Can ICAM and VCAM predict the severity of coronary artery diseases in stable angina?

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Abstract

BACKGROUND: Ischemic heart disease is the leading cause of mortality and morbidity in the world. Vascular inflammation is the noticeable risk factor of ischemic heart disease. In this study, the relation between the intracellular adhesion molecule (ICAM) and vascular adhesion molecule (VCAM) were evaluated as the inflammatory indicators of the coronary involvement extent.

METHODS: In this cross-sectional study, 82 patients with stable angina were studied. Patients were all candidates for angiography. Individuals with acute coronary syndrome, recent surgery, inflammatory disease, drug consumption, kidney and liver disease, phlebitis and pulmonary thromboembolism (PTE) were excluded. Blood sampling was performed for biochemical analysis of VCAM and ICAM. Coronary angiography was then conducted via standard method.

RESULTS: Mean age of the patients was 58.4 ± 10.1 years and males constituted 72% of the studied population. Mean values of ICAM and VCAM were 183.9 ± 78 and 150.3 ± 136 ng/dl, respectively. There was not any correlation between VCAM and ICAM and the severity of coronary artery disease. In linear regression analysis, even with considering hypertension, hyperlipidemia, and diabetes as cofounders, there was not any relation between these factors and cardiovascular disease.

CONCLUSION: According to our findings, inflammatory markers (VCAM and ICAM) did not add any further information about the extent of cardiovascular disease.

Keywords: Intracellular Adhesion Molecule, Vascular Adhesion Molecule, Stable Angina, Severity of Cardiovascular Disease.

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Introduction

Atherosclerosis and its complications are the leading cause of mortality and morbidity in both genders and all races.[1] Atherosclerosis is associated with inflammation. In fact, adherence of circulating leukocytes to endothelium in response to cytokine secretion from the cells of blood vessels is one of the earliest stages of atherosclerosis development.[2] Intracellular adhesion molecules include (ICAMs) and vascular adhesion molecules (VCAMs). Their increase has been shown in plaque endothelial surface molecules in human atherosclerotic lesions.[2] The soluble forms of VCAM and ICAM are isolated from the activated endothelium and can be measured in peripheral blood.[3] In some studies, the increased levels of soluble forms of binding molecules were related to the increased risk of myocardial infarction in healthy subjects and patients with coronary artery disease (CAD).[4,5] Various studies have shown very different results regarding the relations between changes in serum levels of these molecules and the extent of CAD.[6] While some studies indicated these factors as independent risk factors for CAD, some others could not find any association.[5-9] In this study,

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the relationship between serum levels of circulating binding molecules and the severity and extent of CAD were studied in patients with stable angina.

Materials and Methods

This prospective cross-sectional study was conducted in Chamran Hospital, Isfahan University of Medical Sciences, Iran, in 2007. The study population included 82 patients with stable angina who were candidates for diagnostic angiography. Patients were selected by simple sampling method. Stable angina was defined as chest pain or equivalent symptoms (shortness of breath, fatigue, or syncope) which typically lasted for 2 to 10 minutes and improved by taking rest or trinitroglycerin (TNG).[5] At first, a questionnaire containing demographic data (age and gender), history of previous illnesses (diabetes, hypertension, and high blood lipids) was designed. After collecting data, patients with a history of hospitalization due to heart attacks in the past two weeks, unstable angina, active malignancy, acute or chronic liver disease, kidney disease, infection, deep vein thrombosis, asthma, pulmonary embolism were included. On the other hand, patients were excluded if they had undergone a major surgery during the past 2 months, or had any rheumatic disease, were using no steroidal anti-inflammatory drugs NSAIDs or corticosteroids,[10] or had any evidence in favor of chronic heart failure according to New York Heart Association class III or class IV examination and history taking.[11] On the day of angiography, while the patients had been fasting for at least 10 hours, a 20-cc blood sample was taken from each patient and was kept at room temperature for at least 1 hour. The serum was separated by centrifugation and was kept at a temperature of -70°C. The samples were sent to the laboratory of Cellular and Molecular Research Center (Iran University of Medical Sciences, Tehran, Iran). Serum levels of VCAM and ICAM were measured in nanograms per milliliter using enzyme-linked immunosorbent assay (ELISA Reader, Pharmacia, U.S.). Patients with hypertension, hyperlipidemia, and diabetes were identified based on the records or measurements. Diabetes was considered as the state of having a fasting blood sugar level above 126 mg/dl or consuming glucose-lowering drugs.[12] Hyperlipidemia was defined as total cholesterol, triglyceride and low-density lipoprotein cholesterol (LDL-C) levels more than 200, 150, and100 mg/dl, respectively. Abnormal high-density lipoprotein cholesterol (HDL-C) levels were also defined as levels less than 50 mg/dl in women and less than 40 mg/dl in men.[13] Coronary angiography was performed using standard Judkins method via the femoral approach. Angiographic films were read by two cardiologists. If there were no matches, they were examined by the third cardiologist. Patients with normal coronary angiography were excluded from the study. In order to measure the severity and extent of coronary vessels 0-3 points were considered for the number of involved major coronary arteries, i.e. while 0 represented no involved major artery, a score was added for each involved major coronary artery. Two points were added if the left main coronary artery was involved. Therefore, maximum score for each individual in this group was 3. In addition, segments of the involved coronary artery in which stenosis existed were also scored, i.e. 3 for proximal segment, 2 for medial segment, and 1 for distal segment. Each patient could thus score 0-9. Finally, atherosclerotic stenosis was rated as less than 50% (1 point), 50-75% (2 points), and more than 75% (3 points). The overall score for each patient ranged from 0 to 9. Therefore, considering all 3 categories of scoring, total score of each patient could vary between 0 and 21.[14-15]

The obtained data was analyzed by student-t and regression analysis in SPSS (SPSS Inc., Chicago, IL). The characteristics of the studied subjects were presented as mean ± standard deviation (SD) for quantitative factors and number (percentage) for qualitative factors. Spearman's and Pearson's analysis of single-variable correlation coefficients were used to determine the correlations between angiographic scores and other variables (such as VCAM and ICAM). Finally, multiple linear regression analysis was performed to identify the variables determining the angioplasty score (dependent variable) and the effect of each factor in the prediction.

Results

Among the 82 studied patients, 72% were male. Mean age of participants was 58.4 ± 10.1 years. Hypertension, hyperlipidemia, and diabetes were observed in 64.6%, 96.3%, and 34.1% of the subjects. Mean serum levels of ICAM and VCAM were 183.9 ± 78 and 150.3 ± 136 ng/dl, respectively. Mean CAD score was 15.0 ± 4.56 (Table 1).

As table 3 shows, the correlation coefficient tests did not show significant correlations between serum levels of ICAM and VCAM and the intensity and extent of CAD. The variables of hypertension, diabetes, and hyperlipidemia were entered into multiple linear regression models to control their possible confounding effects on the conflict score and serum levels of ICAM and VCAM (Table 3). Even after controlling for potential confounding effects of these

factors, no significant linear relationship was observed between the involvement score and serum levels of ICAM and VCAM (P > 0.05).

Table 1. Basic characteristics of the study population

Characteristics	Values
Age (years)	58.4 ± 10.1
Male	59 (72%)
Hypertension (mm Hg)	53 (64.6%)
Systolic blood pressure (mm Hg)	142 ± 25.9
Diastolic blood pressure (mm Hg)	83 ± 13.3
Hyperlipidemia	79 (96.3%)
Cholesterol (mg/dl)	177 ± 40.5
Low-density lipoprotein cholesterol (mg/dl)	108.9 ± 32.6
High- density lipoprotein cholesterol (mg/dl)	36.2 ± 12.9
Triglyceride (mg/dl)	167 ± 101.7
Diabetes	28 (34.1%)
Fasting blood sugar (mg/dl)	115.9 ± 50.48
Intracellular adhesion molecules	183.9 ± 78.0
Vascular adhesion molecules	150.3 ± 136.6
Angiographic score	15.0 ± 4.56

Values are expressed as mean ± SD or number (%).

Table 2. Correlation coefficients between the angiographic scores and vascular adhesion molecules (VCAM) and intracellular adhesion molecules (ICAM)

		ICAM	VCAM
Coronary involvement score	r*	-0.019	-0.058
	P	0.86	0.6
	r**	0.045	-0.116
	P	0.069	0.3

*Pearson's correlation coefficient
**Spearman's correlation coefficient

Table 3. Regression analysis of coronary involvement score and vascular adhesion molecules (VCAM) and intracellular adhesion molecules (ICAM)

Model	Standardized coefficients Beta	t	P
ICAM	0.038	0.310	0.758
VCAM	-0.001	-0.011	0.992
Age	0.030	0.228	0.821
Gender	-0.117	-0.846	0.400
Diabetes	-0.062	-0.490	0.626
Hypertension	0.102	0.775	0.453
Hyperlipidemia	0.002	0.017	0.987

Discussion

Different studies have reported different results in relation to levels of ICAM and VCAM in patients with CAD. In this study, there was no significant correlation between serum levels of solubleVCAM-1 and ICAM-1 and the severity and extent of coronary artery involvements in patients with stable angina. Ikata et al. found ICAM-1C as a marker of coronary atherosclerosis and progression to coronary disease while VCAM-1 was not significantly different between patients and controls.[16] Oishi et al. evaluated 81 subjects (69 with CAD and 12 in the control group) and concluded that ICAM was associated with severity of coronary atherosclerosis. However, VCAM levels were not different between patients and controls and had no relationship with the severity of CAD.[17] Another study showed higher levels of ICAM (but not VCAM) in patients with CAD compared to the control group.[18] A study on 81 patients with CAD reported soluble ICAM-1 levels to be higher than the control group (n = 75). Therefore, ICAM was solely introduced as an independent factor representing CAD.[7] In the four mentioned case-control studies, there was a relationship between ICAM and CAD. The difference between these studies and our study was the method of performing the study, i.e. we did not include a control group and the relationship was studied between the risk factors and the severity of stenosis. In other studies, different results were obtained. For instance, Semaan et al. suggested higher levels of soluble VCAM (but not ICAM) in 40 patients with CAD compared to the controls (patients with normal coronary angiography and healthy volunteers).[19] In a study in Germany, among binding molecules, only VCAM was related with the extent of atherosclerosis in patients with peripheral artery disease.[8] In our study however, VCAM was correlated with the existence and extent of CAD in patients with stable angina. This different between our findings and those of the two mentioned studies might have been caused by the bigger sample size and having a control group.

On the other hand, several studies reported findings similar to ours. For instance, a Japanese survey evaluated the relation between serum binding molecules and the extent of coronary by comparing 52 CAD patients with 40 individuals with normal coronary angiography. It suggested an insignificant relationship between soluble VCAM and ICAM and CAD. However, there was no relationship between the two molecules and extent of coronary atherosclerosis.[20] In another study, ICAM levels in 74 patients with proven CAD were similar to 27 healthy subjects.[21] Likewise, Nasuno et al. could not establish a relationship between the severity of coronary atherosclerosis and plasma levels of ICAM in patients with stable CAD. However, a weak but significant relationship was found between levels of binding molecules and the number of existing coronary risk factors.[11] It is noteworthy that in the two studies mentioned earlier, the VCAM levels were not

checked. In another study, the relation between levels of binding molecules and the incidence and severity of coronary disease was assessed. It reported the concentration of binding molecules in patients with CAD not to significantly differ from the control group. In addition, none of the molecules had any effects on the severity of CAD.[6] Based on previous cohort studies and meta-analyses published in England about the predictive value of binding molecules in CAD, the values of soluble binding molecules were related with each other and also with other inflammatory markers and some major coronary risk factors. However, it was indicated that measuring the levels of binding molecules would not provide additional predictive information than the previously documented risk factors.

Overall, this study found that binding molecules had no significant correlation with the severity of coronary involvement. Consequently, performing such expensive tests in patients suspected to CAD would be unnecessary. However, designing cohort studies with larger sample size can be helpful to further explore this relationship.

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Conflict of Interests

Authors have no conflict of interests.

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