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Effectiveness of CAR C-Reactive Protein to Albumin Ratio in Predicting the Severity of Coronary Artery Disease in Patients with Non-ST Elevation Myocardial Infarction

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ABSTRACT

Background: *Non-ST elevation myocardial infarction (NSTEMI) is a critical manifestation of coronary artery disease (CAD) requiring timely risk stratification to guide management. Inflammatory and nutritional markers, such as the C-reactive protein to albumin ratio (CAR), have gained attention for their potential to predict CAD severity. This study aimed to evaluate the effectiveness of CAR in predicting the severity of CAD in patients with non-ST elevation myocardial infarction.* ***Methods:*** *This cross-sectional observational study was conducted at the National Institute of Cardiovascular Diseases in Dhaka from May 2018 to April 2019. It included 200 patients with NSTEMI who underwent coronary angiography (CAG) and were equally divided into two groups based on their CAR: Group I with CAR>11 and Group II with CAR≤11. Data analysis was performed using SPSS version 26.0.* ***Results:*** *The mean SYNTAX score (SS) was significantly higher in Group I (CAR>11) compared to Group II (CAR≤11) ($p<0.001$). In Group I, 68% of patients had intermediate-to-high SS (>22), whereas 71% of patients in Group II had low SS (≤22) ($p<0.001$). Diabetes, hypoalbuminemia (albumin<35g/L), and CAR>11 emerged as significant predictors of CAD severity. Notably, CAR>11 was identified as an independent predictor of intermediate-to-high SS in multivariate analysis ($p<0.001$). A significant correlation was observed between CAR and SS ($p<0.001$). The ROC curve analysis demonstrated an area under the curve of 0.878 for CAR ($p<0.001$), with a sensitivity of 77.3% and specificity of 70.0% for predicting intermediate-to-high SS.* ***Conclusion:*** *The C-reactive protein to albumin ratio is a reliable and independent predictor of CAD severity in NSTEMI patients. With its high sensitivity and specificity, CAR stands out as a valuable inflammatory and nutritional biomarker, offering significant potential to enhance risk stratification when used alongside traditional diagnostic methods in NSTEMI management.*

Keywords: *Coronary artery disease, C-reactive protein to albumin ratio, NSTEMI, Effectiveness, Predictor, SYNTAX score*

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INTRODUCTION

Coronary artery disease (CAD) remains the leading cause of morbidity and mortality worldwide, with non-ST elevation myocardial infarction (NSTEMI) being a common clinical presentation. NSTEMI is characterized by acute myocardial injury without persistent ST-segment elevation on electrocardiogram (ECG), and it is associated with significant short- and long-term complications, including heart failure, arrhythmias, and recurrent infarction [1]. The severity of CAD plays a critical role in determining patient outcomes, including the need for invasive interventions such as coronary angiography and revascularization [2]. Therefore, accurate and early identification of patients with high-risk CAD is essential for improving management strategies and reducing adverse cardiovascular events. The identification of reliable biomarkers

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that can predict the severity of CAD in NSTEMI patients has garnered significant attention in recent years. C-reactive protein (CRP) is a well-established marker of inflammation, and its elevation has been associated with an increased risk of cardiovascular events, including myocardial infarction (MI) [3,4]. However, CRP alone may not be sufficient in predicting the severity of CAD. Inflammation plays a central role in the pathogenesis of atherosclerosis and subsequent plaque rupture, which leads to acute coronary syndromes (ACS) like NSTEMI [5]. Albumin, on the other hand, is a negative acute-phase reactant, and its levels are typically reduced in the setting of systemic inflammation [6]. The C-reactive protein to albumin ratio (CAR) has emerged as a novel biomarker that combines these two indicators of inflammation and nutritional status. Several studies have suggested that the CAR ratio could serve as an effective predictor of disease severity in various cardiovascular conditions, including heart failure and ischemic heart disease [7,8]. The CAR ratio has the advantage of being readily available in clinical practice, as both CRP and albumin levels are commonly measured during the initial evaluation of patients presenting with acute chest pain. In the context of NSTEMI, assessing the severity of CAD early on is crucial for guiding therapeutic decisions, such as the need for urgent coronary angiography or medical management with antithrombotic and statin therapies. Several scoring systems, such as the GRACE (Global Registry of Acute Coronary Events) score, have been developed to stratify risk in ACS patients, but there remains a need for simple and cost-effective biomarkers to complement these tools, especially in resource-limited settings [9]. The CAR ratio has shown promise in predicting outcomes in various diseases, but its role in predicting the severity of CAD in NSTEMI patients remains inadequately explored [10]. This study aimed to evaluate the effectiveness of the CAR ratio in predicting the severity of CAD in patients with NSTEMI. By examining the relationship between CAR and angiographic findings, this research seeks to provide valuable insights into the clinical utility of the CAR ratio as a prognostic tool for CAD severity in NSTEMI patients. Early identification of high-risk patients could significantly improve management strategies, reduce complications, and ultimately enhance patient outcomes in this critical population.

METHODOLOGY

This cross-sectional observational study was conducted at the National Institute of Cardiovascular Diseases (NICVD), Dhaka, Bangladesh, from May 2018 to April 2019, involving 200 patients with NSTEMI undergoing coronary angiography (CAG). The sample was selected using a consecutive sampling method. The study included patients experiencing their first NSTEMI who underwent coronary angiography during index hospitalization at NICVD. Exclusion criteria included patients with active infectious or inflammatory diseases, connective tissue diseases, chronic kidney disease, hepatic cirrhosis, malnutrition, congestive heart failure, malignancy, valvular or congenital heart diseases, cardiomyopathy, myocarditis, or pericarditis. The study also excluded patients with a history of previous myocardial infarction, percutaneous coronary interventions (PCI), coronary artery bypass grafting (CABG), or other severe comorbidities. Informed written consent was obtained from all participants before enrollment. CRP levels were measured within 48 hours of admission using a Beckman Coulter Analyzer (Model- OLYMPUS AU 480) with a quantitative method. The patients were divided into two groups based on the CAR: Group I (CAR > 11) and Group II (CAR ≤ 11). Coronary angiography was performed, and the SYNTAX score (SS) was calculated for each patient. Digital angiogram recordings were analyzed using a DICOM viewer by two experienced cardiologists. Only coronary arteries with a diameter greater than 1.5 mm and obstructions over 50% were included in the SS calculation, which was performed using the online SS calculator. The correlations between CRP, albumin, and CAR with SS were assessed using the Pearson correlation coefficient test. ROC curve analysis was used to evaluate the predictive value of CAR for intermediate-high SS. Statistical analysis was conducted using SPSS 25.0, with a significance threshold set at $p < 0.05$.

RESULT

The mean age of the participants was 54.01 ± 8.67 years in Group I and 51.69 ± 9.95 years in Group II, with no statistically significant difference ($p>0.05$). Diabetes mellitus was significantly more prevalent in Group I compared to Group II (59.0% vs. 48.0%, $p=0.038$). The mean albumin levels were 36.15 ± 7.85 g/l in Group I and 40.53 ± 7.89 g/l in Group II. The mean C-reactive protein to albumin ratio (CAR) × 100 was 41.08 ± 17.39 in Group I and 7.95 ± 2.81 in Group II, with a statistically significant difference between the two groups ($p=0.001$). Regarding the severity of coronary artery disease (CAD), 69.0% of patients in Group I had an intermediate to high SYNTAX score (SS ≥ 22), compared to 28.0% in Group II, while 31.0% of Group I patients had a low SS, compared to 72.0% in Group II. This difference was statistically highly

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significant (p<0.001). The mean Syntax score was 23.45 ± 8.13 in Group I and 16.25 ± 9.51 in Group II. The difference in mean Syntax scores between the two groups was statistically highly significant (p<0.001). In Group I, 60.0% of patients had triple vessel disease (TVD), while only 25.0% had TVD in Group II. Conversely, 27.0% of patients in Group II had single vessel disease (SVD), compared to just 7.0% in Group I. The number of involved vessels was significantly different between the two groups (p<0.001). None of the biochemical parameters showed significant differences in their mean values between the two groups (p>0.05). Pearson's correlation coefficient test revealed a moderately positive correlation (r=0.530) between C-reactive protein (CRP) and Syntax score, which was statistically highly significant (p<0.001). Another scatter plot revealed a weak inverse correlation (r = -0.246) between serum albumin and Syntax score, which was statistically significant (p = 0.041). Additionally, a scatter plot showed a moderately positive correlation (r = 0.645) between the C-reactive protein to albumin ratio (CAR) and Syntax score, which was statistically highly significant (p < 0.001). This suggests that patients with higher CAR tend to have higher Syntax scores. Univariate logistic regression analysis of determinants likely associated with severe coronary artery disease (intermediate-high Syntax score) included albumin, but not CRP, due to the strong correlation between CAR and CRP (p < 0.001). Diabetes mellitus (DM), albumin <35 g/l, and C-reactive protein to albumin ratio (CAR) >11 were significant independent predictors of severe coronary artery disease (CAD), with p-values of 0.013, 0.026, and <0.001, respectively. Variables such as age >50 years, hypertension, dyslipidemia, smoking, and family history of CAD were excluded from the multivariate regression analysis as they were found to be statistically insignificant in the univariate analysis. While DM and albumin <35 g/l were significant in univariate analysis, they were deemed insignificant in the multivariate regression analysis (p = 0.080 and 0.114, respectively). After adjustment, CAR >11 emerged as the significant independent predictor of severe CAD in the multivariate logistic regression analysis (p < 0.001). Furthermore, ROC curve analysis showed that CAR >11 predicted severe CAD with sensitivity and specificity of 77.3% and 70.0%, respectively.

Table 1: Comparison of the study patients by CRP, albumin, and CAR

Variables	Group-I (n=100) Mean ±SD	Group-II (n=100) Mean ±SD	p-value
CRP (mg/l)	15.41±8.79	5.32±2.51	0.001[s]
Albumin (g/l)	36.15±7.85	40.53±7.89	0.001[s]
CAR ×100	41.08±17.39	7.95±2.81	0.001[s]

Table 2: Comparison of the study groups by SYNTAX score

Score	Group-I (n=100)		Group-II (n=100)		p-value
	n	%	n	%	
IHSS (>22)	69	69.0	28	28.0	[a] <0.001[s]
LSS (≤ 22)	31	31.0	72	72.0	
Mean ±SD	23.45±8.13		16.25±9.51		[b] <0.001[s]

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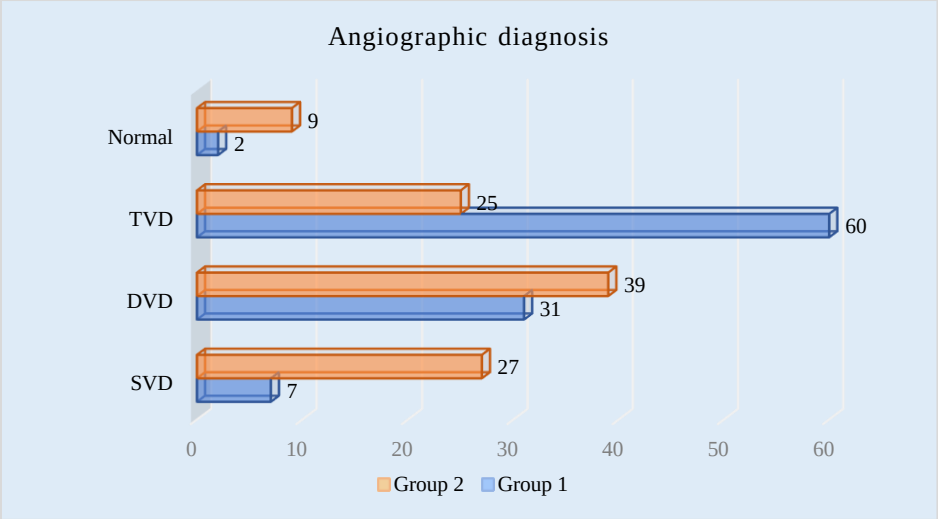

Figure I: Column chart showed comparison of the study groups by the number of involved vessels

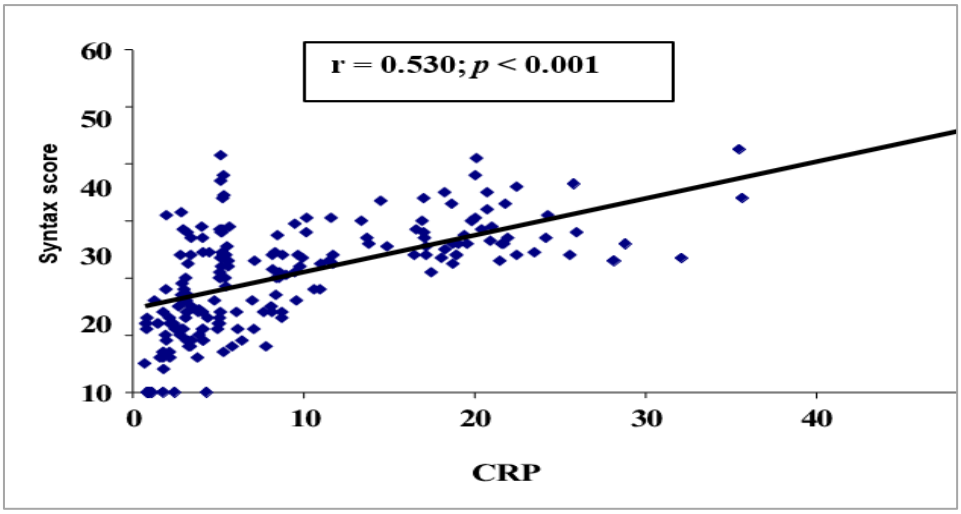

Figure II: Scatter plot showing the correlation between C-Reactive protein and SYNTAX score

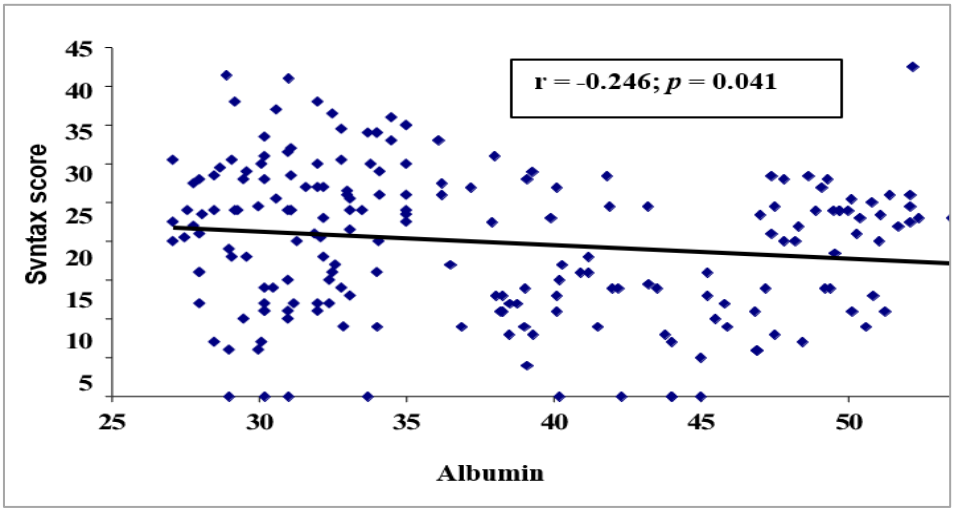

Figure III: Scatter plot showing the correlation between Serum Albumin and SYNTAX score

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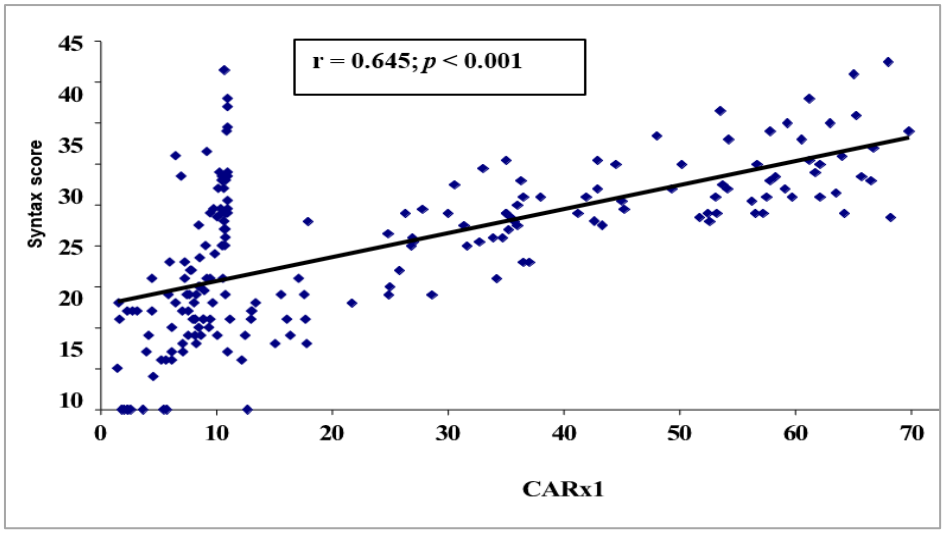

Figure IV: Scatter plot showing the correlation between CAR and SYNTAX score

Table 3: Univariate logistic regression analysis of the determinants of severe CAD (intermediate-high SYNTAX score, SS>22)

Variables	SRC (b)	OR	p-value
Age>50 yrs.	0.394	1.482	0.207[ns]
HTN	0.235	1.265	0.408 [ns]
DM	0.721	2.056	0.013s
Dyslipidemia	0.361	1.435	0.204 [ns]
Smoking	0.316	1.371	0.267 [ns]
Family H/o CAD	-0.219	0.803	0.463 [ns]
Albumin< 35 g/l	0.531	1.36	0.026 s
CAR > 11	1.745	5.724	<0.001s

Table 4: Multivariate logistic regression analysis of the determinants of severe CAD (intermediate-high SYNTAX score, SS>22)

Variables	SRB (□)	OR	p-*value*
DM	0.578	1.783	0.080
Albumin < 35g/l	0.438	1.11	0.114
CAR>11	1.663	5.276	<0.001s

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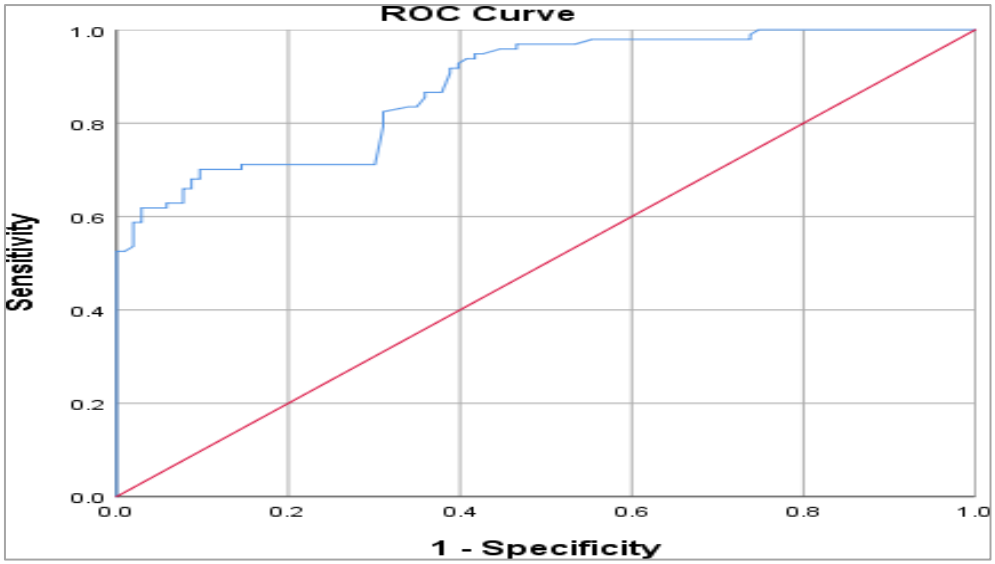

Figure V: Area Under the Curve, Test Result Variable (S): CAR

Table 5: The receiver operating characteristic (ROC) curve analysis of CAR in predicting severe CAD (intermediate– high SYNTAX score (SS>22)

			Asymptotic 95% Confidence Interval	
Area	Std. Error	Asymptotic Sig.	Lower Bound	Upper Bound
0.878	0.023	0	0.832	0.923

Table 6: Cutoff value, sensitivity, and specificity for CAR by ROC curve analysis in predicting angiographic severity of CAD by intermediate- high SYNTAX score (>22) in NSTEMI

	Cut off value	Sensitivity	Specificity
CAR	>11.0	77.3	70

DISCUSSION

In this study, no significant difference was found between Group I and Group II regarding CAD risk factors such as hypertension, dyslipidemia, smoking, and family history of CAD, except for diabetes mellitus (DM). However, major biochemical variables—CRP, albumin, and CAR—showed statistically significant differences between the groups (p=0.001). Group I had mean values of 15.41 ±8.79 mg/l for CRP, 36.15 ±7.85 g/l for albumin, and 41.08 ±17.39 for CAR, while Group II had values of 5.32 ±2.51 mg/l for CRP, 40.53 ±7.89 g/l for albumin, and 7.95 ±2.81 for CAR. Similar findings were reported by Kalyoncuoglu and Durmus [11] for CRP (14.1 ±7.8mg/l vs. 5.9 ±4.5mg/l), albumin (37.7 ±3.8g/l vs. 39.2 ±3.6g/l), and CAR (37.8 ±20.5 vs. 15.8 ±13.3). The study found no significant differences between groups for other biochemical parameters, such as random blood sugar, creatinine, troponin I, and fasting lipid profile, consistent with findings by Karabag et al. [12]. Regarding CAD severity, assessed by the SYNTAX score, Group I showed a significantly higher percentage of severe CAD cases (69.0%) compared to Group II (28.0%), with a p-value of <0.001. The mean SYNTAX score was also significantly higher in Group I (23.45 ± 8.13) than in Group II (p<0.001), aligning with the results of Cagdas et al. [13], who observed a higher mean SYNTAX score in the high CAR group compared to the low CAR group (p<0.001). This study found that 60.0% of patients in Group I had triple-vessel disease (TVD), compared to 25.0% in Group II. Conversely, 27% of Group II patients had single-vessel disease (SVD), while only 7% in Group I had SVD, with a significant difference between the two groups (p<0.001). Similarly, Kalyoncuoglu and Durmus [11] reported a higher number of TVD patients in the high CAR group compared to the low CAR group (p<0.001). However, Cınar et al. [14] did not observe significant differences in TVD prevalence between groups in their STEMI study (p = 0.134). The study also found a significant positive correlation between CAR and the SYNTAX score, indicating that higher CAR values were

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associated with higher SYNTAX scores. A moderately positive correlation was found between CAR and the SYNTAX score ($p<0.001$), along with a moderate positive correlation between CRP and the SYNTAX score ($p<0.001$) and a weak inverse correlation between albumin levels and the SYNTAX score ($p=0.041$). These findings are consistent with those of Cagdas et al. [13], who observed significant correlations between the SYNTAX score and CAR ($p<0.001$), CRP ($p<0.001$), and albumin ($p<0.001$). Similarly, Kalyoncuoglu and Durmus [11] reported a significant positive correlation between CAR and the SYNTAX score ($p<0.001$). Parvez et al. [15] also found a weak inverse correlation between serum albumin and the Leaman score ($p=0.009$) in their NICVD study. In the current study, both univariate and multivariate logistic regression analyses were performed to identify variables contributing to severe CAD. The univariate analysis identified DM, albumin levels <35g/l, and CAR>11 as significant predictors of severe CAD, with CAR>11 being the strongest independent predictor ($p<0.001$). After multivariate analysis, DM and albumin <35g/l were no longer significant predictors, while CAR>11 remained a strong independent predictor of severe CAD with adjusted odds ($p<0.001$). These findings align with those of Kalyoncuoglu and Durmus [11]. ROC curve analysis for CAR in predicting severe CAD (SYNTAX score >22) showed an area under the curve (AUC) of 0.878 ($p<0.001$). A CAR >11 predicted an intermediate-high SYNTAX score with 77.3% sensitivity and 70% specificity. Kalyoncuoglu and Durmus [11] reported an AUC of 0.829 ($p<0.001$) for CAR, while Cagdas et al. [13] found it to be 0.765 ($p<0.001$). In their study, the sensitivity and specificity of CAR >11 for predicting an intermediate-high SYNTAX score were 71.7% and 71.4%, respectively, which aligns with the current study's findings. This comparison, along with observations from other researchers, underscores the significant association between CAR and the angiographic severity of CAD, as assessed by the SYNTAX score, in NSTEMI patients.

CONCLUSION & RECOMMENDATION

In conclusion, this study demonstrates that the C-reactive protein to albumin ratio (CAR) is an effective and independent predictor of coronary artery disease (CAD) severity in patients with non-ST elevation myocardial infarction (NSTEMI). The findings highlight a significant correlation between higher CAR values and elevated SYNTAX scores, indicating more severe coronary involvement. With its strong sensitivity and specificity, CAR can serve as a valuable inflammatory and nutritional marker to complement existing diagnostic tools for risk stratification in NSTEMI patients. Incorporating CAR into clinical practice could enhance the early identification of high-risk patients and guide timely management strategies to improve outcomes. Further studies are warranted to validate these findings in broader populations and diverse clinical settings.

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