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Original Article

Predictive value of CRP/albumin ratio for in-hospital atrial fibrillation development in ST segment elevation myocardial infarction

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Abstract

Aim: Atrial fibrillation(AF) development in ST elevation myocardial infarction (STEMI) patients is associated with increased cardiovascular mortality and morbidity. The CRP to Albumin ratio(CAR) is a new described parameter and it has been suggested that this parameter may also be correlated with cardiovascular diseases. In this study, we investigated the association between AF development and the CAR in STEMI patients undergoing percutaneous coronary intervention.

Material and Methods: This study was conducted in patients presenting to our department with a diagnosis of STEMI retrospectively and undergoing percutaneous coronary intervention. A total of 110 patients were included in the study. The patients were divided into two groups according to AF development and the predictors for AF development were investigated.

Results: The mean age of the patients was 62±5.1 years and 72% of them were males. While CAR, TIMI, CRP, albumin, neutrophil to lymphocyte to ratio, lesion localization, myocardial blush grade and syntax score were associated with the AF development in the univariate analysis, the CAR was determined to be an independent predictor of AF development in the multivariate regression analysis.

Conclusions: We have demonstrated that the CAR was an independent predictor for prediction of AF development and we think that this parameter may be useful in clinical practice.

Keywords: Atrial fibrillation; CRP to albumin ratio; myocardial infarction.

INTRODUCTION

Coronary artery disease (CAD) is an important cause of mortality and morbidity with an increasing frequency. Myocardial infarction is a life-threatening emergency condition occurring usually due to demand and supply mismatch or rupture of the plaque present in the coronary artery in consequence of the progression of coronary artery disease. ST elevation Myocardial Infarction (STEMI) has a high in-hospital mortality rate. While improvements occur in these patients after treatment, congestive heart failure, development of atrial fibrillation(AF) and recurrent myocardial ischemia are more common in them compared to healthy individuals (1-4).

And the occurrence of these conditions also leads to an additional increased risk of cardiovascular mortality. AF is a clinical condition which is an important cause of mortality and morbidity with an increasing incidence with increasing age and determined in 30% of patients developing ischemic stroke (5).

In STEMI patients, AF development can cause to deterioration of heart failure and may lead to myocardial ischemia during tachycardia. As a result, AF development in STEMI patients is associated with an increased mortality (6). Therefore, to detect early the STEMI patients that can develop AF is important for prevent adverse events and risk reduction.

There is a link between inflammation and AF. Inflammation has a key role in AF development and inflammation markers, such as interleukin 6, D-Dimer and the natriuretic peptides can predict cardiovascular events in patients with AF. It has been demonstrated in the previous studies that the CRP/Albumin ratio (CRP) was a sensitive marker of inflammation (7-9). It has been reported that the CAR

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could be more tightly associated with adverse event and mortality compared to CRP and Albumin value alone. Furthermore, it has been suggested in a few studies that this parameter can also be associated with cardiovascular diseases and a good predictor (8). However, there is a limited number of studies showing the association between the CAR and AF development in STEMI patients. In this study, we investigated the association between AF development and the CAR in STEMI patients and in the control group constituted with propensity score matching (PSM) analysis.

MATERIAL and METHODS

The study was approved retrospectively by the ethics committee for retrospective observational studies and performed in suitable STEMI patients according to inclusion and exclusion criteria. Seventy-two patients developing AF and 1100 patients not developing AF were included in the study. After PSM analysis, 110 patients (55 AF+, 55 control) were included in the final analysis (study flow diagram: figure 1). Demographic characteristics and biochemical parameters of the patients before the procedure and adverse events and coronary lesion characteristics after the procedure were recorded. The patients whose file data were not achieved, have malignancy the patients with previous CABG surgery were excluded from the study. Similarly, the patients with active infection, the patients with an autoimmune disease receiving active treatment and the patients receiving a blood transfusion during hospitalization since it could affect the CRP or Albumin level were excluded from the study.

Definitions

Diabetes mellitus was defined as the use of antidiabetic medication due to elevated blood glucose levels, measurement of a fasting blood glucose level of > 126 mg/dL or measurement of a postprandial blood glucose level of > 200 mg/dL or a HbA1c level of > 6.5. Hypertension was defined to have a blood pressure value of > 140/90 mmHg after two consecutive measurements or previous use of antihypertensive medication. CAD was defined as the determination of a lesion in the coronary artery previously with imaging methods or the patients undergoing percutaneous coronary intervention(PCI) or coronary artery bypass graft (CABG) surgery. Current smokers and/or those who smoked at least 1 packs/ year until 1 month ago were described as patients with a history of smoking.

AF diagnosis methods

All patients were followed up to 72 hours with continuous electrocardiogram monitor in coronary care unit. The AF developed patients were detected and included to study.

Angiography

Coronary angiography was performed in all of the patients either via a femoral approach or a radial approach depending on interventionist preference. After taking standard angiographic images, PCI, CABG surgery was performed or medical treatment was administered in all of the patients based on patient and interventionist preference. Thereafter the patients were admitted to coronary intensive care unit and they were discharged after approximately 72 hours.

Blood sampling

A blood sample was obtained via a peripheral venous catheter into EDTA tubes before coronary angiography. Then Hematological analyzes were studied with Sysmex XN 9000, an automated blood cell counter; biochemical parameters with Beckman Coulter AU 5800 device. After calculation of CRP and Albumin values, the CAR value was calculated by dividing the CRP value by the Albumin value. CRP measurement was made by wide range CRP. Albumin measurement was provided by BCG (bromocresol green) method.

Propensity score

Two groups were generated according to AF status (group 1: AF (-), group 2: AF (+)). As the baseline clinical biochemical and angiographical characteristics of the patients in the Group-1 and Goup-2 were different, PSM analysis (using logistic regression model) were performed to decrease potential bias. After propensity score (PS) calculation of each patient, a 1:1 match analysis was performed using the nearest-neighbor matching with a caliper distance of 0.001 without replacement. The model fit was examined with the Hosmer–Lemeshow's goodness-of- fit test and the C-statistic test. The post matching balance was examined by mean standardized difference, in which less than 10% for a given covariate suggested the adequate balance.

Statistical Analysis

The variables distributed normally were expressed as mean± standard deviation and the variables not distributed normally were expressed as median. Categorical variables were expressed as a percentage. While the Mann Whitney U test or Student T test was used for comparison of numeric variables, the Chi Square test was used for comparison of categorical variables. The variables determined to be significant in the univariate analysis were subjected to regression analysis for determination of independent predictor of AF development. The parameters with high autocorrelation were not included in the regression analysis. ROC curve analysis was performed for prediction and clinical decision of AF development. A p value of <0.05 was considered significant. Data were evaluated by using SPSS Statistics 23 package program(SPSS Inc, Chicago, IL, USA).

Results

A total of 110 patients were included in the study using PSM analysis with 1:1 matching. Study flow diagram is shown Figure-1. The mean age of the patients was 62±5.1 years and 72% of them were males. Baseline demographic and biochemical characteristics of the patients are shown in Table 1.In AF + group; CAR, SS, TIMI risk score, neutrophil lymphocyte ratio (NLR), CRP values

were significantly higher in univariate analysis(p values respectively; <0.001, 0.004, 0.007, 0.043, < 0.001) and had more proximal lesions (p: 0.036). In the AF – group albumin was significantly higher (p:0.018).

While the CAR, TIMI, CRP, albumin, neutrophil to lymphocyte to ratio, lesion localization, myocardial blush grade and syntax score were associated with the AF development in the univariate analysis, the CAR was determined to be independent predictor of the AF development in the regression analysis (Table 2). Distribution of the CAR value according to groups is shown in Figure 2. ROC curve analysis was performed for the predictive value of AF development and its clinical use. In ROC curve analysis, the CAR was predicting the cut-off value 1.9 for the development of restenosis with a sensitivity of 84 % and a specificity of 75 % (Figure 3).

Table 1. Baseline demographic, clinical and angiographical characteristics of the study populations

Variables	Group-1 AF(-)	Group-2 AF(+)	P value
CAR	**1.04(0.6-1.38)**	**3.7(1.7-4.9)**	**<0.001**
SS	13.84.4	16.14.5	0.004
Gender(Male %)	82.2	85.6	0.28
Age (years)	569.1	5810	0.48
DM (%)	31.4	30.3	0.74
HT (%)	**35.6**	**38.9**	**0.79**
Smoking (%)	49.6	52.1	0.93
Dyslipidemia (%)	42.7	44.7	0.79
Aspirin (%)	5.2	7.5	0.30
TIMI Risk Score	1(1-3)	2(1-4)	0.007
WBC (*103)	9.23.6	10.1(9.6-14)	0.44
Neutrophils (*103)	7.5(6.7-11.5)	9.1(7-11.2)	0.45
Lymphocytes (*103)	1.5(1.3-2.46)	1.6(1.2-2.4)	0.53
NLR	5(3.7-7.6)	5.6(4.1-8)	0.043
HGB (*103)	14.81.5	14.71.7	0.61
Platelets (*103)	242(209-291)	252(217-298)	0.31
GFR(ml/sec/1.73m2)	0.90.26	0.920.32	0.78
Glucose (mg/dl)	118(105-180)	123(110-181)	0.87
Uric acid (mg/dl)	4.50.2	5.11.1	0.49
Albumin (mg/dl)	3.90.41	3.70.38	0.018
CK (U/L)	261(147-407)	270(160-506)	0.94
CK-MB (U/L)	34(21-46)	45(29-55)	0.027
Troponin T (ng/dl)	1.5(0.31-3.1)	2.1(0.6-4.1)	0.87
LDL(mg/dl)	111(82-129)	110(87-140)	0.33
Triglyceride (mg/dl)	118(79-168)	121(81-161)	0.53
CRP (mg/l)	4.8(3.1-6.4)	12(6.3-19)	<0.001
EF (%)	487.2	467.6	0.81
Left atrium diameter, mm	313.4	334.1	0.59
IRA (%)			
LMCA	0.4	0.4	
LAD	49.8	50.2	
CX	10.7	14.2	0.31
RCA	38.7	34.4	
Others	0.4	0.8	
Localization (%)			
Proximal	49.8	57.3	
Mid region	45.3	41.1	0.036
Distal region	5.5	4.7	
Stent Type (DES, (%)	42	30	0.004
MBG	3(2-3)	2(1-3)	0.045
CTFC	20(15-25)	22(17-27)	0.51

Abbreviations: CAR; CRP to Albumin Ratio, SS; syntax score, MD; diabetes mellitus, HT; hypertension, COPD; chronic obstructive pulmonary disease, WBC; white blood count, HGB; hemoglobulin, NLR; neutrophil lymphocyte ratio,GFR; glomerular filtration rate, CK; creatine kinase, LDL; low density lipoprotein, CRP; C reactive protein, EF; ejection fraction, IRA; infarct related artery, CTFC; corrected TIMI frame count, MBG; myocardial blush grade.

Table 2 Regression analysis performed for predictors of the development of atrial fibrillation

Variables	Univariate OR, 95 CI %	P value	Multivariate OR, 95 CI %	P value
CAR	**1.17(1.14-1.21)**	**<0.001**	**1.2(1.01-1.6)**	**<0.001**
SS	1.3(1.06-1.7)	0.004	0.98(0.89-1.08)	0.756
TIMI Risk Score	1.12(1.05-1.18)	0.007	0.85(0.68-1.06)	0.161
MBG	1.03(1.018-1.06)	0.027	1.07(0.60--1.89)	0.808
NLR	0.89(0.84-0.94)	0.043	0.91(0.81-1.02)	0.106
Stent Type	**0.91(0.85-0.92)**	**0.004**	**0.79(0.30-2.08)**	**0.639**

Abbreviations: CAR; CRP to Albumin Ratio, HT; hypertension, HGB; hemoglobin, CK; creatine kinase-myocardial, NLR; neutrophil lymphocyte ratio.

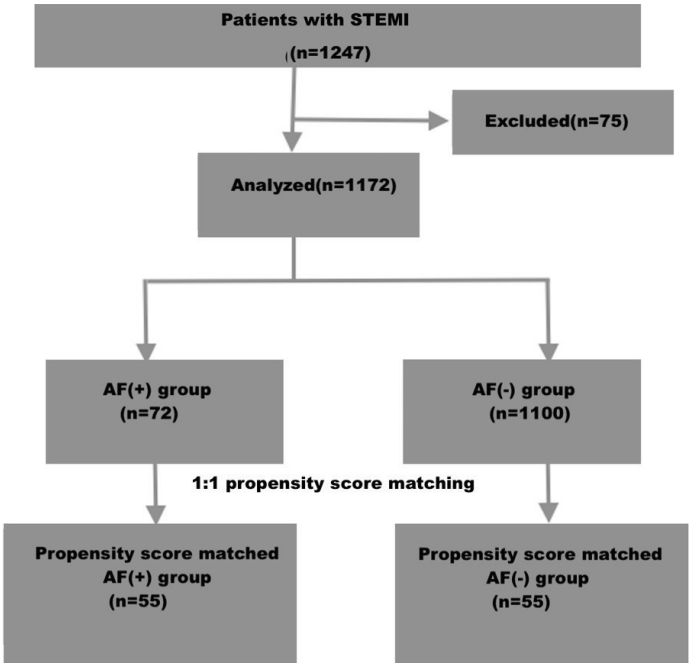

Figure 1. Study flow diagram

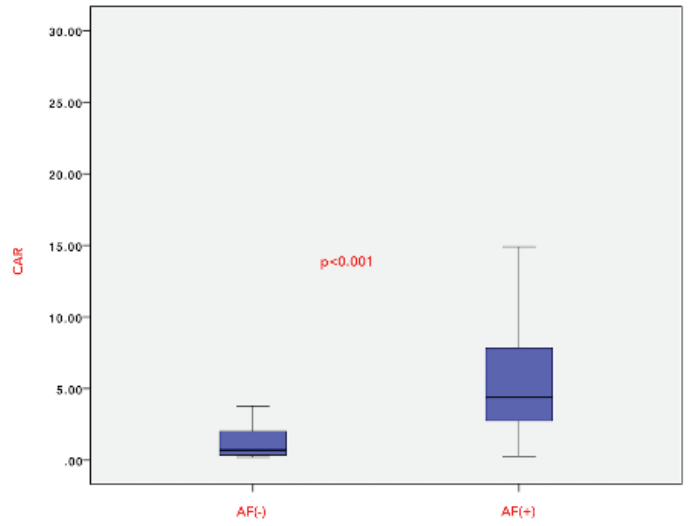

Figure 2. CAR values according to AF status

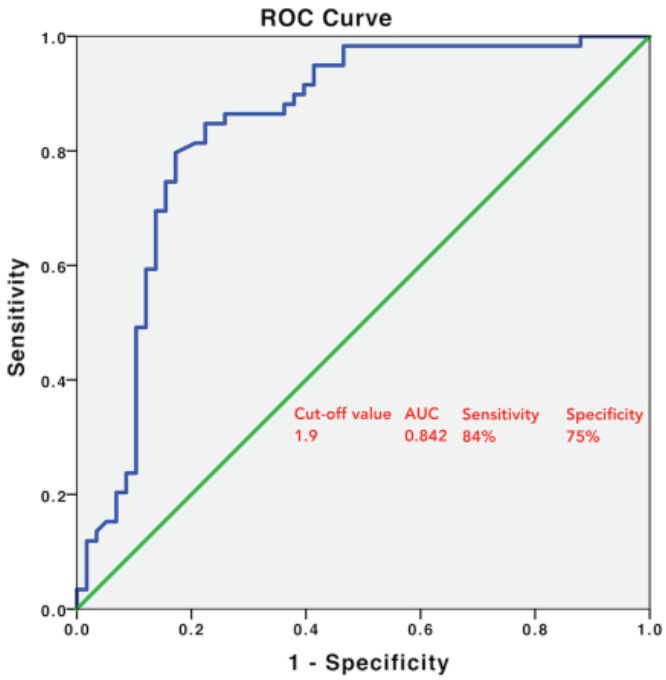

Figure 3. ROC curve analysis performed for CAR values in the prediction of the development of atrial fibrillation

DISCUSSION

In this study, we demonstrated that the CAR was an important parameter for prediction of AF development. To the best of our knowledge, this is the first study demonstrating this relationship.

STEMI is among the leading one of cardiovascular diseases with high mortality and morbidity. Early revascularization is of critical importance in these patients and a reduction has occurred in both disease mortality and incidence of the adverse event during long-term follow-ups with revascularization methods. However, despite improved revascularization options, mortality and adverse events are observed higher in STEMI compared to the other cardiovascular diseases (4,8,10,11). Early determination and aggressive treatment of the patients developing adverse event is a desired and recommended approach in

these patients and various risk scores were developed for the determination of these patients (4,8,10-13). Alvarez et al. determined an increased long-term mortality in patients with STEMI and high SS-II scores (14). In another study, it was shown that the incidence of the one-year adverse event was higher in patients with higher GRACE risk score (15).

CRP is a biomarker considered to be an acute-phase reactant and whose plasma levels rise during inflammation. Plasma concentration of CRP also increases in many inflammatory conditions and this increase is usually considered to be a marker of poor prognosis (16). It has been thought that it could have similar effects also in coronary artery disease and increased levels of CRP were associated with an adverse event in Jupiter study (17). Similarly, also plasma Albumin level changes in the inflammatory conditions as infections in the first place, but this change occurs negatively and it is considered to be a negative acute-phase reactant. Because of this characteristic, plasma Albumin level is used as a prognostic factor in many diseases as liver diseases in the first place. Considering that the CAR is clinically more important rather than dynamic changes of both of parameters in plasma separately during disease, CAR parameter has been introduced in clinical practice. Albumin is a negative acute phase reactant, as opposed to CRP. Therefore, CAR values give us a good combination of acute phase reactants (18,19).

While it has been suggested in a few small-scale studies that CAR could be a more sensitive inflammatory parameter than both of two parameters, it has been especially reported that it could have better clinical predictive values. Xi et al. showed in non-small cell lung cancer patients that CAR might be a better predictor of prognosis compared with other inflammatory markers, but Liu et al. demonstrated that CAR might be a marker of poor prognosis among ovarian cancer patients (20,21). There are very few studies investigating the relationship between the CRP/Alb ratio and coronary artery disease. A significant relationship was determined between CAR and SS in a study investigating the extensiveness of coronary artery disease in acute coronary syndrome patients. Moreover, in the study of Cınar et al. they found that CAR was an independent predictor of all-cause mortality and CAR can be useful as a prognostic tool for predicting a poor prognosis in STEMI patients. They investigated too many in-hospital and long term events, however they did not evaluate the AF development (22). Similarly, this relationship was also shown in patients with stable coronary artery disease (8). Finally, in a study investigating predictors of restenosis development in STEMI patients during long-term follow-up, a significant relationship was determined between elevated CAR and restenosis.

AF development in STEMI patients was associated with increased adverse events. These events are conditions which are likely to develop due to both increased stroke complications and embolic complications and increased coronary ischemia secondary to tachycardia. Therefore, determination and early treatment of these patients is of critical importance for the prevention of development of complications and reduction of the incidence of adverse events that can develop during long-term. It was shown in previous studies that increased myocardial inflammatory condition could be effective in AF development in STEMI patients (5). In our study, marked elevation of CAR in the group developing AF suggested that inflammation could be an important inducer during the process of AF development. Because an increased inflammatory response is observed from the beginning in STEMI patients and the extent of this response is closely associated with the extent of the cardiac injury and wound healing process. The increased myocardial injury may provide an arrhythmogenic effect in AF development both as a substrate and by means of cytokines and hormonal pathways (4,23). In our study, this increase in the incidence of AF development in patients with higher CAR is likely to be associated with the inflammatory condition and this finding is consistent with the literature. In the light of this information, we think that CAR can be used as a good predictor of the development of adverse events in cardiovascular diseases. Additionally, in our study, equating also the patient and control groups with PSM analysis is one of the factors strengthening our hand and increasing the power of our study. In conclusion, the CAR is a simple and easily available parameter. Besides that it does not require detailed calculation as another risk scores, its sensitivity is high and it may give useful information to the clinician in the early period in addition to traditional parameters.

Limitations: Our study has several limitations. Firstly, the study was designed retrospective. Secondly, sample size is relatively small. However, we used PSM analysis to strengthen our study power. Finally, we have not data about the time onset of symptoms and the CAR value.

CONCLUSION

Since the CAR has a better predictive value in prediction of adverse events like AF in STEMI patients, addition of CAR (which is a sensitive marker of inflammation) to the developed risk scores may give useful information to clinician. Moreover, the patients might be enabled to have a maximum benefit and a reduction of their risks by determining them in the early period and by individualizing their treatment strategies.

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