The association between C-reactive protein/albumin ratio and coronary collateral circulation in patients with chronic coronary syndromes and chronic total occlusion

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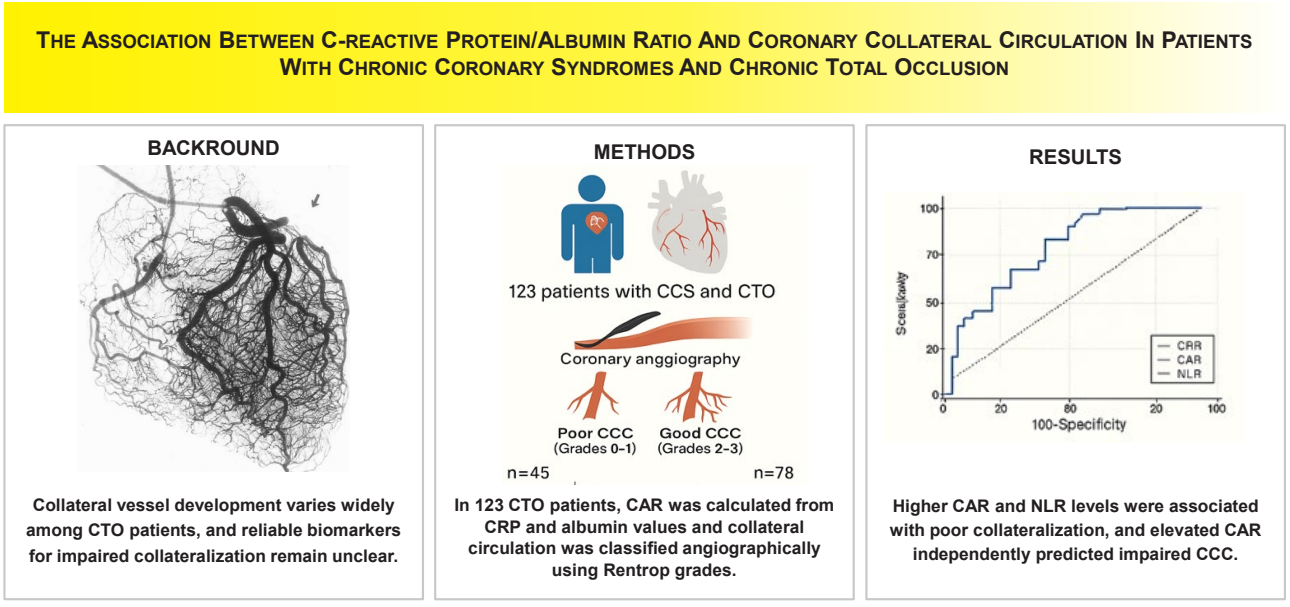
Background. The C-reactive protein-to-albumin ratio (CAR) has recently gained attention as a novel biomarker reflecting both systemic inflammation and nutritional status. Since inflammation plays a critical role in the formation of the coronary collateral circulation (CCC), this study aimed to investigate the association between CAR and the extent of CCC in patients with chronic coronary syndromes (CCS) and chronic total occlusion (CTO).
Methods. A total of 123 consecutive patients with CCS and angiographically documented CTO were included. CCC was assessed using the Rentrop classification and patients were divided into two groups: poor CCC (grades 0–1) and good CCC (grades 2–3). Laboratory data including C-reactive protein (CRP), albumin, lipid parameters, renal and liver function tests, glucose, and complete blood count were recorded. CAR was calculated by dividing CRP (mg/L) by albumin (g/dL), and neutrophil-to-lymphocyte ratio (NLR) was also evaluated.
Results. Patients with poor CCC had significantly higher CRP, CAR, and NLR levels ($P<0.05$ for all). In multivariate logistic regression, both CAR (OR=1.200, 95% CI: 1.102–1.394, $P<0.001$) and NLR were independently associated with poor CCC. ROC analysis showed that CAR had better predictive value (AUC=0.79) than CRP (AUC=0.75, $P=0.02$) and NLR (AUC=0.67, $P=0.03$). A CAR cutoff of 2.36 yielded 67% sensitivity and 68% specificity.
Conclusion. Elevated CAR is independently associated with impaired CCC in patients with CCS and CTO. CAR may serve as a simple and superior marker over traditional inflammatory indices in assessing collateral vessel development.



Key words: C-reactive protein (CRP), albumin, CRP/albumin ratio (CAR), coronary collateral circulation (CCC), inflammation, chronic coronary syndromes (CCS)

Received: July 15, 2025; Revised: January 29, 2026; Accepted: March 30, 2026; Available online: April 16, 2026
https://doi.org/10.5507/bp.2026.010

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INTRODUCTION

Coronary collateral circulation (CCC) represents a vital compensatory mechanism that provides an alternative blood supply to myocardial tissue distal to an occluded coronary artery. In cases of severe coronary stenosis or complete blockage, well-formed collateral arteries may mitigate ischemia damage, decrease infarct size, maintain ventricular function, and eventually enhance survival rates[1]. Despite its clinical significance, the extent of collateral development varies markedly among individuals, even in the presence of similar degrees of coronary obstruction, and the underlying determinants of this variability remain only partially elucidated.

The formation of CCC is governed by complex biological processes, including arteriogenesis and angiogenesis, which are modulated by various mechanical, metabolic, and molecular stimuli. Among these, inflammation has emerged as a key regulatory factor. Low-grade inflammation that persists not only facilitates the onset and advancement of atherosclerosis but also affects vascular remodeling and the development of new collateral arteries[2,3].

Several lines of evidence support a link between systemic inflammatory status and the extent of coronary collateralization. For example, increased circulating monocyte counts, indicative of systemic inflammation, have been linked to improved collateral development, whereas heightened levels of C-reactive protein (CRP), a classic acute-phase reactant, have shown an inverse correlation with collateral the development among individuals with chronic coronary syndromes (CCS) (ref.[4,5]). Both CRP and serum albumin are established markers of inflammation, with CRP reflecting pro-inflammatory activity and albumin representing a negative acute-phase reactant that also reflects nutritional status. Each of these indicators has been linked to the existence and severity of atherosclerosis[6].

Recently, the CRP/albumin ratio (CAR) has gained attention as a composite inflammatory marker that integrates the opposing inflammatory dynamics of CRP and albumin. This ratio has been shown to outperform CRP or albumin alone in predicting adverse outcomes in various cardiovascular settings, including the severity of CAD and the probability of in-stent restenosis[6,7].

Considering the mechanistic interplay between inflammation and collateral vessel formation, we hypothesized that CAR might serve as a useful marker for assessing the extent of CCC. This research aims to examine the correlation between CAR and CCC development in individuals with CCS underwent coronary angiography.

METHODS

Study population

From April 2017 to March 2021, 123 consecutive patients (99 males and 24 females; median age: 65 years, range: 46–78 years) diagnosed with CCS and who underwent diagnostic coronary angiography at Dışkapı Yıldırım Beyazıt Training and Research Hospital were prospectively included in this study. All included patients were found to have a chronic total occlusion (CTO), defined as a complete blockage with TIMI 0 flow for more than three months, in at least one of the major epicardial coronary arteries. The decision to perform coronary angiography was based on clinical symptoms suggestive of myocardial ischemia or abnormal results from non-invasive stress testing.

Patients were excluded if they had any systemic or chronic conditions that might possibly affect inflammatory or nutritional biomarkers. The exclusion criteria were delineated as follows: Active systemic infection, including sepsis; chronic infectious diseases such as tuberculosis or chronic viral hepatitis; autoimmune or inflammatory disorders; ongoing treatment with corticosteroids, immunosuppressive agents, or non-steroidal anti-inflammatory drugs; advanced hepatic dysfunction or clinically active hepatitis; end-stage renal disease necessitating dialysis; history of malignancy; prior coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI); diagnosis of acute coronary syndrome (ACS) within the last 3 months; moderate to severe valvular heart disease; and symptomatic heart failure with a left ventricular ejection fraction (LVEF) below 50%. These criteria were implemented to reduce confounding variables that might influence the inflammatory markers being examined.

Comprehensive demographic, clinical, and laboratory data were gathered upon admission. Conventional cardiovascular risk variables, including age, sex, hypertension (HT), diabetes mellitus (DM), hyperlipidemia, and smoking status, were documented for all individuals. HT is characterized by a systolic blood pressure of ≥140 mmHg, a diastolic blood pressure of ≥90 mmHg, or the current use of antihypertensive medication[8]. DM is characterized by a fasting plasma glucose level above 126 mg/dL, a glycated hemoglobin (HbA1c) level of 6.5% or more, or continuous management with insulin or oral hypoglycemic medications[9]. Smoking status was classified as current, former, or never smoker according to self-report.

The local institutional ethics committee examined and approved the research protocol before its beginning. All subjects furnished signed informed permission prior to their enrollment in the research. The study adhered to the ethical principles established by the Declaration of Helsinki, and all patient data was anonymised to maintain anonymity.

Coronary angiography and collateral circulation assessment

All participants underwent conventional selective coronary angiography, which was performed by experienced interventional cardiologists using the Judkins technique through a transfemoral arterial access. The procedure was conducted under sterile conditions in accordance with institutional protocols. To diminish interobserver variability and improve diagnostic precision, all angiographic record-

ings were assessed separately by two board-certified interventional cardiologists who were unaware of the patients' clinical features and laboratory values.

CCC was assessed using the Rentrop–Cohen classification, a widely utilized and validated angiographic grading system for evaluating collateral vessel development[10]. Collateral flow is categorized on a scale from 0 to 3. Grade 0 signifies the absence of visible collateral filling, grade 1 indicates filling of the side branches of the occluded artery without visualization of the main epicardial segment, grade 2 denotes limited filling of the epicardial artery, and grade 3 represents full filling of the distal vessel via collateral channels. Based on this scoring system, patients were categorized into two groups: those with poor collateral circulation (Rentrop grades 0 and 1) and those with good collateral development (Rentrop grades 2 and 3). In individuals with multivessel coronary artery disease and multiple total occlusions, the occluded artery exhibiting the most prominent collateral filling – whether through antegrade bridging or retrograde recruitment – was selected for scoring to provide a representative estimate of the patient's overall collateral status.

Any discordance in grading between the two independent reviewers was addressed by joint review and consensus decision. This rigorous and standardized evaluation process ensured consistency, objectivity, and reproducibility in the angiographic assessment of coronary collateral circulation across the entire study cohort.

Laboratory measurements

Fasting venous blood samples were collected from all study participants during the early morning hours, prior to the index coronary angiography procedure, to ensure standardization and minimize potential diurnal variations in biochemical parameters. All samples were promptly transported to the central biochemistry laboratory of our institution, where analyses were conducted under uniform conditions using validated methods and calibrated equipment.

The laboratory investigations included a comprehensive panel of routine biochemical and hematological parameters. These consisted of a complete blood count, fasting plasma glucose, serum creatinine, alanine aminotransferase (ALT), lipid profile (including total cholesterol, LDL-C, HDL-C, and triglycerides), serum albumin, and CRP. Measurement of CRP and albumin levels was carried out using an automated Cobas C702 analyzer (Roche Diagnostics, Tokyo, Japan), following the manufacturer's specifications and internal quality control procedures. The normal reference intervals for CRP and albumin were 0.0–5.0 mg/L and 3.5–5.2 g/dL, respectively.

To derive a combined index that reflects both systemic inflammation and nutritional status, the CAR was calculated by dividing the CRP value (mg/L) by the albumin concentration (g/dL). This ratio has been increasingly recognized as a prognostic marker in various cardiovascular and systemic inflammatory conditions due to its ability to integrate two biologically distinct yet interrelated processes.

Renal function was evaluated by estimating the glomerular filtration rate (eGFR), which was calculated using the Cockcroft–Gault equation. This formula incorporates serum creatinine, age, sex, and body weight to provide an approximation of renal clearance capacity. All biochemical and hematological values were interpreted in the context of each patient's clinical profile, ensuring a comprehensive assessment of their metabolic, inflammatory, and nutritional status.

Statistical analysis

All statistical analyses were conducted using IBM SPSS Statistics, version 20.0 (SPSS Inc., Chicago, IL, USA). The distribution of continuous variables was first assessed for normality using the Kolmogorov–Smirnov test. Data exhibiting a normal distribution are represented as means ± standard deviation (SD), whilst non-normally distributed data are summarized as medians with interquartile ranges (IQR), yielding reliable estimations of central tendency and variability. Categorical variables are expressed as frequencies and percentages. Comparisons between groups of individuals with poor and excellent coronary collateral circulation were conducted using suitable statistical tests, chosen according to the distribution features of each variable. The independent samples t-test was used for continuous variables with a normal distribution, whereas the Mann–Whitney U test was used for data that did not meet normality assumptions. The Chi-square test or Fisher's exact test was used for comparisons of categorical data, contingent upon predicted frequency counts. Independent predictors of inadequate collateral development were identified by including factors with a $P<0.10$ from the univariate study into a multivariate logistic regression model. The findings were presented as odds ratios (OR) accompanied by 95% confidence intervals (CI), offering an assessment of the association's strength and accuracy. The efficacy of inflammatory markers – specifically CRP, neutrophil-to-lymphocyte ratio (NLR), and CAR – in detecting inadequate collateral circulation was assessed by receiver operating characteristic (ROC) curve analysis. The area under the curve (AUC) was calculated for each parameter, and the DeLong technique was used to compare AUCs and ascertain statistical differences in predicting accuracy. The ideal cutoff value for CAR was determined by optimizing Youden's index. A two-tailed P below 0.05 was deemed indicative of statistical significance across all tests.

RESULTS

A total of 123 patients (80.5% male; median age: 65 years [range: 46–78]) with CCS were included. Based on the Rentrop classification, 66 patients (53.7%) were classified as having poor CCC (grades 0–1), and 57 patients (46.3%) as having good CCC (grades 2–3).

Baseline demographic, clinical, and angiographic characteristics of the study population are presented in

Table 1. Baseline characteristics and coronary angiographic findings.

	Poor CCC (n=45)	Good CCC (n=78)	*P*
Age, years	67 (46-77)	61 (55–78)	0.75
Gender ,male n (%)	39 (86.7)	60 (76.9)	0.24
Diabetes Mellitus, n (%)	33 (73.3)	43 (54.5)	0.02
Hypertension, n (%)	32 (71.1)	53 (67.9)	0.84
Hyperlipidemia n (%)	31 (68.9)	46 (59)	0.33
Smoking, n (%)	31 (68.9)	50 (64.1)	0.69
Number of vessel disease:			0.15
1-Vessel disease, n (%)	16 (35.6)	42 (53.8)	
2-Vessel disease, n (%)	12 (26.7)	15 (19.2)	
3-vessel disease, n (%)	17 (37.8)	21 (26.9)	
Occluded coronary:			0.50
Occluded LAD, n (%)	19 (42.2)	39 (50)	0.16
Occluded CX, n (%)	10 (22.2)	14 (17.9)	0.10
Occluded RCA, n (%)	16 (35.6)	25 (32.1)	0.10

CCC, coronary collateral circulation; CX, left circumflex artery; LAD, left anterior descending artery; RCA, right coronary artery.

Table 2. Comparison of laboratory parameters between poor and good CCC groups.

	Poor CCC (n=45)	Good CCC (n=78)	*P*
Glucose, mg/dL	198 (108–353)	161 (60–328)	<0.01
Creatinin, mg/dL	1.13 (0.89–1.55)	1.08 (0.93–1.32)	0.81
eGFR (mL/min)	64 (45–103)	61 (50–86)	0.23
C-Reactive protein (mg/L)	10.5 (2.5–14)	5.0 (0.5–15.5)	<0.01
Serum albumin (g/dL)	3.7 (3.0–4.5)	4.1 (3.0–5.1)	<0.01
CRP/albumin ratio	2.8 (0.6–3.8)	1.3 (0.1–4.2)	<0.01
ALT, U/L	33 (26–46)	33 (21–43)	0.02
Total cholesterol, mg/dL	215.3 ± 67.0	202.4 ± 54.1	0.24
LDL-C, mg/dL	130.6 ± 48.2	21.5 ± 40.0	0.26
HDL-C, mg/dL	45.9 ± 7.0	45.7 ± 7.2	0.90
Triglyceride, mg/dL	185 (77–437)	164 (61–341)	0.69
WBC, 103/mm^3	9.4 (5.2–11.5)	9.3 (5.3–11)	0.31
Hemoglobin, g/dL	13.1 (11.1–15.9)	12.7 (10.9–15.5)	0.04
Platelet count, 1000/mm^3	225 (165–292)	252 (177–299)	0.09
NLR	5.0 (1.53–11.1)	3.75 (1.56–10)	0.03

ALT, alanine aminotransferase; CCC, coronary collateral circulation; eGFR, estimated glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; NLR, neutrophil-to-lymphocyte ratio; WBC, white blood cell.

Table 1. The median age was 67 years in the poor CCC group and 61 years in the good CCC group (*P*=0.75). Male sex was observed in 86.7% of the poor CCC group and 76.9% of the good CCC group (*P*=0.24). The prevalence of DM was significantly higher in the poor CCC group (73.3% vs. 54.5%, *P*=0.02). No significant differences were observed in the prevalence of HT, hyperlipidemia, or smoking. The distribution of vessel disease and occlusion sites (LAD, CX, RCA) was also statistically similar between groups.

Laboratory parameters of the two groups are summarized in Table 2. Patients with poor CCC had significantly higher CRP, CAR, and NLR levels (*P*<0.01 for all). Serum albumin levels were significantly lower in this group (3.7 g/dL vs. 4.1 g/dL, *P*<0.01). Glucose levels were also significantly elevated in patients with poor CCC (198 mg/dL vs. 161 mg/dL, *P*<0.01). ALT levels were similar in median value but differed in distribution (*P*=0.02). No significant differences were noted in total cholesterol, LDL-C, HDL-C, triglycerides, WBC, or platelet counts. Hemoglobin was lower in the poor CCC group (13.1 g/dL vs. 12.7 g/dL, *P*=0.04).

In multivariate logistic regression analysis, elevated CAR (OR=1.200, 95% CI: 1.102–1.394, *P*<0.001), NLR (OR=1.640, 95% CI: 1.442–1.926, *P*=0.018), glucose (OR=1.986, 95% CI: 1.974–1.997, *P*=0.012), ALT (OR=1.704, 95% CI: 1.579–1.857, *P*<0.001), and DM (OR=1.216, 95% CI: 1.053–1.877, *P*=0.032) were identified as independent predictors of poor CCC. Hemoglobin showed a borderline association (*P*=0.100).

Table 3. Logistic regression analysis results.

	P	OR	95% CI
NLR	0.018	1.640	1.442–1.926
CAR	<0.001	1.200	1.102–1.394
Glucose	0.012	1.986	1.974–1.997
ALT	<0.001	1.704	1.579–1.857
Hemoglobin	0.100	1.571	0.993–1.813
Diabetes Mellitus	0.032	1.216	1.053–1.877

ALT, Alanine aminotransferase; CAR, C-reactive protein/albumin ratio; CI, Confidence interval; NLR, Neutrophil-to-lymphocyte ratio; OR, Odds ratio.

Receiver operating characteristic (ROC) curve analysis showed that CAR had the highest predictive value for identifying poor CCC with an AUC of 0.79 (95% CI: 0.71–0.87). This was significantly greater than the AUCs for CRP (0.75; 95% CI: 0.51–0.73; *P*=0.02) and NLR (0.67; 95% CI: 0.57–0.77; *P*=0.03). A CAR cutoff value of 2.36 yielded a sensitivity of 67% and specificity of 68%.

DISCUSSION

The CAR has emerged as a potential composite biomarker indicative of both systemic inflammation and nutritional status. Numerous investigations have shown its prognostic significance in several cardiovascular disorders, including chronic coronary syndrome, acute coronary syndromes, and heart failure[11-13]. This research demonstrates for the first time that an increased CAR is independently linked to worse CCC in patients with CCS. Significantly, CAR surpassed both CRP and NLR in forecasting compromised collateral formation, achieving an AUC of 0.79 and a cutoff value of 2.36, yielding 67% sensitivity and 68% specificity.

The development of CCC is a complex and multifactorial process influenced by hemodynamic, metabolic, genetic, and immunologic factors[14-15]. Among these, inflammation has been widely recognized as a central regulator of both atherosclerotic progression and angiogenesis, which are critical in collateral formation. Experimental studies have shown that elevated CRP levels directly impair endothelial function by suppressing nitric oxide (NO) production and inhibiting endothelial cell migration in response to vascular endothelial growth factor (VEGF) (ref.[16,17]). These mechanisms may partly explain the inverse relationship observed between CRP levels and the extent of CCC in clinical settings.

Albumin, the other component of CAR, is a negative acute-phase reactant with antioxidant, anti-inflammatory, and antiplatelet properties. Hypoalbuminemia is associated with increased blood viscosity, oxidative stress, endothelial dysfunction, and increased LDL oxidation—all of which are known contributors to impaired collateral development[18-20]. The combination of high CRP and low albumin yields a high CAR, which amplifies the inflammatory and metabolic burden. This integrated index may therefore provide a more accurate reflection of impaired vascular adaptation capacity than either parameter alone.

Our findings build on previous studies that highlighted the prognostic role of CAR in cardiovascular risk stratification. Karabağ et al. demonstrated an association between CAR and the severity of CAD in patients with stable angina[6]. By demonstrating an independent association between CAR and poor CCC, our study expands this body of evidence and emphasizes the utility of CAR in evaluating ischemic adaptation.

The observed relationship between an elevated CAR and insufficient coronary collateral development may, at least in part, be explained by underlying pathophysiological mechanisms involving endothelial dysfunction, oxidative stress, and impaired vascular remodeling. NO, a critical regulator of vascular tone and endothelial integrity, also facilitates collateral vessel recruitment in response to ischemia. Experimental evidence has demonstrated that CRP can downregulate endothelial nitric oxide synthase (eNOS), thereby reducing NO bioavailability and promoting endothelial impairment, as reported by Verma and colleagues[16]. Additionally, Schneeweis et al. identified that CRP may attenuate the angiogenic response by interfering with VEGF-mediated endothelial cell migration[17]. Taken together, these findings suggest that heightened systemic inflammation – as reflected by increased CRP – may negatively influence collateral formation through the inhibition of angiogenesis-related pathways.

In parallel, hypoalbuminemia has been shown to promote a pro-inflammatory and pro-atherogenic state. It is associated with increased blood viscosity and enhanced LDL oxidation, both of which promote vascular injury and inhibit adaptive vascular remodeling[18]. Albumin also exerts antioxidant and antithrombotic effects that may be essential in maintaining endothelial integrity under ischemic stress[19,20]. Taken together, the combination of high CRP and low albumin may represent a cumulative insult on vascular health, reflected by a high CAR and poor collateral development.

We also confirmed the previously reported association between NLR and poor CCC (ref.[21,22]). NLR, as an established inflammatory marker, has been linked to adverse vascular outcomes in patients with chronic total occlusion (CTO) and CAD (ref[23,24]). Although both CAR and NLR were independent predictors of impaired CCC in our regression analysis, CAR showed superior discriminatory power, suggesting its enhanced utility in clinical risk assessment.

In line with existing evidence, diabetes mellitus emerged as an independent predictor of impaired collateralization, supporting previous reports linking metabolic dysfunction with compromised angiogenic capacity[25,26]. Although hyperglycemia and insulin resistance are generally associated with impaired endothelial function and angiogenesis, paradoxical findings have been reported[25]. One explanation is that patients with long-standing DM may develop adaptive angiogenic responses to chronic ischemia, resulting in enhanced collateralization despite metabolic dysfunction[26].

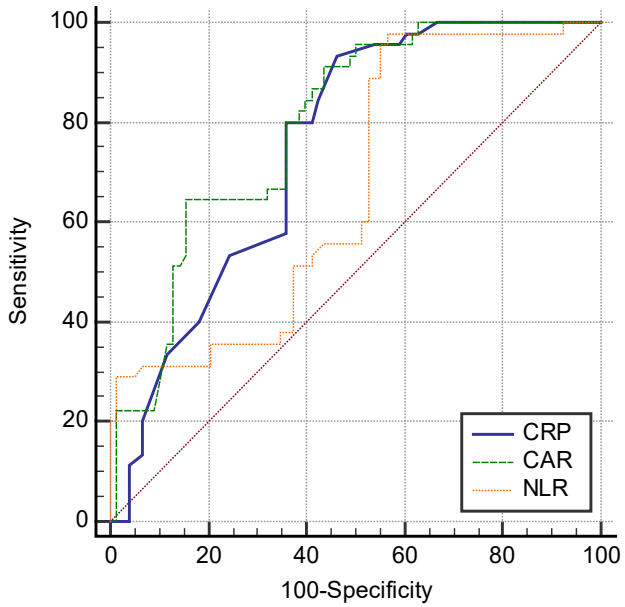

Fig. 1. Receiver operating characteristic (ROC) curve analysis of C-reactive protein/albumin ratio (CAR), C-reactive protein (CRP), and neutrophil-to-lymphocyte ratio (NLR) for the prediction of poor coronary collateral circulation.

Moreover, fasting glucose and ALT levels were independently associated with poor CCC. Elevated ALT, although traditionally a marker of hepatocellular injury, may reflect underlying hepatic steatosis or metabolic syndrome, both of which are associated with endothelial dysfunction and systemic inflammation[27,28]. However, the lack of hepatic imaging and insulin resistance markers in our study limits the interpretability of this finding.

Taken together, our findings suggest that CAR, as a simple and cost-effective biomarker, may be incorporated into clinical evaluation to help identify patients with impaired collateralization capacity. Early identification of such patients may allow for aggressive management of modifiable risk factors, including systemic inflammation, oxidative stress, and metabolic abnormalities. Future studies should explore the longitudinal association between CAR and major adverse cardiovascular events (MACE), as well as the potential therapeutic value of modulating inflammation in improving collateral development. The inclusion of biomarkers such as VEGF, interleukins, and oxidative stress indices may help elucidate the underlying mechanisms linking CAR and vascular remodeling[29].

Although CAR demonstrated promising discriminatory power in identifying patients with impaired collateralization, the clinical relevance of this finding – particularly whether CAR predicts outcomes such as procedural success during CTO PCI, symptom burden, or long-term cardiovascular events – remains to be determined. Therefore, large-scale prospective studies incorporating procedural and prognostic endpoints are warranted to clarify the clinical applicability of CAR-guided risk stratification.

Future directions

The present study establishes a novel link between elevated CAR and impaired CCC in patients with CCS. While these findings provide valuable insights, they also open several avenues for future research.

First, prospective longitudinal studies are needed to confirm the prognostic value of CAR for long-term cardiovascular outcomes such as myocardial infarction, need for revascularization, and mortality in patients with chronic total occlusion. Tracking CAR dynamics over time may further clarify its role as a monitoring tool in therapeutic strategies targeting inflammation and vascular remodeling.

Second, future research should incorporate more comprehensive biomarker profiling, including pro-inflammatory cytokines (e.g., IL-6, TNF-α), oxidative stress markers, and angiogenic mediators like VEGF, to elucidate the pathophysiological mechanisms underlying the association between CAR and collateral development. Integration of these markers may help distinguish patients with impaired adaptive vascular responses despite similar levels of coronary occlusion.

Third, advanced imaging modalities such as myocardial perfusion imaging, cardiac MRI, or 3D coronary CT angiography could complement angiographic assessments to provide more accurate and functional evaluation of collateral circulation. These tools may overcome the inherent limitations of the Rentrop grading system and offer better standardization across studies.

Additionally, interventional studies exploring whether anti-inflammatory therapies, nutritional optimization, or metabolic control can modulate CAR levels and subsequently improve collateral formation could have important clinical implications. Stratifying patients by CAR in clinical trials may help identify high-risk individuals who could benefit from more intensive management strategies.

Finally, studies involving larger, multi-ethnic populations and multi-center designs will be crucial to validate the generalizability and external applicability of CAR as a predictive biomarker of coronary collateral development.

Limitations

This study has several limitations. First, it was designed as a single-center investigation with a relatively limited sample size; therefore, caution is needed when generalizing these findings to broader populations. Second, owing to its cross-sectional design, inflammatory and nutritional markers were assessed only at baseline, and potential changes following successful revascularization could not be evaluated. Third, myocardial viability was not directly assessed using advanced imaging modalities and was instead inferred indirectly through preserved left ventricular systolic function, persistent anginal symptoms despite optimal medical therapy, and the absence of significant regional wall motion abnormalities on echocardiography. Finally, although CAR showed promising diagnostic value, its impact on procedural or long-term clinical outcomes was not examined, limiting direct clinical interpretation of our results. Large-scale, multicenter prospective studies incorporating serial biomarker measurements, viability imaging, post-revascularization changes, and outcome-based analyses are warranted to address these gaps and further elucidate the interplay between

inflammation, metabolic status, and collateral vessel development.

CONCLUSION

In this study, we identified a significant and independent association between an elevated CAR and impaired CCC in patients with CCS. CAR, a composite marker reflecting both systemic inflammation and nutritional status, demonstrated superior predictive value compared to traditional inflammatory markers such as CRP and NLR. These findings highlight the potential clinical utility of CAR as a simple, inexpensive, and reliable biomarker for assessing collateral vessel development in routine cardiovascular risk stratification.

Given the critical role of coronary collaterals in preserving myocardial perfusion, especially in the setting of chronic total occlusion, identifying patients with poor collateralization has important prognostic and therapeutic implications. Early recognition of such patients using readily available laboratory parameters like CAR may help guide the intensity of medical therapy, optimize risk factor control, and prioritize consideration for advanced diagnostic or interventional strategies.

Furthermore, the link between CAR and poor CCC supports the notion that systemic inflammation and metabolic imbalance may impair vascular remodeling and limit adaptive responses to ischemia. These insights open new avenues for exploring targeted interventions aimed at modulating inflammation and improving endothelial function as a means of enhancing collateral growth.

Nevertheless, as this was a cross-sectional, single-center study with a modest sample size, further large-scale, prospective, and multicenter investigations are warranted to confirm our results, assess longitudinal outcomes, and elucidate the mechanistic pathways through which CAR influences vascular adaptation. Incorporation of additional biomarkers and advanced imaging modalities in future studies may also enhance our understanding of the interplay between systemic inflammation, nutritional status, and coronary collateral development.

Author contributions: SI, VOT, CT, SK, KA, BO: contributed to conceptualization; SI, CT, VOT, SK: contributed to data curation and validation; SI, CT, VOT: contributed to investigation and visualization; SI, SK, KA: contributed to resources; SI, CT, VOT, BO: contributed to writing – original draft preparation; CT, VOT, BO: contributed to writing – review and editing; VOT, BO: contributed to supervision; CT, VOT: contributed to project administration. All authors have read and agreed to the published version of the manuscript.

Conflict of interest statement: The authors declare that there are no conflicts of interest regarding the publication of this article.

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