Serum Adhesion Molecule Levels in Acute Coronary Syndrome Among Indonesian Patients

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ABSTRACT

Aim: to observe whether the VCAM and ICAM level in ACS patients were higher than those in coronary heart disease (CHD) patients. In addition, we would like to observe the cut off point of VCAM and ICAM level in ACS patients.

Methods: in observational study, as many as 146 subjects were analyzed, consisting of 84 ACS patients, and 62 coronary heart disease (CHD) patients. This study were conducted at Dr. Cipto Mangunkusumo General Hospital (RSUPN-CM), Persahabatan Hospital, MMC Hospital and Medistra Hospital, Jakarta. The study was carried out from May 2005 to May 2006.

Results: the VCAM level was higher in the group of ACS patients (mean 981.06 ng/mL, SD 319.28, CI 95%: 911.77-1050.35) than in that in the group of CHD (mean 915.23 ng/mL, SD 283.05, CI 95%: 843.35-987.11), but the difference is not significant. At cut-off point of VCAM level ≥ 920.8 ng/mL, the highest sensitivity (57.14%) and highest specificity (67.74%) were found with ROC of 0.58.

The ICAM level was higher in the group of ACS patients (mean 268.08 ng/mL, SD 72.75, CI 95%: 252.29-283.87) than that in the group of CHD (mean 245.18 ng/mL, SD 87.37, CI 95%: 222.99-267.37), but the difference is not significant. At cut-off point of ICAM level ≥ 248.6 ng/mL, the highest sensitivity (54.76%) and highest specificity (66.13%) were found with ROC of 0.62.

Conclusion: it could be concluded that VCAM and ICAM level in ACS were higher than in CHD, but the difference is not significant. The VCAM and ICAM level are not the best parameter to differentiate between acute (ACS) and stable (CHD) condition.

Key words: adhesion molecules, acute coronary syndrome.

INTRODUCTION

Leukocyte adhesion to the endothelial cell in the circulation and transendothelial migration is an important step in the initiation of atherosclerosis.1 This process is partly mediated through cellular adhesion molecule (CAMs) to the endothelial cell membrane as a response to several inflammatory cytokines, such as interleukin-1, tumor necrosis factor, and interferon.2 Pathological study shows an increase of CAM expression in atherosclerotic plaque components3 and clinical data show the role of adhesion molecule in acute atherothrombosis syndrome.4,5

There are currently no studies of adhesion molecule levels in acute coronary syndrome (ACS) patients among Indonesians. This study is conducted as part of a serial studies on inflammatory response in acute coronary syndrome patients. The objective of this study is to determine the cut-off point of VCAM and ICAM value in ACS patients in Indonesian population.

METHODS

We used comparative observational cross-sectional study design. Comparison was done between ACS patients with coronary heart disease (CHD) patients. Measurement of VCAM and ICAM serum level could demonstrate both endothelial dysfunction and indirect inflammatory response in acute coronary syndrome (ACS).

Data of ACS patients was taken from inpatient data from ICCU in Continuing Medical Health, Faculty of Medicine University of Indonesia, Persahabatan Hospital, MMC Hospital, and Medistra Hospital. Patients are matched for age and sex. Data of CHD was collected from Outpatient Clinics at Department of Internal Medicine CMH/FMUI and Integrated Cardiac Service Outpatient Clinic CMH. The study was carried out between May 2005 and May 2006.

Patients are included in the study if they have ACS that occurs less than 72 hours, and CHD patients who visit the Cardiology Outpatient Clinic Department of
Internal Medicine CMH/FMUI and Integrated Cardiac Service Outpatient Clinic CMH.

Patients who currently in acute or chronic infection, having diseases associated with inflammatory response such as autoimmune disease, connective tissue disease, neoplasm, trauma or surgery in the previous month, receiving corticosteroid, NSAID, or immunosuppressive therapy, receiving thiazolidindione therapy, having chronic kidney or liver disease are excluded from the study. Statin use is permitted after collection of blood sample in ACS group only.

A written informed consent was obtained from each patient after formal explanation from the investigator/assistant investigator.

**Sample Size**

Sample size is determined with power (b) 0.84. The total subject’s recruited is 146 patients.

**Analyses of Inflammatory Response**

We analyzed the inflammatory response based on the mean VCAM and ICAM level from Mulvihill et al.³ Serum VCAM and ICAM was measured using enzyme immunoassay method, Quantikine® reagen from R&D System, Inc. 614 McKinley Place NE Minneapolis, MN 55413, USA. Normal VCAM value 349-991 ng/mL. Intraassay variability 4.3-5.9% and interassay variability 8.5-10.2%. Normal ICAM value 115-306 ng/mL. Intraassay variability 3.3-4.8% and interassay variability 6.0-10.1%.

In order to measure the ability of VCAM and ICAM serum level as a predictor of ACS, the sensitivity and specificity of this parameter towards ACS in various VCAM and ICAM serum levels were calculated.

**RESULTS**

Demographic analysis showed that there was no difference in ages among the two groups (ACS and CHD). The risk factors of dyslipidemia, hypertension and lipid profile in the two groups did not differ significantly. Waist circumference and BMI, systolic and diastolic blood pressures in the two groups did not also differ significantly.

**Cut-off Point of Serum VCAM level in ACS Group Compared to CHD Group**

In this study the VCAM serum level is higher in ACS patients (mean 981.06 ng/mL, SD 319.28, 95 % CI 911.77-1050.35) compared to CHD patients (mean 915.23 ng/mL, SD 283.05, 95 % CI 843.35-987.11).

Highest sensitivity and specificity was found using VCAM serum level ≥ 920.8 ng/mL as cut-off point. The sensitivity and specificity values for VCAM serum level 920.8 ng/mL above is illustrated in Figure 1.

**Figure 1.** ROC VCAM serum level in acute condition (ACS) compared with non-acute condition (CHD)

**Cut-off Point of serum ICAM level in ACS Group Compared to CHD Group**

In this study the ICAM serum level is higher in ACS patients (mean 268.08 ng/mL, SD 72.75, 95 % CI 252.29-283.87) compared to CHD patients (mean 245.18 ng/mL, SD 87.37, 95 % CI 222.99-267.37).
Highest sensitivity and specificity was found at ICAM serum level ≥ 248.6 ng/mL as cut-off point. The sensitivity and specificity values for ICAM serum level at 248.6 ng/mL above is illustrated as a receiver operating characteristic (ROC) curve 0.62 as seen in Figure 2.

Our study shows that the cut-off point of VCAM level ≥ 920.8 ng/mL can predict the incidence of ACS in our population, with 57.14 % sensitivity and 67.74% specificity. Based on the ROC curve, the VCAM does not seem to be an ideal measurement in differentiating between acute and stable condition (low sensitivity, specificity, and ROC).

**Serum ICAM Levels in ACS Group**

ICAM-1 is a protein from transmembrane immunoglobulin superfamily group in which its expression occurs due to activation of endothelial cell, leukocyte, fibroblast, vascular smooth muscle cell, cardiomyocyte, and other types of non-cardiac cells. Interleukin adhesion molecule-1 (ICAM-1) is expressed by the endothelial cell during activity and resting, and promotes neutrophil, monocyte, and lymphocyte adhesion.

In this study, the ACS group shows higher serum ICAM level compared to CHD group. Increased ICAM level in ACS group is a response to increase IL-6 as proinflammatory cytokine due to injury, which will stimulate ICAM expression. Mulvihill et al. studied 91 ACS patients (56 UAP patients and 35 Non-Q MI patients) and reported that the VCAM and ICAM level is significantly higher compared to the control group at admission, after 3 months, and after 6 months. After 6 months the serum ICAM and VCAM level tend to decrease.

In order to predict the incidence of ACS, we found the cut-off point of ICAM level ≥ 248.6 ng/mL, with 54.76 % sensitivity and 66.13 % specificity. Cut-off for ICAM level is illustrated in the receiver operating characteristic curve as seen in Figure 2. Based on the ROC curve, the ICAM does not seem to be an ideal measurement in differentiating between acute and stable condition.

**CONCLUSION**

The VCAM and ICAM levels in ACS are higher compared to CHD, but the difference is not significant. The VCAM and ICAM levels are not the best parameters to differentiate between acute (ACS) and a stable (CHD) condition.

**REFERENCES**


