

RELATIONSHIP BETWEEN C-REACTIVE PROTEIN TO ALBUMIN RATIO AND THE EXTENT OF CORONARY ARTERY DISEASE SEVERITY IN PATIENTS WITH NON ST ELEVATED MYOCARDIAL INFARCTION

By

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ABSTRACT

Background: Coronary artery diseases (CAD) are as atherosclerotic heart disease, atherosclerotic cardiovascular diseases, coronary heart diseases (CHD), or ischemic heart disease (IHD). CAD is the largest contributor of cardiovascular diseases (CVDs), and mortality rate is due in prevalence to atherosclerosis, a chronic inflammatory condition of the arterial wall.

Objective: To assess the relationship between C reactive protein /albumin ratio and the extent of coronary coronary disease assessed by the syntax score I in patients with non ST elevated myocardial infarction.

Patients and methods: This was a prospective cohort study carried out at Cardiology Department of Al-Azhar University, and Al-Agouza Cardiology Department, and enrolled 100 patients admitted with non ST-elevation myocardial infarction and underwent coronary intervention during the period from January 2019 to February 2020.

Results: There was a non-statistically significant relation regarding gender and age. There was statistically significant relation regarding diabetes mellitus (DM) and dyslipidemia (cholesterol and LDL). There was also a statistically significant relation regarding syntax score, CRP and also CRP/Alb ratio.

Conclusion: There was a correlation between CRP/ Albumin ratio and the severity of coronary artery disease assessed by syntax score I.

Keywords: C-reactive protein, Albumin Ratio, Coronary Artery Disease, Non ST elevated myocardial infarction

INTRODUCTION

Non-ST-segment elevation myocardial infarction (NSTEMI) remains the leading causes of death in individuals with coronary artery disease (*Yeh et al., 2010*).

Coronary artery disease severity is closely related to mortality, and the Synergy between Percutaneous Coronary Intervention with TAXus and cardiac surgery (SYNTAX) score (SS), the most

commonly used scoring system for determining CAD severity (*Farooq et al., 2013*).

The developed SS II, designed by adding clinical variables identified by applying a Cox proportional hazards model to the results of the SYNTAX trial, provides greater prognostic accuracy in clinical settings for patients with CAD and acute myocardial infarction (*Magro et al., 2011*).

Identifying the factors associated with intermediate–high SS and high SS II may improve the prognosis of patients with NSTEMI by enabling early referral for timely coronary angiography and revascularization, as well as close monitoring during hospital stay and after discharge. Inflammation plays a major role in the progression and destabilization of atherosclerotic plaque (*Karadeniz et al., 2015*).

The relationship between CRP, SS, and CAD severity were determined in previous studies. Inflammation plays an important role in all stages of atherosclerosis. They are markers of inflammation that are frequently used in clinical practice (*Çağdaş et al., 2017*).

Decreased albumin level may be associated with increased risk of morbidity and mortality in a range of cardiovascular diseases. *Kurtul and colleagues (2016)* demonstrated that decreased albumin level is an independent predictor of high SS and in-hospital mortality in patients with acute coronary syndrome.

The inflammatory status can be measured using acute phase reactants (APRs). The commonly used parameters,

C-reactive protein (CRP) and albumin, known as positive and negative APRs, respectively, are associated with the presence of CAD, CAD severity (*Taniguchi et al., 2010*).

CRP to albumin ratio (CAR) is believed to be more accurate indicator of the inflammatory status than CRP or albumin alone. Furthermore, high CAR was associated with worse prognosis in patients with critical illness and malignancy (*Fairclough et al., 2010*).

The aim of the present study was to evaluate the possible relationship of coronary artery disease severity (identified using the syntax score I) and C-reactive protein to albumin ratio.

PATIENTS AND METHODS

This prospective cohort study was carried out at cardiology department of Al AGouza hospital and Al-Hussein Hospital at the period from January 2019 to February 2020.

This study included one hundred (100) patients who admitted to Al- Agouza Hospital and Al-Hussein hospital with clinical features of non ST- elevation myocardial infarction and undergone coronary intervention.

Inclusion criteria: All patients with non-ST segment elevation myocardial infarction.

Exclusion criteria: Patients with a history of previous coronary artery disease treated with percutaneous coronary intervention or coronary artery bypass grafting, e.g. malignancy, active infection, connective tissue disorder, patient with Chronic kidney disease, and patient with hepatic disease.

All patients subjected to the following:

A. Full history taking: with special emphasis on:

1. Demographic criteria including Age, sex.
2. A detailed medical and cardiac history including cardiovascular risk factors: History of smoking, hypertension diagnosed and /or treated with medications, diet and/or exercise, diabetes Mellitus, dyslipidemia, and family history of ischemic heart disease or sudden cardiac death.

B. General and local examination:

Pulse, blood pressure, neck veins, edema of lower limbs, chest and abdominal examination, and cardiac examination including inspection, palpation and auscultation.

C. Laboratory investigations:

1. Serum creatinine and blood urea: detected by Cobas 6000 C501 electro chemiluminescent assay before and after (from 12 to 48 hours) coronary intervention.
2. Complete blood cell count using Sysmex S. F3000 automated analyzer.
3. Random blood sugar level.
4. Lipid profile: This included total cholesterol, low-density lipoproteins, high-density lipoproteins, and triglycerides using Cobas Integra instrument - spectrophotometry method serum albumin.
5. Reactive protein (CRP ELISA Kit 5/11 Catalog Number: CRP31- K01, USA).

6. C-reactive protein to albumin ratio: The albumin and CRP levels will be measured. The CAR will be calculated as the ratio of CRP to the albumin level.

D. Resting surface 12 ECG leads:

Surface ECG was done on admission at a paper speed of 25mm/s and amplification of 10 mm/mv. Depicted ECG changes were either, ST depression > 0.5 mm in 2 contiguous leads, T wave inversion or normal ECG (no ST deviation).

E. Transthoracic Echo Doppler study:

Detailed transthoracic echocardiography was performed to all patients using GE Vivid 9. The conventional Echo was performed by experienced echo cardiographer in accordance with the recommendations of the American Society of Echocardiography (ASE) and European Association of Echocardiography (EAE). The mean of three measurements was used in the analysis. The echocardiogram was performed with the patient breathing quietly and lying in the left lateral position.

- F. Coronary angiography:** Approach either femoral or radial if available, and assessment if lesion in 2 orthogonal views.

G. Calculating syntax score.

Statistical analysis:

Statistical presentation and analysis of the present study was conducted, using the mean, standard deviation, student t- test, Linear Correlation Coefficient and Analysis of variance [ANOVA] tests by SPSS V20. Quantitive data are presented

as mean, standard deviation and range and were compared by Mann-Whitney test. Quantitative data are presented as

number and frequency. $P < 0.05$ was considered significant.

RESULTS

The mean age of the study group was 54.520 ± 7.889 years and 37 patients (37%) were females. In our study population, 28 patients (28%) were suffering from diabetes mellitus (all type II), 39 (39%) had arterial hypertension, and 64 (64%)

were smokers. The mean body mass index (BMI) of the study group was $28.010 \pm 2.545 \text{ kg/m}^2$. In our study, there were 28% diabetic patients, 39% hypertensive patients, 64% smoking and 62% dyslipidemia patient (**Table 1**).

Table (1): Basic demographic data and risk factors

Demographic Data		N	%
Sex	Male	63	63.00
	Female	37	37.00
Age	Range	40-68	
	Mean \pm SD	54.520 ± 7.889	
Height	Range	167-183	
	Mean \pm SD	175.790 ± 4.812	
Weight	Range	70-97	
	Mean \pm SD	86.240 ± 8.115	
BMI	Range	20-33	
	Mean \pm SD	28.010 ± 2.545	
Risk Factors			
HTN	Yes	39	39.00
	No	61	61.00
Dyslipidemia	Yes	62	62.00
	No	38	38.00
DM	Yes	28	28.00
	No	72	72.00
Smoking	Yes	64	64.00
	No	36	36.00

ECG criteria on examination

Sixty four patients (64%) had ECG changes in the form of 14 patients ST

segment depression, 50 patients inverted T wave (**Figure 1**).

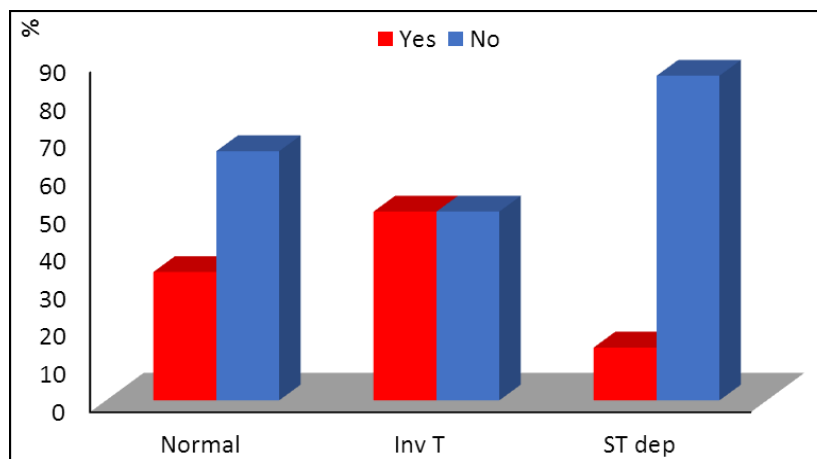


Figure (1): ECG criteria on examination.

According to SYNTAX I score of severity of coronary artery disease, there were 40 (40) single vessel disease. There were 9 (9%) patients two vessel disease. There were 44 (44%) patients three vessel disease. There were 7 (7%) patients with four vessel disease.

Echocardiographic data on examination: Mean left ventricular

ejection fraction (EF) was $53.090 \pm 15.792\%$. According to LVEF, patients with LVEF ($>50\%$) was noticed in 61 patients 61%, with midrange LVEF (40-49%) noticed in 10 patients (10%), and patients with heart failure with reduced LVEF ($<40\%$) noticed in 29 patients (29%). No RSWMA was observed in 76 patients (76%) (Table 2).

Table (2): Coronary angiographic data and echocardiography data regarding RWMA, EF

Affected vessel		N
LM	Yes	17
	No	83
LAD	Yes	92
	No	8
LCX	Yes	49
	No	51
RCA	Yes	60
	No	40
Number of diseased vessels	One vessels	40
	Two vessels	9
	Three vessels	44
	Four vessels	7
Syntax score 1	Range	6-49
	Mean \pm SD	23.200 ± 13.266
Echocardiography		N
RWMA	Yes	24
	No	76
EF %	Range	25-74
	Mean \pm SD	53.090 ± 15.792

RWMA: regional wall motion abnormality, LVEF: left ventricular ejection fraction.

There were no significant relations between CAR ratio and hypertension (P value 0.157), smoking (p-value 0.764), but there were significant relations between CAR and DM (P value .002), Dyslipidemia (p-value .001). There was a significant relation between CAR ratio

and ST depression ECG finding (P value .005). There was no significant relation between CAR ratio and RWMA. There was no significant relation between CAR ratio and Number of diseased vessels (**Table 3**).

Table (3): Correlation between CAR ratio and risk factors, ECG findings, and RWMA and Number of diseased vessels in our study group

Parameters	CAR	N	Median (IQR)	Mann-Whitney Test
Risk Factors:				
HTN	Yes	39	2.6(1.4-5)	0.924
	No	61	2.5(1.58-4.75)	
Dyslipidemia	Yes	62	3.3(1.6-5.375)	0.005*
	No	38	1.85(1.4-3.15)	
DM	Yes	28	3.1(1.6-8.875)	0.043*
	No	72	2(1.515-4)	
Smoking	Yes	64	2(1.56-5)	0.634
	No	36	3.1(1.625-4.875)	
ECG:				
Normal	Yes	34	3.2(1.52-5)	0.564
	No	66	2(1.56-4.25)	
Inv T	Yes	50	2(1.56-4.25)	0.402
	No	50	2.85(1.59-5)	
ST dep	Yes	14	3.1(1.9-3.625)	0.485
	No	86	2(1.56-5)	
Echocardiography RWMA	Yes	24	3.3(1.57-5)	0.240
	No	76	2(1.56-4.375)	
				Kruskal-Wallis Test
Number of diseased vessels	One vessels	40	1.95(1.4-4.725)	0.097
	Two vessels	9	4(2.85-8.5)	
	Three vessels	44	2(1.56-5)	
	Four vessels	7	3.1(1.9-3.1)	

There was a significant relation between CAR ratio and severity of SYNTAX score I, cholesterol and LDL with significant P value = 0.003, 0.001 and 0.001 respectively. There was a strong

positive linear relationship between CAR ratio and Severity of coronary artery disease assessed by SYNTAX I score (Table 4).

Table (4): Correlation between CAR ratio and severity of SYNTAX I score & Labs.

Correlations \ CAR	r	P-value
Syntax score 1	0.214	0.003
Age	-0.019	0.851
Height	0.116	0.252
Weight	0.098	0.332
BMI	-0.067	0.506
Echocardiography EF %	-0.437	<0.001
LAB CRP	0.667	<0.001
LAB Albumin	0.115	0.256
TG	0.901	<0.001
Cholesterol	0.880	<0.001
HDL	-0.879	<0.001
LDL	0.910	<0.001

DISCUSSION

Among individuals with an acute phase of CAD, serum albumin is also reported as a strong prognostic factor *Hartopo et al. (2014)* evaluated small number patients with acute coronary syndrome (ACS) from a single center. Hypoalbuminemia (<3.5g/dL) measured upon admission was associated with in hospital adverse events, including death, acute heart failure, cardiogenic shock, and reinfarction.

In our study, as regarding the age, the mean age was 54.520±7.889 years with non-statistically significant. Regarding gender, there were 63% males and 37% females with non-statistically significant difference between the two groups. *Yahagi et al. (2015)* stated that most of the underlying systemic risk factors for coronary artery disease are similar between men and women. However, the impact of various risk factors is different

between men and women, with smoking being a stronger risk in women than men, especially in younger women. Furthermore, the influence of the menopause is also unique and important in women: incidence of plaque rupture is higher in older women as compared to younger.

Our results showed a statistically significant relation as regarding DM and dyslipidemia (cholesterol, LDL-C) and non-significant difference with the other risk factors. Presence of DM, elevated values of cholesterol, LDL-C and CAR were found to be independent predictors of high SS (*Caixeta et al., 2014*).

In our study as regarding serum cholesterol, the mean was 174.300±34.157 with statistically significant. For Serum LDL, the mean was 108.260±19.461 with statistically significant. Our results were concordant

with *Suzuki et al. (2019)*, who stated that there was a statistical significant relation as regarding total cholesterol and LDL, with non-significant difference as regard HDL.

Our results showed that Syntax Score, the mean was 23.200 ± 13.266 , and for CRP, the mean was 12.473 ± 9.448 with statistically significant differences.

We also showed significant correlation between CRP/ ratio, CRP, Albumin and syntax score / Albumin ratio and CRP while non-significant correlation with Albumin.

Kurtul et al. (2016) assumed that increased CRP/albumin ratio indicates a higher inflammatory state and may be superior to CRP and albumin alone in determining the prevalence and severity of CAD. They also stated that elevated CAR levels in CAD patients were independent predictors of intermediate-high SS group, and the predictive accuracy of CAR was better than CRP and albumin level, as per the comparison of the ROC curves.

Oh et al. (2017) stated that the relationships between albumin, CRP level, and SS were similar to that reported in previous trials. Merging albumin and CRP into a single index demonstrated to be associated with poor prognosis in a variety of disorders including cancer and sepsis.

The inflammatory status, reflected by the decreased albumin level, increased CRP level, and higher CAR, were closely related to severe CAD, which was determined using the SS. The CAR was found to be a more accurate predictor of intermediate-high SS than CRP or albumin (*Çağdaş et al., 2017*).

CONCLUSION

There was a correlation between CRP/ Albumin ratio and the severity of coronary artery disease assessed by syntax score I.

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العلاقة بين نسبة البروتين التفاعلى سى الى الزلال ومدى مرض الشريان التاجى لدى المرضى الذين يعانون من إحتشاء عضلة القلب غير المرتفع اس تى

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خلفية البحث: يعتبر مرض قصور الشريان التاجى سبب رئيسى للوفيات حول العالم ويمثل عبء اقتصادى على أنظمه الصحة وقصور الشريان التاجى غالبا ما يكون بسبب مرض تصلب الشرايين ويلعب الالتهاب دوراً مهماً فى نشوء وزيادة تصلب الشرايين. ويرتبط شدة مرض قصور الشريان التاجى بمعدل الوفيات. ويعد معيار سينتاكس الاشهر إستخداماً لتحديد شدة إصابة الشريان التاجى، وزيادة رقم هذا المعيار يؤدي إلى زيادة الوفيات لمرضى إحتشاء عضلة القلب الغير مرتفع الاس تى.

الهدف من البحث: تقييم العلاقة الممكنة بين نسبة البروتين التفاعلى سى إلى الزلال، ومدى شدة مرض الشريان التاجى فى مرضى إحتشاء عضله القلب غير مرتفع الاس تى.

المرضى وطرق البحث: كانت الدراسة عبارة عن دراسة جماعية مرتقبة أجريت فى قسم أمراض القلب بجامعة الأزهر وقسم العجوزة لأمراض القلب، وتم تسجيل 100 مريض تم قبولهم بإحتشاء عضلة القلب غير المرتفع اس تى، وخضعوا للقسطرة التشخيصية التداخلية للشرايين التاجية فى الفترة من يناير 2019 إلى فبراير 2020.

نتائج البحث: اثبتت النتائج عدم وجود علاقته ذات قيمة احصائية من حيث العمر والجنس و الضغط، فى حين أثبتت وجود علاقة ذات قيمة إحصائية من حيث

السكر والكوليسترول. أثبتت الدراسة وجود علاقة ذات قيمة إحصائية بين نسبة البروتين التفاعلي سي إلى الزلال ومدى مرض الشريان التاجي.

الاستنتاج: هناك إرتباط بين نسبة البروتين التفاعلي سي إلي البيومين في تحديد درجة إعتلال الشريان التاجي.

الكلمات الدالة: بروتين سي التفاعلي، نسبة الألبومين، مرض الشريان التاجي، إحتشاء عضلة القلب غير المرتفع اس تي.