

ORIGINAL RESEARCH

Association of the C-reactive protein/albumin ratio with major adverse cardiovascular events following elective PCI in elderly patients with unstable angina pectoris

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Abstract

Background: This study aimed to investigate the predictive value of C-reactive protein (CRP)/albumin (ALB) ratio (CAR) for the occurrence of major adverse cardiovascular events (MACE) following elective percutaneous coronary intervention (PCI) in elderly patients with unstable angina (UA). **Methods:** A retrospective analysis was conducted on 307 patients with UA who underwent elective PCI between January 2021 and September 2023. The patients were followed up for one year post-operation and categorized into two groups: the MACE group (62 cases) and non-MACE group (245 cases) based on the occurrence of adverse cardiovascular events. Multivariate logistic regression analysis was used to screen the factors influencing the occurrence of MACE, and receiver operating characteristic (ROC) curves were used to analyze the predictive value of CRP, ALB and CAR for MACE. **Results:** Compared to the non-MACE group, patients in the MACE group exhibited significantly lower albumin (ALB) levels ($p < 0.05$) and significantly higher CRP and CAR values ($p < 0.05$). ROC curve showed that the area under the curve (AUC) for CRP and ALB in predicting MACE was 0.869 and 0.792, respectively with a sensitivity of 74.19% and 70.97%, and a specificity of 86.53% and 76.73%. The AUC of CAR for predicting MACE was 0.918, significantly higher than that of CRP ($Z = 3.820, p < 0.001$) and ALB ($Z = 3.490, p < 0.001$), with a sensitivity and specificity of 87.10% and 87.76%, respectively. Multifactorial logistic regression analysis revealed smoking history, multiple coronary lesions, age, neutrophil-to-lymphocyte ratio (NLR) and elevated CAR as significant risk factors for MACE after elective PCI in elderly UA patients ($p < 0.05$). **Conclusions:** CAR is a strong predictor of MACE following elective PCI in elderly patients with UA, and elevated CAR values are associated with an increased likelihood of MACE.

Keywords

C-reactive protein; Albumin; Unstable angina; Percutaneous coronary intervention; Adverse cardiovascular events

1. Introduction

Unstable angina (UA) is a serious manifestation of coronary artery disease, characterized by a complex pathogenesis involving the instability, rupture and thrombosis of coronary atherosclerotic plaques [1]. Percutaneous coronary intervention (PCI) is one of the safe and effective treatments for patients with UA as it can rapidly restore coronary blood flow and myocardial tissue perfusion, thereby reducing myocardial injury and restoring cardiac function [2]. Despite its efficacy, PCI inevitably causes myocardial cell damage. Along with the gradual weakening of organ function in elderly patients, some patients are still at risk of major adverse cardiovascular events (MACE) after the procedure, which negatively impacts their prognosis [3]. Therefore, it is crucial to identify effective indicators that can predict the occurrence of MACE after elective

PCI in elderly UA patients.

C-reactive protein (CRP) is a well-established inflammatory response protein associated with oxidative stress, inflammation, monocyte infiltration and plaque progression [4, 5]. Albumin (ALB), on the other hand regulates a variety of physiological functions such as maintaining colloid osmotic pressure and transporting nutrients and drugs [6]. Low serum ALB levels are closely associated with an increased risk of cardiovascular disease [7]. The CRP/ALB ratio (CAR) has emerged as a novel inflammation indicator that reflects the balance between CRP and ALB, and has the significance of reflecting the systemic inflammatory state. Several studies have shown that CAR is superior to CRP or ALB alone in reflecting cardiovascular inflammation [8–11]. However, the relationship between CAR and coronary artery disease is un-

clear. Therefore, this study aimed to investigate the prognostic significance of CAR for the occurrence of MACE in elderly patients with UA undergoing elective PCI. By exploring this relationship, this study hopes to provide a reference for the prognostic assessment of UA patients.

2. Materials and methods

2.1 Patients

A retrospective analysis was carried out among 307 patients with UA who underwent elective PCI between January 2021 and September 2023. Inclusion criteria for patients' enrollment were: (1) meeting the relevant diagnostic criteria and clinically diagnosed with UA [12]; (2) successfully undergoing elective PCI; (3) aged 60 years or older; (4) received anticoagulant and antiplatelet treatments post-surgery. Patients were excluded from the study if they had: (1) malignant tumors and psychiatric disorders; (2) history of bleeding from vital organs in the last 6 months; (3) abnormal coagulation function; (4) severe cardiopulmonary insufficiency; (5) abnormal liver and renal function indexes; (6) congenital heart disease or other cardiovascular and cerebral vascular disorders; and (7) history of previous cardiac surgery.

2.2 Calculation of sample size

Prior to the conduct of this study, a power analysis was conducted using G*Power software (latest ver. 3.1.9.7; Heinrich-Heine-Universität Düsseldorf, Düsseldorf, NRW, Germany) in order to determine the appropriate sample size scientifically. Parameters such as the predicted effect size, a significance level of $\alpha = 0.05$, and statistical efficacy (Power = 0.8) were entered into the statistical software, yielding a minimum required sample size of 280 cases. During the recruitment process, we fully considered the possibility of sample loss (e.g., missing data). At the same time, in order to make the sample more representative, we also expanded the recruitment scope. The final number of UA patients included in the study was 307, which ensured that the actual sample size met the minimum sample size standard required for the power analysis, thereby providing sufficient statistical efficacy to the study.

2.3 Data collection

General information including patients' age, gender, body mass index (BMI), smoking history, alcohol consumption history, comorbid underlying diseases, number of branches of coronary artery lesions, left ventricular ejection fraction (LVEF) and left ventricular end-diastolic internal diameter (LVEDD) were collected at the time of admission, Venous blood sample was collected in the early morning of the day following the patient's admission and tested for various parameters, including CRP, ALB, red blood cell distribution width (RDW), white blood cell count (WBC), platelet count (PLT), neutrophils/lymphocytes (NLR) and platelets/lymphocytes (PLR). The CAR percentage was calculated using the formula: $\text{CAR (\%)} = \text{CRP (mg/L)}/\text{ALB (g/L)} \times 100\%$.

2.4 Follow-up

The 307 patients with UA included in this study were regularly followed up after undergoing elective PCI treatment. Follow-up methods included telephone interviews and outpatient visits, with the follow-up period spanning from the date of PCI to one year post-procedure. MACE events monitored during this period included cardiovascular death (including but not limited to death from myocardial infarction, heart failure, malignant arrhythmia, etc.), nonfatal myocardial infarction, target vessel revascularization (including re-PCI or coronary artery bypass grafting), in-stent restenosis or vascular occlusion. In-stent restenosis was defined as a stenosis of $\geq 50\%$ of the blood vessel diameter within 5 mm of the stent or its edge. Vessel occlusion was defined as complete occlusion of the vessel on coronary angiography with no antegrade flow (thrombolysis in myocardial infarction flow grade 0 or 1). Patients were categorized into the MACE group (62 patients) and the non-MACE group (245 patients) based on the results of the 1-year postoperative follow-up.

2.5 Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics (Version 16.0. Armonk, NY, USA: IBM Corp), and a p value < 0.05 was considered statistically significant. Proportions of nominal variables between treatment and control groups were compared using Chi-square test or Fisher's exact tests. Continuous variables were presented either as mean and standard deviation, or median and range. They were compared between the groups using t -test. The predictive effect of CAR on MACE in patients with UA following PCI treatment was analyzed using logistic regression model.

3. Results

3.1 Comparison of clinical data

There were no significant differences in gender distribution, BMI, history of alcohol consumption, prevalence of hypertension, percentage of hyperlipidemia, WBC, PLT, PLR and LVEDD between the MACE and non-MACE groups ($p > 0.05$). However, compared to the non-MACE group, patients in the MACE group were significantly older, had a higher prevalence of smoking history, diabetes, percentage of multi-branch coronary artery lesions, as well as higher RDW, and NLR values ($p < 0.05$). Additionally, LVEF was significantly lower in the MACE group ($p < 0.05$, Table 1).

3.2 Comparison of CRP, ALB and CAR

Compared with the non-MACE group, patients in the MACE group had significantly lower ALB levels ($p < 0.05$), while both CRP levels and CAR were significantly higher ($p < 0.05$, Table 2, Fig. 1).

3.3 Predictive value of CAR for the occurrence of MACE after elective PCI in elderly UA patients

The ROC results (Table 3) showed that the AUC for CRP and ALB for predicting the occurrence of MACE after elective PCI

TABLE 1. Comparison of clinical data.

Parameter	MACE group (n = 62)	Non-MACE group (n = 245)	<i>t</i> / χ^2	<i>p</i>
Sex (n (%))				
Male	35 (56.45)	118 (48.16)	1.360	0.244
Female	27 (43.55)	127 (51.84)		
Age (yr)	71.26 ± 5.73	69.56 ± 5.18	2.255	0.025
BMI (kg/m ²)	23.42 ± 1.18	23.11 ± 1.49	1.544	0.124
Smoking history (n (%))				
Yes	24 (38.71)	60 (24.49)	5.034	0.025
No	38 (61.29)	185 (75.51)		
History of alcohol consumption (n (%))				
Yes	21 (33.87)	64 (26.12)	1.484	0.223
No	41 (66.13)	181 (73.88)		
Comorbid underlying disease (n (%))				
Diabetes mellitus	23 (37.10)	58 (23.67)	4.590	0.032
Hypertension	21 (33.87)	55 (22.45)	3.465	0.063
Hyperlipidemia	16 (25.81)	50 (20.41)	0.854	0.355
Number of coronary artery lesions (n (%))				
Single	28 (45.16)	160 (65.31)	6.005	0.014
Multiple	34 (54.84)	85 (34.69)		
RDW (%)	15.05 ± 2.09	14.32 ± 1.79	2.797	0.005
WBC (×10 ⁹ /L)	10.02 ± 1.67	9.55 ± 1.99	1.704	0.089
PLT (×10 ⁹ /L)	222.02 ± 24.54	218.07 ± 30.07	0.957	0.339
NLR	5.51 ± 1.13	4.56 ± 0.88	7.085	<0.001
PLR	114.17 ± 10.89	112.49 ± 12.74	0.958	0.339
LVEF (%)	41.52 ± 8.06	44.96 ± 6.25	3.639	<0.001
LVEDD (mm)	46.23 ± 5.85	45.88 ± 5.08	0.462	0.645

MACE: major adverse cardiovascular events; BMI: body mass index; RDW: red blood cell distribution width; WBC: white blood cell count; PLT: platelet count; NLR: neutrophils/lymphocytes; PLR: platelets/lymphocytes; LVEF: left ventricular ejection fraction; LVEDD: left ventricular end-diastolic internal diameter.

TABLE 2. Comparison of CRP, ALB and CAR.

Group	n	CRP (mg/L)	ALB (g/L)	CAR (%)
MACE group	62	8.31 ± 2.12	31.75 ± 6.28	27.11 ± 8.29
non-MACE	245	5.02 ± 1.99	38.18 ± 4.65	13.33 ± 5.41
<i>t</i>		11.500	9.008	15.899
<i>p</i>		<0.001	<0.001	<0.001

CRP: C-reactive protein; ALB: albumin; CAR: C-reactive protein/albumin ratio; MACE: major adverse cardiovascular events.

in patients with UA were 0.869 and 0.792, respectively. These values corresponded to sensitivities of 74.19% and 70.97%, and specificity of 86.53% and 76.73%, suggesting that both CRP and ALB have a certain predictive value for the occurrence of adverse cardiovascular events. In contrast, the AUC for CAR was 0.918, which was significantly higher than that of CRP ($Z = 3.820$, $p = 0.0001$) and ALB ($Z = 3.490$, $p = 0.0005$). The sensitivity and specificity of CAR were 87.10% and 87.76%, respectively (Table 3).

3.4 Predictive performance of CAR in the single-branch coronary lesion group versus the multibranch coronary lesion group

UA patients were categorized into two groups based on the number of coronary lesion branches: the single coronary lesion group (n = 190) and the multiple coronary lesion group (n = 117). In the single-branch coronary lesion group, MACE occurred in 28 cases (14.74%). The ROC results showed (Table 4) that the AUCs for CRP, ALB and CAR in predicting the

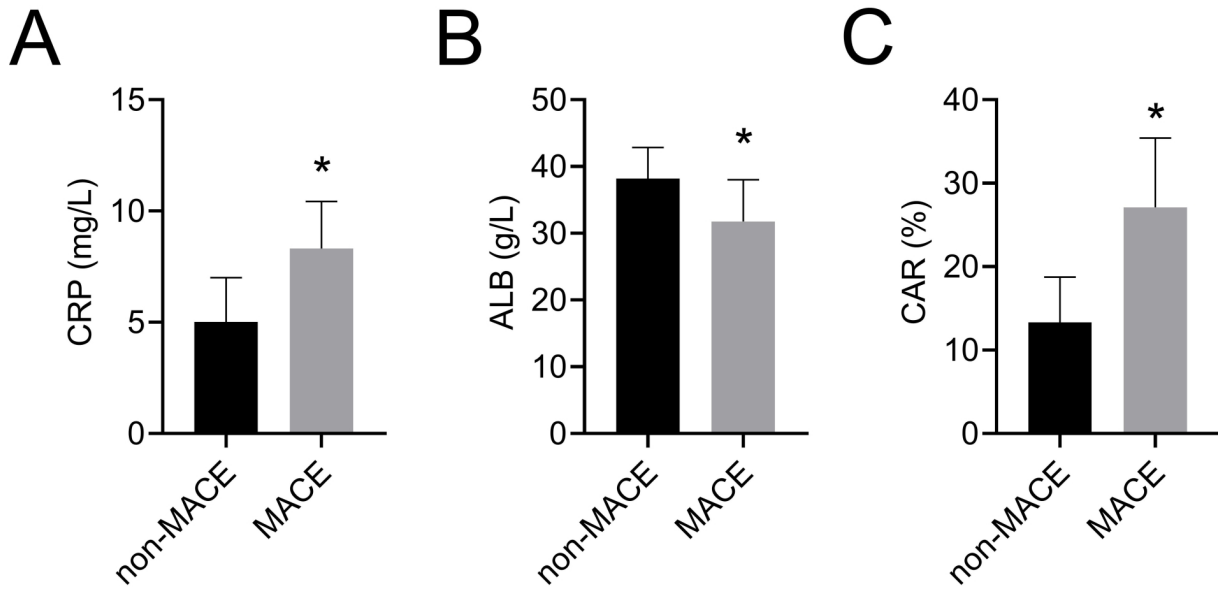


FIGURE 1. Comparison of CRP, ALB and CAR between MACE group and non-MACE group. (A) CRP; (B) ALB; (C) CAR. *: $p < 0.05$. MACE: major adverse cardiovascular events; CRP: C-reactive protein; ALB: albumin; CAR: C-reactive protein/albumin ratio.

TABLE 3. Predictive value of CAR for adverse cardiovascular events after elective PCI in elderly patients with UA.

Indicators	AUC	95% CI	Youden index	Cut-off value	p	Sensitivity (%)	Specificity (%)
CRP	0.869	0.826–0.905	0.607	>7.27	<0.001	74.19	86.53
ALB	0.792	0.742–0.836	0.477	≤34.60	<0.001	70.97	76.73
CAR	0.918	0.881–0.946	0.749	—	<0.001	87.10	87.76

AUC: area under the curve; CI: confidence interval; CRP: C-reactive protein; ALB: albumin; CAR: C-reactive protein/albumin ratio.

TABLE 4. Predictive efficacy of CAR in UA patients with single-vessel coronary disease.

Indicators	AUC	95% CI	Youden index	Cut-off value	p	Sensitivity (%)	Specificity (%)
CRP	0.878	0.823–0.921	0.662	>6.1	<0.001	96.43	69.75
ALB	0.814	0.751–0.866	0.528	≤30.8	<0.001	57.14	95.68
CAR	0.900	0.849–0.939	0.771	—	<0.001	85.71	91.36

AUC: area under the curve; CI: confidence interval; CRP: C-reactive protein; ALB: albumin; CAR: C-reactive protein/albumin ratio.

occurrence of MACE after elective PCI in patients were 0.878, 0.814 and 0.900, respectively. These values corresponded to sensitivities of 96.43%, 57.14% and 85.71%, and specificities of 69.75%, 95.68% and 91.36%, respectively. These results suggest that CAR has a good predictive efficacy in UA patients with single-branch coronary lesions.

In the multi-branch coronary lesion group, MACE occurred in 34 cases (29.06%). The ROC results showed (Table 5) that the AUCs for CRP, ALB and CAR in predicting the occurrence of MACE after elective PCI in patients were 0.808, 0.777 and 0.850, respectively. These values corresponded to sensitivities of 64.71%, 67.65% and 76.47%, and specificities of 90.36%, 79.52% and 87.95%, respectively, suggesting a good predictive value of CAR also in UA patients with multiple coronary lesions.

3.5 Multivariate analysis of adverse cardiovascular events after elective PCI in elderly UA patients

After excluding covariance indicators, a multivariate logistic regression model was constructed with the occurrence of adverse cardiovascular events after PCI as the dependent variable. Independent variables included smoking history, comorbid diabetes mellitus, number of coronary lesions branches, age, RDW, NLR, LVEF and CAR. The results showed that smoking history, multiple coronary lesions, age, NLR and CAR were independent risk factors for the occurrence of MACE in elderly patients with unstable angina ($p < 0.05$, Table 6).

TABLE 5. Predictive efficacy of CAR in UA patients with multi-vessel coronary lesions.

Indicators	AUC	95% CI	Youden index	Cut-off value	<i>p</i>	Sensitivity (%)	Specificity (%)
CRP	0.808	0.725–0.875	0.551	>7.55	<0.001	64.71	90.36
ALB	0.777	0.690–0.849	0.472	≤34.30	<0.001	67.65	79.52
CAR	0.850	0.772–0.909	0.749	—	<0.001	76.47	87.95

AUC: area under the curve; CI: confidence interval; CRP: C-reactive protein; ALB: albumin; CAR: C-reactive protein/albumin ratio.

TABLE 6. Multivariate analysis.

Factors	β	S.E.	Wald	OR	95% CI	<i>p</i>
Age	0.112	0.045	6.178	1.119	1.024–1.223	0.013
Smoking history	1.424	0.505	7.936	4.152	1.541–11.178	0.005
Multiple coronary artery disease	1.184	0.497	5.681	3.267	1.234–8.649	0.017
NLR	1.062	0.284	14.007	2.891	1.658–5.041	<0.001
CAR	0.336	0.050	45.428	1.400	1.269–1.543	<0.001

β : regression coefficient; S.E.: standard error; OR: odds ratio; CI: confidence interval; NLR: neutrophils/lymphocytes; CAR: C-reactive protein/albumin ratio.

4. Discussion

Elderly patients with UA are often accompanied by a variety of underlying diseases, such as hypertension and diabetes mellitus, which make their coronary artery lesions more complex and variable. This makes the occurrence of MACE after PCI a significant clinical challenge [13]. Therefore, identifying effective predictive indicators to assess the risk of MACE after PCI in elderly UA patients is important. Such indicators can guide the development of individualized treatment strategies and enable clinicians to implement timely interventions, ultimately improving patient outcomes and prognosis.

Coronary atherosclerosis is the basis for the development and progression of coronary heart disease. Inflammation, endothelial dysfunction and oxidative stress are among the major causes of atherosclerosis, leading to the development and progression of many cardiovascular diseases. CRP is a non-specific acute time-phase response protein synthesized by the liver, which increases rapidly in response to inflammation, infection and tissue injury. In cardiovascular diseases, CRP serves not only as a marker of inflammatory response, but also plays a direct role in the development of atherosclerosis [14]. Elevated CRP levels have been shown to be closely associated with adverse cardiovascular events such as myocardial infarction, heart failure, and cardiac death [15, 16]. ALB, the most abundant plasma protein, plays a multifaceted role in the physiological processes of the body [17]. ALB can regulate coagulation factors activity and platelet surface receptors function. By binding to some glycoprotein receptors on the platelet surface, ALB alters the spatial conformation of the receptor, which reduces its affinity for fibrinogen and thereby inhibiting the aggregation reaction between platelets. Additionally, ALB's antioxidant properties reduces the degree of platelet activation and decreases the possibility of platelet aggregation by maintaining the redox balance. ALB is also considered to be an important indicator for assessing the nutritional status. Low levels of ALB reflects a deteriora-

tion in nutritional status, reduced stress capacity, impaired recovery and are often associated with a poor prognosis [18–20]. CAR comprehensively reflect the inflammatory state and nutritional status of the organism, providing a new perspective for predicting cardiovascular events. In this study, CAR demonstrated high predicting value in the occurrence of MACE after PCI in elderly UA patients, and patients with elevated CAR were more likely to experience adverse events such as myocardial infarction and heart failure following PCI. We hypothesize that high levels of CAR may reflect an imbalance in the body's inflammatory and nutritional status, which may impair the normal functioning of vascular endothelial cells, such as decreasing nitric oxide (NO) production and increasing endothelin-1 (ET-1) release, leading to vasodilatory dysfunction, vasoconstriction, and an increased propensity for thrombosis. Together, these changes contribute to the destabilization of atherosclerotic plaques, ultimately elevating the risk of cardiovascular events.

Many factors may influence the occurrence of MACE after PCI. This study identified smoking history, multiple coronary artery lesions, age and NLR as risk factors for adverse cardiovascular events after elective PCI in elderly UA patients. Long-term smoking leads to increased blood viscosity and affects normal glycolipid metabolism. Abnormal glycolipid metabolism can impair vascular endothelial function and increase the release of inflammatory factors, leading to disruption of coagulation and fibrinolytic homeostasis, increasing the risk of arterial plaque rupture and the occurrence of MACE [21]. Multi-branch coronary lesions are one of the common pathologic features in elderly patients with UA, and their complexity lies in the fact that the lesions may involve multiple coronary arteries at the same time, leading to extensive and severe myocardial insufficiency [22]. Compared with single-branch lesions, patients with multi-branch lesions are more prone to complications such as myocardial ischemia-reperfusion injury, in-stent restenosis, and heart failure after PCI. The body's physiological functions gradually decline with

age, and the function of each organ also declines. Previous study has demonstrated decreased elasticity and increased brittleness of the vascular wall in elderly patients, increasing the incidence of complications such as vascular perforation and entrapment during the procedure [23]. At the same time, the weakening of the immune system in elderly patients makes them less tolerant to surgical stress, making highly susceptible to postoperative complications such as infections. Those patients have very less chance to postoperative recovery. Neutrophils play a key role in the inflammatory response, and an increase in their number reflects the body's enhanced stress response to injury [24]. Lymphocytes, on the other hand, are involved in immunoregulatory processes, and a decrease in their number may reflect a decline in immune function [25]. In elderly patients with UA, elevated NLR levels tend to signal a more severe inflammatory response and a higher risk of cardiovascular events.

The study has some limitations: Firstly, there was some selection bias in including patients only with unstable angina; Secondly, this study, as a single-center, retrospective analysis, had a short follow-up period for patients. In addition, only general research directions was proposed for inflammation and immunoregulatory mechanisms, endothelial function and coagulation mechanisms, which have not yet been supported by specific experimental data. To address these limitations, future studies need to incorporate larger sample sizes and more extensive data to confirm the findings of this study and to explore in depth the linkage of related mechanisms.

5. Conclusions

In conclusion, CAR has been proven to be a reliable predictor of MACE in elderly patients with UA undergoing PCI. Regular monitoring of CAR levels postoperatively can facilitate the early identification of patients at heightened risk for MACE. This early detection provides strong clinical support for the development of individualized treatment strategies and optimizing therapeutic regimens, ultimately improving patient outcomes and prognosis.

AVAILABILITY OF DATA AND MATERIALS

The authors declare that all data supporting the findings of this study are available within the paper and any raw data can be obtained from the corresponding author upon request.

AUTHOR CONTRIBUTIONS

JHC, YPM—designed the study and carried them out, prepared the manuscript for publication and reviewed the draft of the manuscript. JHC, MNF, LLF, XHC—supervised the data collection, analyzed the data, interpreted the data. All authors have read and approved the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval was obtained from the Ethics Committee of Hangzhou Ninth People's Hospital (Approval no. 2024-088). Written informed consents were obtained from a legally authorized representative for anonymized patient information to be published in this article.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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