
hs-CRP	2.505(0.702–8.934)	0.157
LVEF	0.856(0.235–3.119)	0.814

Variables assignment: sOSCAR <117.4 pg/mL =0, ≥117.4 pg/mL =1; NT-proBNP <181.3 pg/mL =0, ≥181.3 pg/mL =1; hs-CRP <3.4 mg/L =0, ≥3.4 mg/L =1; LVEF <63% =0, ≥63% =1. Soscar, soluble osteoclast-associated receptor; NT-proBNP, N-terminal pro-brain natriuretic peptide; hs-CRP, hypersensitive C-reactive protein; LVEF, left ventricular ejection fraction; ACS, acute coronary syndrome.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: This study was approved by the Ethics Committee of The Second Affiliated Hospital of Nantong University (IRB number: 2018041).

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