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RESEARCH

The predictive role of the CALLY index for contrast-associated acute kidney injury in patients with stable angina pectoris

CALLY indeksinin koroner anjiyografi sonrası kontrast ilişkili akut böbrek hasarı öngörüsündeki rolü

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Abstract

Purpose: This study aimed to evaluate the predictive role of the C-reactive protein-albumin-lymphocyte (CALLY) index, which integrates systemic inflammation, nutritional status, and immune response for contrast-associated acute kidney injury in patients undergoing elective coronary angiography.

Material and Methods: This retrospective, single-center study included 945 patients who underwent elective coronary angiography for stable angina pectoris between 2020 and 2024. Patients with an ejection fraction <50%, those who required intra-aortic balloon pump support were excluded. Contrast-associated acute kidney injury was defined as an increase in serum creatinine ≥25% or ≥0.5 mg/dL within 72 hours after contrast exposure. Clinical characteristics, laboratory parameters, and the CALLY index were analyzed.

Results: Among 945 patients, 332 (35.1%) were female, median age was 58 years. Contrast-associated acute kidney injury developed in 150 patients (15.9%). In the multivariate CALLY-based model, advanced age, diabetes, lower albumin, lower bicarbonate, higher mean corpuscular volume, higher contrast volume and lower CALLY index were independent predictors, while C-reactive protein and uric acid lost significance.

Conclusion: The CALLY index independently predicted contrast-associated acute kidney injury but showed modest diagnostic strength. It may serve as a complementary immunonutritional marker rather than a standalone tool. Bicarbonate exhibited the highest diagnostic accuracy, supporting the role of metabolic acidosis in contrast-associated acute kidney injury.

Keywords: Contrast-associated acute kidney injury, coronary angiography, c-reactive protein

Öz

Amaç: Bu çalışmanın amacı, sistemik inflamasyon, beslenme durumu ve immün yanıtı birlikte değerlendiren C-reaktif protein (CRP)-albümin-lenfosit (CALLY) indeksinin, elektif koroner anjiyografi uygulanan hastalarda Kİ-ABH'yi öngörmedeki rolünü değerlendirmektir.

Gereç ve Yöntem: Bu retrospektif, tek merkezli çalışmaya 2020–2024 yılları arasında stabil anjina pektorisi nedeniyle elektif koroner anjiyografi uygulanan 945 hasta dahil edilmiştir. Ejeksiyon fraksiyonu <%50 olanlar ve intraaortik balon pompası gereksinimi bulunan hastalar çalışma dışı bırakılmıştır. Kontrast ilişkili akut böbrek hasarı, kontrast maruziyetinden sonraki 72 saat içinde serum kreatinin düzeyinde ≥%25 veya ≥0.5 mg/dL artış olarak tanımlanmıştır. Klinik özellikler, laboratuvar parametreleri ve CALLY indeksi analiz edilmiştir.

Bulgular: Toplam 945 hastanın 332'si (%35.1) kadın olup medyan yaş 58 idi. Kontrast ilişkili akut böbrek hasarı, 150 hastada (%15.9) gelişti. CALLY temelli çok değişkenli modelde ileri yaş, diyabet, düşük albümin, düşük bikarbonat, yüksek ortalama korpüsküler volüm, yüksek kontrast volümü ve düşük CALLY indeksi bağımsız prediktörlerdi; C-Reaktif Protein ve ürik asit ise anlamını yitirdi.

Sonuç: CALLY indeksi kontrast ilişkili akut böbrek hasarını bağımsız olarak öngörmüş olsa da tanısal gücü ılımlı düzeyde bulundu. Bu nedenle, tek başına bir belirteçten ziyade tamamlayıcı bir immün-nütrisyonel gösterge olarak değerlendirilebilir. Bikarbonat en yüksek tanısal doğruluğu göstermiş olup metabolik asidozun kontrast ilişkili akut böbrek hasarı gelişimindeki rolünü desteklemektedir.

Anahtar kelimeler: Kontrast ilişkili akut böbrek hasarı, koroner anjiyografi, C-reaktif protein

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INTRODUCTION

Contrast-associated acute kidney injury (CA-AKI) is a subtype of acute kidney injury characterized by a marked increase in serum creatinine levels within 48–72 hours following exposure to iodinated contrast agent, and it remains a critical complication, particularly after coronary angiography[1,2]. Despite advances in contrast media and procedural techniques, CA-AKI continues to impose a substantial clinical burden. It is associated with increased morbidity and mortality, prolongation of hospitalization, and higher healthcare costs[1]. Therefore, early identification of high-risk individuals is essential for implementing preventive strategies and optimizing periprocedural management.

The development of CA-AKI is multifactorial. Classical clinical risk factors include advanced age, diabetes mellitus, pre-existing renal impairment, anemia, high contrast volume, hypotension, and congestive heart failure[3]. In terms of pathophysiology, several mechanisms have been implicated, including direct renal tubular toxicity induced by the contrast agent, micro-atherothrombotic embolization, intrarenal vasoconstriction secondary to endothelial dysfunction, oxidative stress, and inflammatory responses[1,4]. Among these, inflammation has gained increasing attention as both a key contributor to kidney injury and a potentially measurable target for improved risk prediction.

To improve CA-AKI risk stratification beyond individual clinical parameters, several scoring systems have been developed. The SYNTAX Score II (SSII), which integrates angiographic features together with clinical variables, has been shown to predict both CA-AKI development and long-term mortality in patients undergoing primary percutaneous coronary intervention for ST-elevation myocardial infarction[5,6]. The Mehran score, one of the most widely used tools in clinical practice, provides risk stratification by incorporating variables such as age, diabetes, anemia, contrast volume, and baseline renal function[7]. Although these models provide valuable prognostic information, they also have practical limitations. SSII requires detailed angiographic evaluation, while the Mehran score largely incorporates procedural and periprocedural variables that may not be fully available before angiographyv[3,5,7]. Consequently, truly early identification of at-risk individuals prior to contrast exposure remains challenging, and additional markers that are readily accessible in routine practice may improve pre-procedural risk estimation.

In recent years, additional biomarkers and composite indices have been investigated to enhance the predictive performance of CA-AKI models. Among these, inflammation-based parameters have emerged as promising candidates. Various inflammatory markers and composite indices, such as the neutrophil-to-lymphocyte ratio (NLR) and the systemic immune-inflammation index (SII), have been reported to be associated with the development of CA-AKI[8,9]. While many biomarkers reflect only a single aspect of systemic inflammation, composite indices may provide a more integrated picture of the inflammatory milieu and its interaction with metabolic and immune status.

The C-reactive protein (CRP)–albumin–lymphocyte (CALLY) index is a composite marker that integrates systemic inflammation (CRP), nutritional status (albumin), and immune response (lymphocyte count) into a single parameter. Unlike isolated inflammatory markers, the CALLY index simultaneously reflects inflammatory activity and the host's nutritional and immunological reserves. Initially introduced as a prognostic marker in oncology, the CALLY index has subsequently been evaluated in other clinical settings, including sepsis, liver diseases, and cardiovascular disorders, where it has been associated with disease severity and adverse outcomes[10-14]. Because it is inexpensive and easy to calculate, the CALLY index represents an attractive biomarker for risk stratification before coronary angiography. Due to its simplicity, low cost, and reliance on routinely available laboratory parameters, the CALLY index represents an attractive candidate biomarker for pre-procedural risk stratification in patients undergoing coronary angiography.

The aim of this study was to investigate the predictive value of the CALLY index for the development of CA-AKI in patients undergoing elective coronary angiography for stable angina pectoris. We hypothesized that a lower CALLY index would be independently associated with an increased risk of CA-AKI and could provide complementary risk stratification alongside traditional clinical predictors.

MATERIALS AND METHODS

Study design and sample

This retrospective, single-center observational study was conducted at Harran University Faculty of Medicine Hospital**,** a tertiary-care academic center in Türkiye. The hospital performs routine coronary angiography procedures for stable angina pectoris under standardized institutional protocols. All eligible cases between 2020 and 2024 were retrospectively reviewed using the hospital's electronic medical record system. Coronary angiography procedures were performed by experienced interventional cardiologists in the catheterization laboratory according to routine clinical practice, and contrast administration was carried out by the catheterization team.

Between 2020 and 2024, a total of 1,308 patients underwent coronary angiography for stable angina pectoris at the hospital. After screening, 363 patients were excluded due to the following reasons: left ventricular ejection fraction (EF) <50% (n=152), intra-aortic balloon pump (IABP) support (n=101), maintenance hemodialysis (n=57), history of kidney transplantation (n=4), clinical evidence of active infection (n=17), and missing laboratory or clinical data (n=32). The final study cohort consisted of 945 patients.

The study included all consecutive eligible patients who underwent coronary angiography for stable angina pectoris during the study period and met the inclusion/exclusion criteria. Therefore, no a priori sample size calculation or power analysis was performed, and the final sample size (n=945) was determined by the number of eligible patients available in the institutional database.

Procedure

The study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was obtained from the Harran University Clinical Research Ethics Committee (approval code: HRÜ/24.01.40; approval date: 12/02/2024).

Coronary angiography was performed in the cardiac catheterization laboratory according to routine institutional practice by experienced interventional cardiologists. A non-ionic, low-osmolar contrast agent, iohexol (Omnipaque 350; GE Healthcare, Princeton, NJ), with a measured osmolality of 0.844 osm/kg H_2O, was used in all patients. Contrast volume (mL) administered during the procedure was recorded in the catheterization laboratory system and retrieved from the electronic medical records.Serum creatinine was measured as part of standard care prior to coronary angiography (baseline) and reassessed within 72 hours after contrast exposure. CA-AKI was defined as an increase in serum creatinine by ≥25% or ≥0.5 mg/dL from baseline within 72 hours following contrast administration[3].

Demographic, clinical, and laboratory variables were obtained from the electronic medical record system and represented values recorded at the time of admission and/or prior to the procedure. Patients with missing key procedural or laboratory data required for CA-AKI assessment were excluded to ensure data completeness and reliability.

Data collection

Clinical and laboratory parameters such as age, sex, presence of diabetes mellitus, hypertension, hyperlipidemia, hemoglobin, albumin, CRP, creatinine, uric acid, electrolytes, and contrast volume were recorded. To ensure data reliability, records with missing or inconsistent laboratory/clinical information were excluded, and key variables (serum creatinine values and contrast volume) were verified from the electronic system.

Inflammatory indices and calculations

The CALLY index, derived from the combination of CRP, albumin, and lymphocyte count[15], as well as other inflammatory markers including NLR, platelet-to-lymphocyte ratio (PLR), and CRP-to-albumin ratio (CAR), were calculated using the following formulas and included in the analyses.

$$\mathrm{NLR} = \frac{\text{Neutrophil } (10^3/\mu\mathrm{L})}{\text{Lymphocyte } (10^3/\mu\mathrm{L})}$$

$$\mathrm{PLR} = \frac{\text{Platelet } (10^3/\mu\mathrm{L})}{\text{Lymphocyte } (10^3/\mu\mathrm{L})}$$

$$\mathrm{CAR} = \frac{\text{C-reactive protein (mg/dL)}}{\text{Albumin (g/dL)}}$$

$$\text{CALLY Index} = \frac{\text{Albumin (g/dL)} \times \text{Lymphocyte } (10^3/\mu\mathrm{L})}{\text{CRP (mg/dL)} \times 10^4}$$

Statistical analysis

All statistical analyses were performed using Jamovi software (version 2.6, 2024). Continuous variables were assessed for normality using the Shapiro–Wilk test. Normally distributed variables were summarized

as mean ± standard deviation (SD), whereas non-normally distributed variables were presented as median (minimum–maximum). Categorical variables were expressed as counts and percentages.

For comparisons between patients with and without CA-AKI, continuous variables were analyzed using the Student's t-test when normally distributed and the Mann–Whitney U test when the normality assumption was not met. Categorical variables (e.g., sex, diabetes mellitus, hypertension, hyperlipidemia) were compared using the chi-square test**.**

For regression modeling, CA-AKI was used as the dependent variable. Candidate predictors were selected based on (i) clinical relevance and prior evidence, and (ii) statistical association in univariate logistic regression analyses. Variables with $p < 0.20$ in univariate analysis were considered eligible for inclusion in the multivariable models. To avoid instability due to multicollinearity, variance inflation factor (VIF) was assessed and variables with VIF > 10 were excluded.

Two separate multivariable logistic regression models were constructed using composite inflammatory indices: a CALLY-based model and a CAR-based model**.** In the CALLY-based model, CRP and CAR were excluded due to collinearity, and albumin and lymphocyte count were excluded because they are directly incorporated into the CALLY index formula. In the CAR-based model, CRP was excluded due to severe collinearity and albumin was excluded to avoid overlap with the CAR construct. Accordingly, each final model included the respective index (CALLY or CAR) together with the remaining non-collinear covariates meeting entry criteria.

Predictive performance was evaluated using receiver operating characteristic (ROC) curves, and the area under the curve (AUC), cutoff values, sensitivity, and specificity were reported. A two-sided p value < 0.05 was considered statistically significant.

RESULTS

A total of 945 patients were included in the study. Among them, 332 (35.1%) were female, and the median age was 58 years. CA-AKI developed in 150 patients (15.9%). Among the 945 patients, 9 individuals (0.95%) required acute hemodialysis following contrast exposure. The mean age of patients who developed CA-AKI was significantly higher compared to those who did not ($p = 0.011$). Diabetes mellitus was more common in the CA-AKI group ($p = 0.019$) (Table 1). The contrast volume used was significantly greater among patients who developed CA-AKI ($p = 0.029$). Regarding laboratory parameters, CRP ($p < 0.001$), CAR ($p < 0.001$), uric acid ($p = 0.041$), and mean corpuscular volume (MCV) ($p < 0.001$) were significantly higher in the CA-AKI group. Conversely, albumin ($p < 0.001$), bicarbonate ($p < 0.001$), and high-density lipoprotein (HDL) ($p = 0.002$) levels were significantly lower in patients who developed CA-AKI. The CALLY index was also significantly lower in the CA-AKI group ($p < 0.001$). Comparisons of laboratory parameters are presented in Table 1.

In univariate logistic regression analysis, age, diabetes mellitus, albumin, triglyceride and HDL levels, MCV, lymphocyte count, CRP, CAR, the CALLY index, serum bicarbonate and contrast agent volume were associated with CA-AKI at $p<0.20$ and were therefore included in the multivariate analysis.

In the multivariate CALLY-based model, independent predictors of CA-AKI were older age ($p=0.046$), presence of diabetes mellitus ($p = 0.048$), lower albumin ($p = 0.042$), lower bicarbonate ($p < 0.001$), higher MCV ($p = 0.043$), higher contrast volume ($p = 0.005$), lower CALLY index ($p = 0.028$). In contrast, CRP and lymphocyte count did not retain significance after adjustment. When a separate model was tested using CAR instead of CALLY, the elevated CAR (OR 1.245, 95% CI: 0.991-1.564, $p=0.059$) showed borderline significance and did not demonstrate a definitive independent predictive effect. The results of the logistic regression analyses based on the CALLY model are presented in Table 2.

ROC analysis demonstrated that the CALLY index had a modest discriminative ability for predicting CA-AKI (AUC= 0.618; cutoff ≈ 0.002), with lower CALLY values being associated with an increased risk. In addition, ROC analyses of other biochemical parameters showed variable discriminative performance, including albumin (AUC = 0.641), bicarbonate (AUC = 0.779), MCV (AUC = 0.608), with bicarbonate demonstrating the highest predictive accuracy. The comparative ROC curves and related statistical metrics are presented in Table 3 and Figure 1

Table 1. Baseline demographic, clinical, and laboratory characteristics according to CA-AKI status

Variable	CA-AKI (+)	CA-AKI (–)	p value
Age (min-max)	61.00 (35–88)	57.00 (21-101)	0.011*
Gender (F/M), n	54/96	278/517	0.881
Diabetes mellitus, n (%)	60 (40%)	238 (29.9%)	0.019*
Hypertension, n (%)	85 (56.6%)	429 (53.9%)	0.603
Creatinine (mg/dL)	0.80 (0.40–2.1)	0.80 (0.40–4.20)	0.131
eGFR (ml/min/1.73m²)	95.0 (31.4–136)	95.1 (16.1–142)	0.736
Uric acid (mg/dL)	5.40 (3.7-11.5)	5.10 (3.4-11.7)	0.041*
Albumin (g/dL)	4.10 (2.80–4.90)	4.30 (2.40–5.90)	0.000*
Triglyceride (mg/dL)	140.00 (101.00–227.00)	156.00 (104.00–213.00)	0.914
HDL (mg/dL)	35.00 (29.00–39.00)	37.00 (32.00–43.00)	0.002*
LDL (mg/dL)	105.40 (27.20-252.00)	102.90 (38.00–195.00)	0.807
Total Cholesterol (mg/dL)	178.00 (153.00–300.00)	179.00 (147.00–348.00)	0.882
Neutrophil (×10³/μL)	5.28 (0.4–19.1)	5.30 (0.1–25.1)	0.653
Lymphocyte (×10³/μL)	2.27 (0.36–5.40)	2.20 (0.29–6.40)	0.161
Monocyte (×10³/μL)	0.60 (0.50–0.80)	0.60 (0.47–0.80)	0.299
Hemoglobin (g/dL)	14.00 (8.70–18.10)	14.00 (8.10–18.10)	0.962
MCV (fL)	86.00 (69.60-102.00)	84.00 (60.80–103.00)	0.000*
PLT (10⁹/L)	270.00 (90.00-674.00)	260.00 (119.00–470.00)	0.242
CRP (mg/dL)	0.72 (0.02–13.9)	0.37 (0.09–31.9)	0.000*
CAR	0.184 (0.004-4.0)	0.08 (0.002-8.89)	0.000*
NLR	2.16 (0.219-42.8)	2.32 (0.005-53.2)	0.270
PLR	116 (43.5-1020)	121(10.5-707)	0.377
CALLY index	0.001 (0.0001–0.084)	0.002 (0.0001–0.136)	0.000*
HCO_3^- (mEq/L)	23.10 (14.00-27.90)	25.00 (16.20–34.10)	0.000*
Contrast agent volume (mL)	100 (30-320)	90 (30–380)	0.029*
Contrast volume/eGFR	1.24 (0.251-5.98)	1.06 (0.257-9.95)	0.610

Categorical variables are expressed as counts (–/+) or (F/M), and continuous variables are presented as median (min-max). *: $p < 0.05$ was considered statistically significant; CAR, C-reactive protein/albumin ratio; CALLY, C-reactive protein- albumin-lymphocyte index; CA-AKI, contrast-associated acute kidney injury; CRP, C-reactive protein; F, female; eGFR, estimated glomerular filtration rate; HCO_3^-, bicarbonate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; M, male; MCV, mean corpuscular volume; NLR, neutrophil/lymphocyte ratio; PLR, platelet/lymphocyte ratio; PLT, platelet count; SD, standard deviation.

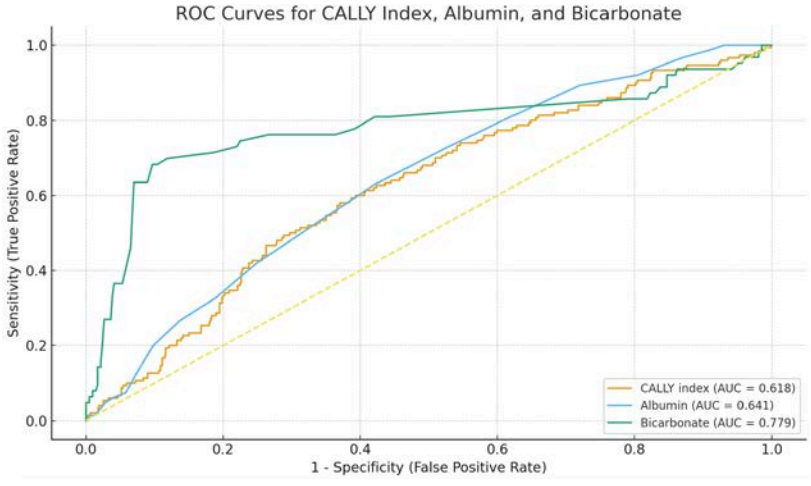

Figure 1. ROC curves of the CALLY index, serum albumin, and bicarbonate levels for predicting CA-AKI.

The CALLY index demonstrated modest discriminative ability (AUC = 0.618), whereas serum albumin (AUC = 0.641) and bicarbonate (AUC = 0.779) showed better predictive performance. The diagonal dashed line represents the reference line (AUC = 0.5), indicating random classification. All curves lying above this line reflect positive discriminative power, with bicarbonate providing the highest diagnostic accuracy among evaluated parameters.

Table 2. Univariate and multivariate logistic regression analyses for independent predictors of CA-AKI

Univariate			Multivariate		
Parameters	**OR (95% CI)**	**P**	**Parameters**	**OR (95% CI)**	**P**
Age	1.021 (1.006-1.037)	0.008†	Age	1.026 (1.001–1.054)	0.046*
Gender	1.046 (0.727-1.505)	0.808	Gender		
DM	1.560 (1.088-2.237)	0.016†	DM	1.801 (1.004–3.232)	0.048*
HT	1.116 (0.785-1.586)	0.542	HT		
Creatinine (mg/dL)	0.632 (0.311-1.284)	0.204	Creatinine (mg/dL)		
Uric Acid (mg/dL)	1.031 (0.969-1.098)	0.338	Uric Acid (mg/dL)		
Albumin (g/dL)	0.349 (0.235-0.520)	<0.001†	Albumin (g/dL)	0.454 (0.212–0.971)	0.042*
Triglyceride (mg/dL)	1.001 (1.000-1.002)	0.187†	Triglyceride (mg/dL)	1.001 (0.999-1.004)	0.246
HDL (mg/dL)	0.975 (0.957-0.993)	0.006†	HDL (mg/dL)	0.970 (0.937–1.006)	0.103
LDL (mg/dL)	1.000 (0.995-1.004)	0.849	LDL (mg/dL)		
TC (mg/dL)	1.000 (0.996-1.005)	0.875	TC (mg/dL)		
MCV (fL)	1.057 (1.026-1.089)	<0.001†	MCV (fL)	1.057 (1.002–1.117)	0.043*
PLT (10^9/L)	1.001 (0.999-1.003)	0.337	PLT (10^9/L)		
Neutrophil ($\times10^3/\mu L$)	0.992 (0.938-1.050)	0.791	Neutrophil ($\times10^3/\mu L$)		
Lymphocyte ($\times10^3/\mu L$)	1.160 (0.962-1.397)	0.118†	Lymphocyte ($\times10^3/\mu L$)	1.343 (0.966-1.869)	0.079
Monocyte ($\times10^3/\mu L$)	0.999 (0.990-1.007)	0.794	Monocyte ($\times10^3/\mu L$)		
Hemoglobin (g/dL)	1.001 (0.908-1.103)	0.990	Hemoglobin (g/dL)		
CRP (mg/dL)	1.052 (0.994-1.113)	0.079†	CRP (mg/dL)	0.950 (0.848–1.065)	0.384
CAR	1.222 (0.992-1.506)	0.059	CAR		
NLR	1.007 (0.968-1.048)	0.733	NLR		
PLR	1.001 (0.999-1.003)	0.319	PLR		
CALLY index	0.0001 (0.0001-0.0132)	0.014†	CALLY index	0.0001 (0.0001-0.126)	0.028*
HCO_3^- (mEq/L)	0.538 (0.441-0.657)	0.000†	HCO_3^- (mEq/L)	0.497(0.398-0.622)	<0.001*
Contrast agent volume (mL)	1.003 (1.000-1.005)	0.027†	Contrast agent volume (mL)	1.006(1.002-1.011)	0.005*
Cv/eGFR	1.066(0.900-1.264)	0.454	Cv/eGFR		

CALLY was used in the main multivariate model. In a separate CAR-based multvariate model, CAR remained borderline (OR 1.245, 95% CI: 0.991-1.564, p=0.059) and did not demonstrate independent predictive strength; †: Variables with $p < 0.20$ in univariate analysis were included in the multivariate model. * : $p < 0.05$ was considered statistically significant.; CAR, C-reactive protein/albumin ratio; CALLY, C-reactive protein- albumin-lymphocyte index; CA-AKI, contrast-associated acute kidney injury; CRP, C-reactive protein; DM, diabetes mellitus; HCO_3^-, bicarbonate; HDL, high-density lipoprotein; HT, hypertension; LDL, low-density lipoprotein; MCV, mean corpuscular volume; NLR, neutrophil/lymphocyte ratio; PLR, platelet/lymphocyte ratio; PLT, platelet count; TC, total cholesterol.

Table 3. ROC analysis: AUC, cutoff, sensitivity, and specificity values for albumin, HCO_3, MCV, and CALLY

Parameters	AUC	Cut-off	Sensitivity (%)	Specificity (%)
Albumin	0.641	4.24	63.3	57.6
HCO_3^-	0.779	23.75	68.3	89.8
MCV	0.608	84.95	61.4	55.9
CALLY index	0.618	0.00197	61.3	59.3

For albumin and HCO_3, the AUC direction was adjusted considering the association with lower values; AUC, area under the curve; CALLY, C-reactive protein-albumin-lymphocyte index; HCO_3^-, bicarbonate; MCV, mean corpuscular volume.

DISCUSSION

In this study, the role of the CALLY index in predicting CA-AKI was investigated in 945 patients who underwent elective coronary angiography for stable angina pectoris. Among classical clinical and biochemical markers, increased age, presence of diabetes mellitus, lower albumin, lower bicarbonate, higher MCV and greater contrast volume, and the lower CALLY index were identified as independent predictors. Although the discriminative performance of the CALLY index was modest (AUC ≈ 0.618), lower values were associated with a higher risk of CA-AKI.

In the literature, the incidence of CA-AKI ranges from 2% to 14% in the general population, while in high-risk groups this rate may increase to as high as 20–30%[16]. Moreover, age ≥75 years, diabetes mellitus, and high contrast volume have been identified as independent risk factors for the development of CA-AKI[7]. In our study, CA-AKI occurred in 15.9% of patients, and the findings that age, diabetes mellitus, and contrast volume were significantly higher in the CA-AKI group are consistent with the risk profiles reported in the literature.

In our study, serum bicarbonate levels were found to be significantly lower in patients who developed CA-AKI (23.1 mmol/L vs. 25.0 mmol/L, $p < 0.001$), and this parameter also emerged as an independent predictor in multivariate analysis (OR 0.497, 95% CI: 0.398-0.622, $p = 0.001$). This finding is consistent with established metabolic-acidosis mechanisms in AKI, where low bicarbonate levels are known to reduce intracellular pH, promoting oxidative stress and mitochondrial dysfunction in renal tubular cells[17]**.** While bicarbonate has been primarily studied for its preventive therapeutic role in hydration protocols[18], its high predictive accuracy in our risk model (AUC = 0.779) supports its clinical utility as a potent indicator of increased metabolic vulnerability to contrast exposure, rather than a novel pathophysiological observation.

In addition, MCV values were found to be higher in the group that developed CA-AKI ($p = 0.001$). This association was significant in the univariate analysis and also remained statistically significant in the multivariate model (OR 1.057, 95% CI 1.002–1.117, $p = 0.043$). Nevertheless, a limitation stemming from the retrospective nature of this study is the lack of available data for corroborating hematological markers, such as RDW or MCHC, which constrains the definitive interpretation of the MCV finding. While MCV is not an established biomarker for CA-AKI, considering the evidence linking elevated MCV with increased mortality in chronic kidney disease populations[19], it can be hypothesized that higher MCV may reflect subclinical nutritional deficiencies, oxidative stress, or impaired erythropoietic response, thereby increasing susceptibility to contrast exposure. Indeed, oxidative stress has been reported to disrupt erythropoiesis and alter erythrocyte volume by triggering eryptosis processes[20].

Moreover, the role of certain biochemical parameters in predicting CA-AKI risk has been emphasized in the literature. Hypoalbuminemia has been identified as an independent risk factor in patients with acute coronary syndrome, and serum albumin levels have been found to be inversely associated with the development of CA-AKI[21]. The CAR, representing an integrated indicator of inflammation and nutritional status, has been shown to be a significant predictor of CA-AKI in patients undergoing percutaneous intervention for acute myocardial infarction, with higher CAR values demonstrating a strong correlation with the occurrence of CA-AKI[22]. Elevated uric acid levels have been identified as a significant predictor of increased CA-AKI risk, particularly among patients with type 2 diabetes[22]. In our study, low albumin levels were significantly associated with CA-AKI development, whereas the associations of uric acid and CRP lost statistical significance after adjustment, and CAR demonstrated only a borderline trend toward increased risk rather than a definitive independent effect.

In previous studies investigating the predictive value of NLR and PLR for CA-AKI, Kurtul et al.[23] reported that NLR significantly predicted the risk of CA-AKI in patients with acute coronary syndrome, while a meta-analysis by Jiang et al.[24] demonstrated that PLR levels measured at admission were significantly higher in patients who developed CA-AKI following contrast exposure, suggesting that PLR may serve as a potential predictor. In our study, however, neither NLR nor PLR was found to be associated with the development of CA-AKI. This may be attributed to the fact that our study population consisted of patients with stable angina pectoris, a clinical setting characterized by a relatively lower inflammatory burden. The limited acute-phase response in stable angina pectoris may attenuate the prognostic value of inflammatory markers. Similarly,

in a prospective study by Wannamethee et al., inflammatory biomarkers such as CRP, interleukin-6, and fibrinogen were significantly associated with the risk of myocardial infarction and coronary death but not with uncomplicated angina pectoris[25].

This suggests that systemic inflammation is less pronounced in stable coronary disease compared to acute coronary syndromes, and that the prognostic value of inflammatory markers may therefore be limited. Ratios such as NLR and PLR primarily reflect acute systemic inflammation and may have lower sensitivity than composite indices that also encompass chronic inflammatory processes and nutritional status. Consequently, composite markers incorporating nutritional parameters such as albumin (for example, the CALLY index or the CAR) may provide greater utility in assessing CA-AKI risk and offer complementary value to traditional risk factors. Because albumin reflects not only nutritional status but also acts as a negative acute-phase reactant, these composite indices can more comprehensively represent both inflammatory and nutritional conditions. This dual property may enhance risk prediction, particularly in patients where subclinical inflammation and nutritional deficiency coexist.

In this context, the CALLY index provides a simple risk indicator by integrating inflammation, nutrition, and immune response into a single metric[10]. Its prognostic value has been demonstrated in malignancies, sepsis, cirrhosis, and cardiovascular populations[11,14,26]. In our study, the CALLY index was significantly lower in the CA-AKI–positive group ($p < 0.001$) and remained an independent predictor in the multivariate analysis (OR 0.0001, $p = 0.028$). ROC analysis showed a balanced sensitivity and specificity and a modest discriminative ability with an AUC of 0.618, a cutoff value of approximately 0.002, sensitivity of 61.3%, and specificity of 59.3%. Although lower CALLY values were independently associated with the development of CA-AKI, an AUC below 0.65 indicates limited clinical utility as a standalone predictive marker. Therefore, the prognostic value of the CALLY index should be interpreted with caution. Because the present study did not evaluate its incremental predictive performance over established risk models such as the Mehran score or other angiography-based risk stratification tools we cannot conclude that the CALLY index provides meaningful additive value beyond existing predictors. Taken together, these findings suggest that the CALLY index may serve as a supportive immuno-nutritional indicator rather than a primary diagnostic tool, and its clinical role should be considered complementary and hypothesis-generating. Future studies incorporating integrated prediction models are needed to clarify its true incremental benefit.

ROC analyses in our study demonstrated that, in addition to the CALLY index, serum albumin (AUC = 0.641), CRP (AUC = 0.632), CAR (AUC = 0.639), MCV (AUC = 0.608), and particularly bicarbonate (AUC = 0.779) levels were associated with the development of CA-AKI. The fact that bicarbonate had the highest AUC value supports the role of metabolic acidosis in the pathophysiology of CA-AKI. In contrast, the CALLY index, by integrating both CRP and albumin, offers a more comprehensive biological perspective that simultaneously reflects inflammatory and nutritional status.

To the best of our knowledge, no study to date has evaluated the CALLY index in the context of CA-AKI, making our study a novel contribution to the literature. Current risk scores, such as the Mehran and SYNTAX Score II, are primarily based on demographic and procedural parameters. Our findings suggest that incorporating inflammatory and immuno-nutritional markers into these models may enhance their predictive accuracy. Given its modest predictive performance in the present analysis, the CALLY index should currently be interpreted as a supportive immuno-nutritional marker; however, future prospective studies are needed to determine whether it could help identify patients who may benefit from closer monitoring or targeted preventive strategies before contrast exposure.

This study has several limitations. First, its retrospective and single-center design may limit generalizability and introduce selection bias. The retrospective nature also carries the possibility of residual confounding due to unmeasured clinical factors and variability in periprocedural management. Second, CA-AKI was defined solely based on changes in serum creatinine, as additional renal biomarkers (e.g., NGAL or cystatin C) were not routinely available. Third, key clinical outcomes such as percutaneous coronary intervention status, length of hospital stay, and short-term mortality could not be evaluated due to incomplete recording in the database. Fourth, detailed data on nephroprotective strategies (e.g., standardized hydration protocols, sodium bicarbonate use, or medication adjustments) were not uniformly available, which may have

influenced the observed incidence of CA-AKI. In addition, since the study included consecutive eligible cases within the study period, no a priori power analysis was performed and the sample size was determined by the available patient records, which may limit the precision of effect estimates for some variables. Finally, long-term renal outcomes were not available.

Despite these limitations, the relatively large cohort and systematic assessment of routinely available clinical and laboratory parameters strengthen the reliability and clinical applicability of our findings.

In conclusion, our findings suggest that the CALLY index is an accessible inflammation-based marker associated with the development of contrast-associated acute kidney injury in patients undergoing coronary angiography for stable angina. Although its discriminative performance was modest, CALLY may provide complementary value when interpreted alongside routinely available clinical parameters such as serum bicarbonate, albumin, and contrast volume. Future prospective, multicenter studies should validate these findings, evaluate whether the integration of CALLY into risk prediction models improves pre-procedural stratification, and investigate whether CALLY-guided nephroprotective strategies (e.g., individualized hydration protocols and periprocedural management) can reduce CA-AKI incidence and improve short- and long-term renal outcomes.

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