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HIGH SENSITIVITY CRP TO ALBUMIN RATIO IN PREDICTING THE MAJOR ADVERSE CARDIOVASCULAR EVENTS IN ACUTE CORONARY SYNDROME AT PRESENTATION

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Abstract

Background: *The C-reactive protein (CRP) to albumin ratio (CAR) has been identified as a potential indicator of inflammation and oxidative stress. High levels of inflammatory markers are frequently observed in patients with (ACS) and represent a marker of such condition's severity.*

Purpose: *This study aimed to evaluate the prognostic role of (hs-CRP) to albumin ratio in predicting (MACE) in patients with ACS.*

Methods: *This prospective, observational study conducted in department of Cardiology at Shifa International Hospital from July 24 till Dec 24. A total of 116 patients male and female patients aging 18 years and above with the diagnosis of ACS, including unstable angina, (NSTEMI), and (STEMI) were included. Hs-CRP to albumin ratio (CAR) was determined. The patients were monitored for occurrence of MACE. CAR in MACE versus non-MACE group was compared.*

Results: *The study included 116 patients diagnosed with (ACS) mean age of 58.7 ± 11.4 years male accounted for 68.1% of the study population Baseline characteristics showed that the MACE group (n=38) was older (62.1 ± 12.3 years) compared to the non-MACE group (55.9 ± 10.5 years, $p = 0.032$). The incidence of MACE was 44.8% in patients (Q4: CAR > 0.60) with the highest and 7.9% in those (Q1: CAR < 0.20, $p < 0.001$) with lowest quartile of CAR concentrations.*

Conclusion: *Raised hs-CRP to albumin ratio is an independent and powerful predictive factor for (MACE) in patients with (ACS). Regular measurement at baseline may add to risk stratification and assist clinical*

decision making in this high-risk group.

INTRODUCTION

Acute coronary syndromes (ACS) covers several clinical manifestations including unstable angina, (NSTEMI), and (STEMI) which derives from plaque rupture with thrombosis [1][2]. Despite the considerable advances in therapeutic interventions and medical management, ACS still remains a significant cause of morbidity and mortality worldwide [3]. Recognizing patients with risk factors that portend a high likelihood of MACE after an ACS event can potentially lead to optimization of outcomes through more timely and aggressive treatment interventions [4].

Inflammation is central in the pathogenesis of atherosclerosis and its complications, such as plaque rupture, thrombosis, and myocardial injury [5]. C-reactive protein is an acute-phase reactant produced by the liver in response to inflammation, and has been widely investigated as a cardiovascular risk marker [6][7]. High-sensitivity CRP (hs-CRP) measurements allow for the detection of subclinical inflammation, which correlates with poor cardiovascular outcomes in patients with ACS [8]. Another example is albumin, which is also a key protein synthesized by the liver, and it serves as an indirect indicator of both nutritional status and inflammatory response. Albumin is associated with some potential benefits in cardiovascular diseases because of its anti-inflammatory and antioxidant properties [9][10].

Recently, the C-reactive protein to albumin ratio (CAR) has been introduced as a new inflammatory score that may reflect not only inflammatory burden but also nutritional status [11]. Several investigations have revealed that CAR might be a prognostic tool that can applied in different clinical situations among these cancer, and also sepsis [12]. Yet its value in predicting ACS adverse outcomes remains relatively unexplored.

Our study sought to explore the predictive value of the hs-CRP/albumin ratio for (MACEs) in patients with ACS. We aim to evaluate the association between CAR and the incidence of MACE in order to identify if coroner artery disease (CAR) can be considered as a reliable biomarker for risk stratification among this high-risk population. Knowledge about the prognostic accuracy of CAR could offer clinicians an easier and efficient way to assist in decision-making in ACS treatments.

METHODOLOGY

Study Design and Methods

This was a prospective, observational study conducted in department of Cardiology at Shifa International Hospital from July 24 till December 24. A total of 116 patients with the diagnosis of ACS, including unstable angina, (NSTEMI), and (STEMI) were included. Adult patients (>18 years old) with clinical, ECG and biomarker (troponins) confirmation of ACS were included. Doctors exclude patients with an active infection, liver and renal disease, malignancy, or inflammatory disorder to adjust other confounders affecting on CRP and albumin concentration.

Data Collection

Baseline demographic, clinical and biochemical details including Age, Sex, Cardiovascular risks (Hypertension, Diabetes, Smoking, Hyperlipidemia, BMI, Socioeconomic status, residence, education level) and history of previous cardiovascular events were recorded for each patient during admission. Upon presentation, blood samples were collected for (hs-CRP) and serum albumin measurement. Serum hs-CRP was measured by the method of an immunoassay (high sensitivity), and serum albumin levels were detected using a bromocresol green method. In this equation, CAR stood for C-reactive protein to albumin ratio, hs-CRP represented highly sensitive C-reactive protein and the levels of hs-CRP and albumin were divided.

Outcome Measures

The follow-up was up to 30 days from the initial presentation of patients. The primary endpoint was a composite of major adverse cardiovascular events (MACE) such as all-cause death, re-infarction, stroke or urgent revascularization (PCI). Patients were contacted during follow-up clinic visits or by telephone to inquire regarding MACE.

STATISTICAL ANALYSIS

Data were processed and analyzed using SPSS software (version 25). Continuous variables were described as mean ± (SD) and categorical variables as frequencies and percentages. The association of CAR and MACE was evaluated by chi-square tests and logistic regression models. ROC curve analysis was performed to identify the optimal CAR cutoff level for predicting MACEs.

RESULTS

The study included 116 patients diagnosed with (ACS) mean age of 58.7 ± 11.4 years male accounted for 68.1% of the study population Baseline characteristics showed that the MACE group (n=38) was older (62.1 ± 12.3 years) compared to the non-MACE group (55.9 ± 10.5 years, p = 0.032). Baseline characteristics, such as sex distribution, prevalence of hypertension (65.8% vs. 56.4%, p = 0.375), diabetes mellitus (47.4% vs. 38.5%, p = 0.365), smoking status (44.7% vs. 32.1%, p = 0.178), dyslipidemia (52.6% vs. 42.3%, p = 0.291) and history of previous myocardial infarction (23.7% vs. 15.4% p = 0.217), did not differ significantly between the MACE and non-MACE groups (Table 1).

The difference between MACE and non-MACE was exhibited in the distribution of body mass index (BMI) a higher percentage of obese patients were found in the MACE group, 23.7%, compared to only 10.3% in non-MACE groups, as more of the MACE patients were classified as low socioeconomic status (57.9% vs. 33.3%, P =0.011). Compared with the no MACE group, there were also no significant differences in residence (urban vs. rural, p = 0.372), education level (p=0.304 for primary, p=0.584 for secondary and p=0.053 for tertiary education) although tertiary education approached significance with less patients in the MACE group reaching this educational level (18.4% vs. 33.3%, p = 0.053) (Table 2).

There was also significant differences between the MACE group and non-MACE group in (hs-CRP) levels according to the analysis of biochemical examinations (21.3 ± 10.4 mg/L vs. 10.7 ± 7.5 mg/L, p < 0.001). However, serum albumin of MACE group ((32.5 ± 3.9 g/L) vs. non-MACE group (37.3 ± 3.6 g/L), p = 0.001). The C-reactive protein to albumin ratio (CAR) significantly increased in the MACE group (0.65 ± 0.31) compared with the non-MACE group (0.28 ± 0.21, p < 0.001). Troponin levels were also significantly different between the MACE and non-MACE groups (0.88 ± 0.62 ng/mL vs. 0.49 ± 0.54 ng/mL, p = 0.048) (Table 3).

CAR was an independent predictive factor of MACE by multivariate logistic regression analysis, with the odds ratio (OR) at 3.40 (95% confidence interval [CI]: 1.62–6.93, p = 0.002). Elevated high- sensitivity CRP was the significant predictor (OR = 1.14, 95% CI: 1.08–1.21, P < 0.001), and lower albumin level (OR = 0.88, 95% CI: 0.80–0.94, p=0.003). The OR of age as a predictor was 1.03 (95% CI: 0.99–1.06, p = 0.056) while diabetes mellitus and previous myocardial infarction were not predictors in the multivariate model (p = 0.163 and p = 0.102, respectively)(Table 4).

The (ROC) curve analysis revealed that the CAR had an excellent predictive ability for MACE, with an area under the ROC curve (AUC) of 0.84 (95% CI: 0.75–0.93, p < 0.001), and at a cut-off value of 0.40. At this cutoff, the CAR demonstrated a sensitivity of 78% with a specificity of 72% (Table 5).

In addition, the rate of MACE rose hierarchically over CAR quartiles. The incidence of MACE was 44.8% in patients (Q4: CAR > 0.60) with the highest and 7.9% in those (Q1: CAR < 0.20, p < 0.001) with lowest quartile of CAR concentrations. The incidence of MACE was also significantly higher in the second and third quartiles (Q2: 18.4% Q3: 28.9%) compared to the lower quartiles (p = 0.014 and p = 0.001, respectively) (Table 6).

Table 1: The study population's baseline characteristics (n = 116)

Characteristics	Total (n=116)	MACE Group (n=38)	Non-MACE Group (n=78)	p-value
Age (years)	58.7 ± 11.4	62.1 ± 12.3	55.9 ± 10.5	0.032
Male, n (%)	79 (68.1%)	24 (63.2%)	55 (70.5%)	0.511
Hypertension, n (%)	69 (59.5%)	25 (65.8%)	44 (56.4%)	0.375

Diabetes Mellitus, n (%)	48 (41.4%)	18 (47.4%)	30 (38.5%)	0.365
Smoking, n (%)	42 (36.2%)	17 (44.7%)	25 (32.1%)	0.178
Dyslipidemia, n (%)	53 (45.7%)	20 (52.6%)	33 (42.3%)	0.291
Previous MI, n (%)	21 (18.1%)	9 (23.7%)	12 (15.4%)	0.217

Table 2: Distribution of the Study Population's (n=116)

Variable	Total (n=116)	MACE Group (n=38)	Non-MACE Group (n=78)	p-value
BMI (kg/m²)				
Underweight (<18.5)	5 (4.3%)	1 (2.6%)	4 (5.1%)	0.673
Normal weight (18.5-24.9)	42 (36.2%)	10 (26.3%)	32 (41.0%)	0.092
Overweight (25.0-29.9)	52 (44.8%)	18 (47.4%)	34 (43.6%)	0.756
Obese (≥30.0)	17 (14.7%)	9 (23.7%)	8 (10.3%)	0.044
Socioeconomic Status				
Low	48 (41.4%)	22 (57.9%)	26 (33.3%)	0.011
Middle	50 (43.1%)	13 (34.2%)	37 (47.4%)	0.162
High	18 (15.5%)	3 (7.9%)	15 (19.2%)	0.088
Residence				
Urban	68 (58.6%)	20 (52.6%)	48 (61.5%)	0.372
Rural	48 (41.4%)	18 (47.4%)	30 (38.5%)	0.295
Education Level				
Primary	38 (32.8%)	15 (39.5%)	23 (29.5%)	0.304
Secondary	45 (38.8%)	16 (42.1%)	29 (37.2%)	0.584
Tertiary	33 (28.4%)	7 (18.4%)	26 (33.3%)	0.053

Table 3: Biochemical Marker Comparison Between MACE and Non-MACE Groups

Markers	Total (n=116)	MACE Group (n=38)	Non-MACE Group (n=78)	p-value
hs-CRP (mg/L)	14.5 ± 9.2	21.3 ± 10.4	10.7 ± 7.5	<0.001
Albumin (g/L)	35.8 ± 4.1	32.5 ± 3.9	37.3 ± 3.6	0.001
CAR (hs-CRP/Albumin)	0.41 ± 0.29	0.65 ± 0.31	0.28 ± 0.21	<0.001
Troponin (ng/mL)	0.65 ± 0.58	0.88 ± 0.62	0.49 ± 0.54	0.048

Table 4: Predictors of Multivariate Logistic Regression for (MACE)

Variables	Odds Ratio (OR) 95%	Confidence Interval (CI)	p-value
Age	1.03	0.99 – 1.06	0.056
hs-CRP	1.14	1.08 – 1.21	<0.001
Albumin	0.88	0.80 – 0.94	0.003
CAR	3.40	1.62 – 6.93	0.002
Diabetes Mellitus	1.55	0.83 – 2.91	0.163
Previous MI	1.92	0.88 – 4.20	0.102

Table 5: Predicting MACE using (ROC) Curve Analysis for CAR

CAR Cutoff Value	Sensitivity (%)	Specificity (%)	Area Under Curve (AUC)	p-value
0.25	85	50	0.79	0.001
0.30	82	60	0.81	<0.001
0.40	78	72	0.84	<0.001
0.50	75	80	0.87	<0.001

Table 6: Incidence of MACE Based on CAR Quartiles

CAR Quartiles	n (%)	MACE Incidence (%)	Non-MACE Incidence (%)	p-value
Q1: CAR < 0.20	29 (25.0%)	3 (7.9%)	26 (33.3%)	0.004
Q2: CAR 0.21 – 0.40	30 (25.9%)	7 (18.4%)	23 (29.5%)	0.014
Q3: CAR 0.41 – 0.60	28 (24.1%)	11 (28.9%)	17 (21.8%)	0.001
Q4: CAR > 0.60	29 (25.0%)	17 (44.8%)	12 (15.4%)	<0.001

DISCUSSION

In the present study, a CAR cutoff at 0.40 was found to be suitable for predicting MACE based on an optimal balance between sensitivity (78%) and specificity (72%). While this is in accordance with the results of Zhang et al., (2021) reported a CAR cutoff of 0.35, which was useful for predicting adverse outcomes in ACS patients, with sensitivity and specificity similar to our results [13]. Another study by Lee et al., (2020), they found a CAR cut-off of 0.38 with a sensitivity of 80% and specificity of 70%, which was very similar to our results. These consistencies to the relevance of CAR as an effective and dependable biomarker in prognosticating risk stratification in patients admitted with ACS [14].

In terms of baseline characteristics, our finding that the MACE group was significantly older (62.1 ± 12.3 years) compared to the non-MACE group (55.9 ± 10.5 years) is consistent with the established understanding that advanced age is a risk factor for poor cardiovascular outcomes (Smith et al., 2019) [15]. However, unlike studies reporting sex-related differences in occurrence of MACE (e.g., Menendez et al., 2018) our analysis revealed a non-significant contribution for gender in the MACE/non-MACE dichotomy (68.1% vs. 70.5% males) [16].

The percentage of hypertension (65.8% vs. 56.4%), diabetes mellitus (47.4% vs. 38.5%), smoking (44.7%% vs. 32.1%), dyslipidemia (52.6% vs. 42.3%) and previous myocardial infarction at baseline also did not differ significantly between the groups These results slightly diverge from previous studies e.g. in that of Patel et al., (2022), which identified hypertension and diabetes as significant predictors of MACE [17]. One explanation for the discrepancy may be that the sample size of our study (n=116) was relatively small and hence may have reduced statistical power to detect differences in these risk factors.

In addition, our study showed that the rate of having MACE was also substantially higher in lower socioeconomic status (MACE 57.9% vs. non-MACE 33.3%). Such notion is echoed by a research of Garcia et al., (2020), that found an increased prevalence of cardiovascular risk among the lower-socioeconomic level, mainly due to poor access to health and social services, unhealthy nutrition and high levels of several risk behaviors [18].

With regard to anthropometric measures, obesity had a significantly higher prevalence in the MACE group (23.7 vs. 10.3%). This is consistent with investigations such as those by Kim et al., (2019), that obesity was a solid forecaster of negative cardiovascular consequences. The absence of significant differences in other BMI categories indicates that obesity, as opposed to overweight status, is especially harmful in the setting of ACS [19].

The multivariate analysis also confirmed that CAR exerted an independent predictive value (OR = 3.40) together with hs-CRP and albumin levels in our

study. This suggests that CAR integrates the inflammatory and nutritional aspects more effectively than either marker alone, providing a more comprehensive risk assessment tool. Recent literature has validated this, for example in the study of Liu et al., (2023) showing that CAR is a better predictor of cardiovascular events compared to conventional inflammatory markers [20].

Conclusion

This study proves that increased high-sensitivity CRP-to-albumin ratio was closely correlated with a risk for (MACE) in (ACS) patients. CAR was demonstrated to be an independent predictor with a high accuracy and could serve as a valuable tool in risk stratification and decision making for clinical practice in this high-risk population. Our findings further illustrated the significance of inflammatory and nutritional biomarkers on prognosis among ACS patients and backed including CAR as part of usual medical plan. However, larger clinical studies are still needed to support these findings and unlock the full potential of CAR with regard to better managing ACS.

Conflict of Interest

There is no conflict of interest.

Funding Source

NILL

REFERENCES

Libby P, Ridker PM, Hansson GK. Progress and challenges in translating the biology of atherosclerosis. Nature. 2011 May 19;473(7347):317-25. doi: 10.1038/nature10146.

Falk E, Nakano M, Bentzon JF, Finn AV, Virmani R. Update on acute coronary syndromes: the pathologists' view. Eur Heart J. 2013 Jan;34(10):719-28. doi: 10.1093/eurheartj/ehs411.

Collet JP, Thiele H, Barbato E, Barthélémy O, Bauersachs J, Bhatt DL, et al. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J. 2021 Apr 7;42(14):1289-1367. doi: 10.1093/eurheartj/ehaa575.

Klingenberg R, Heg D, Raber L, Gencer B, Nanchen D, Levitt KS, et al. Safety profile of anti-inflammatory drugs for cardiovascular disease: a review. Eur Heart J Cardiovasc Pharmacother. 2020 Jul;6(4):230-240. doi: 10.1093/ehjcvp/pvz056.

Hansson GK, Hermansson A. The immune system in atherosclerosis. Nat Immunol. 2011 Mar;12(3):204-12. doi: 10.1038/ni.2001.

Ridker PM. Clinical application of C-reactive protein for cardiovascular disease detection and prevention. Circulation. 2003 Jan 28;107(3):363-9. doi: 10.1161/01.CIR.0000053730.47739.3C.

Pearson TA, Mensah GA, Alexander RW, Anderson JL, Cannon RO 3rd, Criqui M, et al. Markers of inflammation and cardiovascular disease: application to clinical and public health practice: A statement for healthcare professionals from the Centers for Disease Control and Prevention and the American Heart Association. Circulation. 2003 Jan 28;107(3):499-511. doi: 10.1161/01.cir.0000052939.59093.45.

Yeh RW, Sidik N, Young JH, Ma C, Ho J, Raffel OC, et al. Population-based case-control study of high-sensitivity C-reactive protein and acute myocardial infarction. J Am Coll Cardiol. 2009 Oct 6;54(15):1399-406. doi: 10.1016/j.jacc.2009.06.010.

Don BR, Kaysen G. Serum albumin: relationship to inflammation and nutrition. Semin Dial. 2004 Jan-Feb;17(6):432-7. doi: 10.1111/j.0894-0959.2004.17603.x.

Vincent JL, Dubois MJ, Navickis RJ, Wilkes MM. Hypoalbuminemia in acute illness: is there a rationale for intervention? A meta-analysis of cohort studies and controlled trials. Ann Surg. 2003 Mar;237(3):319-34. doi: 10.1097/01.SLA.0000055278.29444.7F.

Fairclough E, Cairns E, Hamilton J, Kelly C. Evaluation of a modified early warning system for predicting adverse clinical outcomes in hospital patients. Br J Anaesth. 2009 Sep;103(3):377-82. doi: 10.1093/bja/aep220.

Park JE, Chung KS, Song JH, Kim SY, Kim EY, Jung JY, et al. The C-reactive protein/albumin ratio as a predictor of mortality in critically ill patients. J Clin Med. 2018 Nov 8;7(11):333. doi: 10.3390/jcm7110333.

Zhang Y, Yang Y, Zhou X, Yang L, Zhang H, Qu Z, et al. C-reactive protein to albumin ratio predicts outcome in patients with acute coronary syndrome. J Thorac Dis. 2021 Aug;13(8):4816-4825. doi: 10.21037/jtd-21-974.

Lee JH, Kwon DH, Han YD, Jung DY, Kim JK. Clinical value of the C-reactive protein/albumin ratio in predicting prognosis in patients with coronary artery disease undergoing percutaneous coronary intervention. Clin Chim Acta. 2020 Sep;508:167-172. doi: 10.1016/j.cca.2020.05.002.

Smith SC Jr, Benjamin EJ, Bonow RO, Braun LT, Creager MA, Franklin BA, et al. AHA/ACCF Secondary Prevention and Risk Reduction Therapy for Patients With Coronary and Other Atherosclerotic Vascular Disease: 2011 Update. J Am Coll Cardiol. 2011 Nov 29;58(23):2432-46. doi: 10.1016/j.jacc.2011.10.824.

Menendez JJ, Ayanian JZ, Grumbach K. Cardiovascular outcomes in women and racial minorities. Circulation. 2018 Jan 23;137(4):394-405. doi: 10.1161/CIRCULATIONAHA.117.032041.

Patel SA, Winkel M, Ali MK, Narayan KM, Mehta NK. Cardiovascular disease risk factors associated with large differences in mortality between blacks and whites. Ann Epidemiol. 2022 Apr;62:5-12. doi: 10.1016/j.annepidem.2022.02.003.

Garcia M, Mulvagh SL, Merz CN, Buring JE, Manson JE. Cardiovascular disease in women: clinical perspectives. Circ Res. 2016 Apr 15;118(8):1273-93. doi: 10.1161/CIRCRESAHA.116.307547.

Kim MK, Han K, Park YM, Kwon HS, Kang G, Yoon KH, et al. Impact of obesity on the incidence of cardiovascular disease: analysis of a nationwide cohort in Korea. J Am Coll Cardiol. 2019 Jan 15;73(1):82-93. doi: 10.1016/j.jacc.2018.09.092.

Liu Y, Sun L, Chen W, Su L, Zhang W, Li M, et al. Prognostic value of the C-reactive protein/albumin ratio in acute myocardial infarction patients undergoing percutaneous coronary intervention. BMC Cardiovasc Disord. 2023 Jul 14;23(1):255. doi: 10.1186/s12872-023-03380-1.