Research Article

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Serum tumor marker carbohydrate antigen 125 levels and carotid atherosclerosis in patients with coronary artery disease

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Abstract: Objective: We assessed the correlation between serum carbohydrate antigen 125 (CA125) and carotid intima-media thickness (cIMT) in patients with coronary artery disease (CAD). Methods: We collected 518 CAD patients from the cardiovascular disease center in our hospital, and all cIMT values were measured in patients with CAD. Results: The serum CA125 concentrations were found to be increased in CAD patients with early carotid atherosclerosis compared with patients without early carotid atherosclerosis (20.1±7.72 vs. 17.7±6.41 U/mL, p<0.001). The cIMT values were increased in patients with higher serum CA-125 levels than those with lower serum CA-125 concentrations (1.16±0.32 vs. 0.98±0.29 mm, p<0.001). There was a positive correlation between serum CA125 and cIMT in CAD patients (r=0.262, p<0.001). Moreover, the serum CA125 concentrations also were positively correlated with cIMT in subjects with early carotid atherosclerosis and without early carotid atherosclerosis (r=0.255, p<0.001; r=0.189, p=0.002). We found that serum CA-125 concentrations were independently correlated with cIMT (beta = 0.293, p<0.001) in multiple linear regression analysis. Conclusions: We found that serum CA125 concentrations were positively correlated with cIMT in CAD patients, serum CA125 might be a potential biochemical marker for the estimation of atherosclerosis in patients with CAD.

Keywords: Serum carbohydrate antigen 125; Carotid intima-media thickness; Coronary artery disease

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Serum carbohydrate antigen 125 (CA125) is a molecular-weight glycoprotein manufactured by mesothelial cells and the coelomic epithelium, and it is used as a tumor marker in patients with ovarian cancer [1]. Some studies have confirmed that increased serum CA125 concentrations were related with poor prognosis in patients with ovarian cancer [2]. Serum CA125 levels were higher in other malignancies such as melanoma, non-Hodgkin's lymphoma and acute leukemia [3-5]. Moreover, increased CA125 concentrations have been reported in patients with non-malignant diseases including nephrotic syndrome, liver cirrhosis and pelvic inflammatory disease [6-8]. Recent studies have showed that serum CA125 levels were increased in chronic heart failure patients [9]. Recently, CA125 has been considered as a tool for risk stratification in heart diseases [10], and increased serum CA125 concentrations have been found to be correlated with cardiac function in patients with coronary artery disease (CAD) [11].

It is well known that atherosclerosis is implicated in the pathogenesis and development of CAD, and atherosclerosis is the complex process of inflammation and oxidative stress [12-13]. Carotid intima-media thickness (cIMT) is a non-invasive marker for patients with early atherosclerosis [14]. Clinical application of cIMT may provide a prediction for CAD and stroke in large-scale general population studies [15-16], and increased cIMT values are associated with poor prognosis in patients with CAD [17]. In fact, inflammation and oxidative stress may accelerate the development of atherosclerosis, even in the general population [18]. Further, the increase in serum CA125 is correlated with the inflammatory and oxidative stress stimulation. Therefore, we assessed the correlation between serum CA125 and cIMT in patients with CAD.

1 Materials and methods

We collected 518 CAD patients from the cardiovascular disease center in the First Affiliated Hospital, Xinjiang

Medical University. The diagnosis of CAD was determined by coronary angiography in all patients. Patients with following conditions were excluded: liver dysfunction, chronic obstructive pulmonary disease, aortic dissection, immune diseases, acute and chronic infections, malignant tumor and psychosis. All the subjects completed the clinical examinations, including anthropometric assessments, carotid ultrasonography examinations and laboratory tests. The study was approved by the ethics committee of the First Affiliated Hospital, Xinjiang Medical University.

We collected information about physical examinations such as age, gender, body mass index (BMI) and drug use histories. Fast plasma glucose (FPG), total protein (TP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), triglyceride (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) levels were tested by using automatic biochemistry analyzer. High-sensitivity C-reactive protein (hs-CRP) concentrations were tested by automatic immune analyzer. In addition, serum CA125 levels were measured with chemiluminescent analyzer. The cIMT values were obtained from ultrasonic examination results.

2 Statistics analysis

The data analyses were performed by using 19.0 SPSS software (SPSS Inc., Chicago, IL, USA). Continuous variables and categorical variables were presented as mean± standard deviation and proportions, repectively. Differences between two groups were analyzed by using the Student's t test, U test and Chi-square test. The correlation between CA-125 and cIMT in patients CAD was analyzed by Pearson or Spearman method. Multivariate linear regression was used to further evaluate this link between CA125 and cIMT. P values of less than 0.05 were accepted as significant.

3 Results

3.1 The clinical characteristics in all patients with CAD

The study population consisted of 518 patients with CAD. The mean cIMT values were 1.1±0.31 mm. Further, when the concentrations of serum CA 125 were divided by the median, the cIMT values were increased in patients with higher serum CA-125 levels than those with lower serum CA-125 concentrations (1.16±0.32 vs. 0.98±0.29 mm, p<0.001).

3.2 The serum CA125 concentrations divided by the threshold of cIMT values

We decided to divide all patients with CAD into two groups: subjects with early carotid atherosclerosis (cIMT > 1.0 mm) and without early carotid atherosclerosis (cIMT ≤ 1.0 mm). The serum CA125 concentrations were found to be increased in CAD patients with early carotid atherosclerosis compared with patients without early carotid atherosclerosis (20.1±7.72 vs. 17.7±6.41 U/mL, p<0.001). There were statistical differences for age, body mass index, diabetes mellitus, anti-platelet agent use and high-sensitivity C-reactive protein, as shown in Table 1.

3.3 The correlation analysis between serum CA125 and laboratory indexes

The correlation analysis showed that serum CA125 concentrations were positively correlated with BMI, LDL-C, Cr and hs-CRP in patients with CAD (r=0.113, p=0.010; r=0.095, p=0.031; r=0.098, p=0.026; r=0.124, p=0.005) (Table 2). There was a positive correlation between serum CA125 and cIMT in CAD patients (r=0.262, p<0.001) (Figure 1). Moreover, we assessed the correlations between serum CA125 and cIMT in subjects with early carotid atherosclerosis and without early carotid atherosclerosis, the serum CA125 concentrations also were positively correlated with cIMT in the two groups (r=0.255, p<0.001; r=0.189, p=0.002).

3.4 Multiple linear regression analysis between serum CA125 and cIMT in all patients

In the multiple linear regression analysis, adjustment for sex, age, BMI, blood glucose, LDL-C,HDL-C, TC, TG, hs-CRP, ALT, AST, diabetes mellitus, hypertension and medications uses, we found that serum CA-125 concentrations were independently correlated with cIMT (beta = 0.293, p<0.001) in multiple linear regression analysis (Table 3). The correlation between serum CA-125 and cIMT in all patients with CAD reappeared when cIMT variable was included in dependent variable in the multiple linear regression analysis (beta=0.258, p<0.001) (Table 4).

Table 1: Clinical and laboratory parameters in with and without early carotid atherosclerosis

	>1.0 N=262	≤1.0 N=256	p-values
Gender (M)	222(84.7%)	203(79.3%)	0.107
Age(yr)	55.8±13.07	48.5±8.96	<0.001
Body mass index (kg/m2)	23.9±3.01	23.1±2.80	0.009
Diabetes mellitus	102(38.9%)	75(29.3%)	0.021
Hypertension	116(44.3%)	103(40.2%)	0.352
Calcium channel blockers	27(10.3%)	16(6.2%)	0.094
Anti-platelet agent use	259(98.9%)	239(93.4%)	0.001
Nitrates	156(59.5%)	164(64.1%)	0.290
B-blockers	213(81.3%)	195(76.2%)	0.154
ACEI/ARB	223(85.1%)	225(87.9%)	0.355
Alanine transaminase (U/L)	17.4±7.81	16.6±7.32	0.256
Aspartate transaminase (U/L)	18.0±4.55	17.9±4.83	0.772
Low density lipoprotein cholesterol (mmol/L)	2.5±0.87	2.5±0.84	0.471
High density lipoprotein cholesterol (mmol/L)	1.2±0.32	1.2±0.34	0.796
Total cholesterol (mmol/L)	4.1±1.12	4.0±1.01	0.318
Triglycerides (mmol/L)	1.0±0.33	1.0±0.37	0.348
Blood glucose (mmol/L)	5.6±2.06	5.4±1.88	0.244
High-sensitivity C-reactive protein (mg/L)	1.8±1.74	1.5±1.49	0.025
Creatinine (umol/L)	64.6±17.22	65.0±17.20	0.803
Serum carbohydrate antigen 125 (U/mL)	20.1±7.72	17.7±6.41	<0.001

Table 2: The correlation between serum CA125 and laboratory parameters in all patients

Items	r	p-values
Body mass index	0.113	0.010
High sensitivity C-reactive protein	0.124	0.005
Low-density lipoprotein cholesterol	0.095	0.031
Creatinine	0.098	0.026
Carotid intima-media thickness	0.262	<0.001

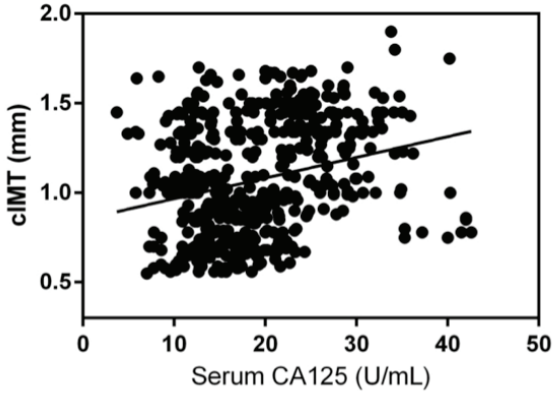

Figure 1: Serum CA 125 concentrations and cIMT in the patients with CAD

4 Discussion

The cIMT measurements have been recommended as a screening method for high-risk populations with cardiovascular events such as older adults, type 2 diabetes mellitus and systemic lupus erythematosus [19-21]. There was evidence that cIMT is an independent predictor of stroke in persons without a history of cardiovascular disease [22]. In addition, serum CA125 has been associated with the diagnosis and prognosis of tumor diseases such as ovarian cancer [1], variant prostate carcinoma [3], non-Hodgkin's lymphoma [23]. Interestingly, our study

Table 3: Serum carbohydrate antigen 125 as dependent variable in multivariable linear regression analysis

	Unstandardized cofficients		Standardized cofficients	t	P-value
	B	Std Error	Beta		
Creatinine	0.057	0.018	0.136	3.228	0.001
High sensitivity C-reactive protein	0.440	0.190	0.099	2.312	0.021
Carotid intima-media thicknes	6.708	0.991	0.293	6.773	<0.001

Table 4: Carotid intima-media thickness as dependent variable in multivariable linear regression analysis

	Unstandardized cofficients		Standardized cofficients	t	P-value
	B	Std Error	Beta		
Age	0.008	0.001	0.289	7.204	<0.001
Body mass index	0.015	0.004	0.140	3.516	<0.001
Blood glucose	0.020	0.006	0.123	3.099	0.002
Triglycerides	0.080	0.036	0.089	2.238	0.026
Serum carbohydrate antigen 125	0.011	0.002	0.258	6.496	<0.001

first found that the increased serum CA125 concentrations were positively correlated with cIMT in the study population, and serum CA125 may be a well marker for subclinical atherosclerosis in patients with CAD. However the mechanism for the correlation between serum CA-125 concentrations and cIMT still remains unclear. Inflammation may contribute to explain this relationship. It is known that the atherosclerosis is considered to be the accumulation of lipoproteins and the stimulation of inflammation in the arterial wall, and low-density lipoprotein molecules are the main inducement for the pathological processes [24]. Indeed, the inflammation plays a key role in the regulation of the atherosclerotic development. Some studies have shown that some inflammatory cytokines were related with carotid atherosclerosis [25]. The production of CRP has been found to promote the formation of atherosclerosis directly [26]. Recent studies have found that serum CA125 concentrations were related to inflammatory cytokines in patients with heart failure and atrial fibrillation, such as interleukin-6 (IL-6), interleukin-1 (IL-1) and tumor necrosis factor-α (TNF-α), and increased CA125 levels might be the activation of inflammatory cytokines in the early stages of atherosclerosis [9, 27-28]. Therefore, the inflammatory conditions may increase serum CA125 concentrations in patients with CAD, and links the relationship between serum CA125 and cIMT in study subjects.

The screening and detection of subclinical atherosclerosis is a primary prevention, which can reduce the occurrence of cardiovascular events. Compared with carotid ultrasound, serum CA125 is an objective and convenient biochemical parameter, which is rarely affected by subjective factors. In our study, we found correlation between serum CA125 and cIMT in patients with CAD. Therefore, we believe that serum CA125 may provide useful information for the assessment of atherosclerosis in patients with CAD.

We noted several limitations in this study. First, a longitudinal study is needed to assess the relationship between serum CA125 and cIMT in patients with CAD. Second, our study did not assess the link of serum CA125 and clinical outcomes in patients with CAD. Finally, the present study did not provide the evidence between serum CA125 and anti-inflammatory treatments in patients with CAD. In conclusion, we found that serum CA125 concentrations were positively correlated with cIMT in CAD patients, and serum CA-125 may be a potential biochemical marker for the atherosclerosis in patients with CAD.

Interest declarations: The authors have no financial conflicts of interes

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