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The Association Between the Gamma-Glutamyl Transferase-to-Albumin Ratio and the No-Reflow Phenomenon in Patients With Acute Coronary Syndrome Undergoing Percutaneous Coronary Intervention

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Abstract

Background

Reopening the culprit epicardial artery by percutaneous coronary intervention (PCI) does not invariably restore myocardial perfusion in acute coronary syndrome (ACS). Gamma-glutamyl transferase (GGT) and albumin reflect different aspects of inflammatory and oxidative status. We investigated whether the GGT/albumin ratio (GAR) was related to angiographic no-reflow after PCI.

Methods

The analysis included 241 patients with ACS who underwent PCI. No-reflow was assigned when the final Thrombolysis in Myocardial Infarction flow grade was ≤ 2. We compared clinical and laboratory data by final flow status, examined covariates with univariable and multivariable logistic regression, and assessed GAR discrimination using receiver operating characteristic analysis.

Results

Thirty-one of 241 patients (12.9%) had no-reflow. Compared with the remaining patients, this group had lower left ventricular ejection fraction (LVEF) and albumin, together with higher white blood cell (WBC) count, C-reactive protein (CRP), GGT, and GAR. In the adjusted analysis, LVEF, the CRP/albumin ratio (CAR), and GAR retained statistical significance. GAR yielded an area under the curve of 0.748 (95% CI 0.645–0.852, $p < 0.001$).

Conclusions

In patients with ACS treated by PCI, GAR was related to angiographic no-reflow independently of the other variables entered into the model. Because GAR can be calculated from routine admission tests, it may provide additional information during assessment of no-reflow risk.

Introduction

Percutaneous coronary intervention (PCI) is used to re-establish flow in the culprit artery during acute coronary syndromes (ACS) [1, 2]. Epicardial patency, however, does not guarantee effective perfusion at the myocardial level. When tissue flow remains inadequate despite treatment of the epicardial lesion, the resulting no-reflow state is clinically important because it accompanies poorer functional recovery, left ventricular dysfunction, heart failure, malignant ventricular arrhythmias, greater infarct size, and higher mortality [3, 4, 6].

No-reflow arises from a combination of microvascular events rather than a single mechanism. Vasoconstriction, distal embolization of atherothrombotic material, endothelial damage, leukocyte accumulation, platelet activation, oxidative injury, and reperfusion-related damage have all been implicated [5, 6]. This convergence of inflammation and microvascular injury creates a rationale for evaluating laboratory measurements obtained at presentation.

The C-reactive protein (CRP)/albumin ratio (CAR) has already been linked to no-reflow in ACS [7]. Gamma-glutamyl transferase (GGT) is associated with inflammatory and oxidative pathways and with adverse cardiovascular outcomes, whereas albumin conveys information about inflammatory burden and vascular homeostasis [8]. Combining these measurements as the GGT/albumin ratio (GAR) may therefore capture complementary biological processes. The present study examined the relationship between GAR and angiographic no-reflow in patients with ACS undergoing PCI.

Methods

Study Population: Hospital records were reviewed for 300 patients with ACS who underwent PCI in our cardiology department from January 2026 through March 2026. We excluded patients treated medically without PCI, those with cirrhosis or another chronic liver disorder, patients with cancer, and individuals whose hospital data were incomplete. After these exclusions, 241 patients constituted the study cohort. The protocol was approved by the Ankara Etlik City Hospital Scientific Research Evaluation and Ethics Committee (approval number: AEŞH-BADEK2-2026-395). The committee waived informed consent because the study used retrospective data. All procedures conformed to the Declaration of Helsinki.

Laboratory Measurements

Blood was drawn after admission and before PCI. Albumin, GGT, creatinine, complete blood count, and the other routine biochemical and hematological variables were measured from these samples. Local laboratory reference intervals were 0–60 U/L for GGT and 3.5–5.5 g/dL for albumin. GAR was obtained by dividing the serum GGT value by the serum albumin value.

Coronary Angiography

Coronary angiography was undertaken with the Judkins technique using either radial or femoral access. Balloon dilatation and stent placement were applied to the culprit lesion when required. Two experienced interventional cardiologists reviewed the digital angiograms; discordant interpretations were settled by agreement. Coronary flow was graded before and after PCI on the Thrombolysis in Myocardial Infarction (TIMI) scale from 0 to 3. The no-reflow group comprised patients whose final TIMI grade was ≤ 2.

Medications

At emergency department presentation, patients were given 300 mg aspirin as a loading dose. Once PCI had been selected, 180 mg ticagrelor and a single intravenous dose of unfractionated heparin (40–70

U/kg) were administered in the catheterization laboratory, with an activated clotting time target of 200–250 seconds. Subsequent in-hospital ACS therapy followed current guideline recommendations.

Statistical Analysis

Distributional assumptions for continuous variables were checked with the Kolmogorov–Smirnov and Shapiro–Wilk tests. Variables satisfying normality were summarized by mean ± standard deviation and contrasted with the independent-samples t test; non-normal variables were summarized by median (minimum–maximum) and contrasted with the Mann–Whitney U test. Counts and percentages were used for categorical data, with Pearson's χ^2 or Fisher's exact test selected according to cell frequencies. Univariable logistic regression was followed by multivariable logistic regression to examine relationships with no-reflow. The discriminatory performance of GAR was quantified by receiver operating characteristic analysis. Calculations were completed in IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA), and two-sided p values below 0.05 were considered significant.

Results

Of the 241 patients analyzed, 31 (12.9%) fulfilled the angiographic definition of no-reflow and 210 did not.

Clinical, demographic, and laboratory comparisons are detailed in Table 1. Mean age was greater in the no-reflow group (66.77 ± 12.50 vs. 62.67 ± 10.39 years, p = 0.047), while the proportion of men did not differ between groups. Diabetes mellitus was recorded in 10 patients (32.2%) with no-reflow and 55 patients (26.2%) without no-reflow (p = 0.477). Hypertension frequencies were likewise comparable [20 (64.5%) vs. 116 (55.2%), p = 0.331]. LVEF was lower among patients with no-reflow (40.10 ± 9.46% vs. 47.64 ± 9.96%, p < 0.001).

Table 1
Baseline demographic, clinical, and laboratory characteristics according to no-reflow status

Variable	No-reflow (n = 31)	No-reflow absent (n = 210)	p value
Age, years	66.77 ± 12.50	62.67 ± 10.39	0.047
Male sex, n (%)	23 (74.2%)	161 (76.7%)	0.762
Diabetes mellitus, n (%)	10 (32.2%)	55 (26.2%)	0.477
Hypertension, n (%)	20 (64.5%)	116 (55.2%)	0.331
LVEF, %	40.10 ± 9.46	47.64 ± 9.96	< 0.001
WBC (×10³/μL)	11.53 ± 3.19	9.88 ± 3.75	0.001
Hemoglobin (g/dL)	13.94 ± 0.90	14.34 ± 1.44	0.013
Platelet (×10³/μL)	251.45 ± 68.35	249.69 ± 67.49	0.976
Sodium (mmol/L)	137.58 ± 3.30	138.34 ± 2.98	0.212
Potassium (mmol/L)	4.44 ± 0.72	4.30 ± 0.33	0.294
Neutrophil (×10³/μL)	8.67 ± 2.58	8.20 ± 3.20	0.212
Lymphocyte (×10³/μL)	1.77 ± 0.82	2.05 ± 0.80	0.031
Monocyte (×10³/μL)	0.79 (0.36–1.64)	0.65 (0.09–2.11)	0.077
Creatinine (mg/dL)	0.88 (0.68–2.05)	0.88 (0.44–2.93)	0.680
AST (U/L)	51.0 (10–1518)	40.5 (10–1750)	0.014
ALT (U/L)	46.0 (5–1155)	26.0 (5–1854)	< 0.001
Uric acid (mg/dL)	5.82 ± 1.34	5.68 ± 1.33	0.607
BNP (pg/mL)	465.82 (323.00–683.02)	262.46 (159.76–611.09)	0.008
GGT (U/L)	39.0 (6–295)	23.5 (4–747)	< 0.001
CRP (mg/L)	21.5 (2.0–164.5)	7.29 (0–237.2)	< 0.001
Albumin (g/dL)	4.30 (3.00–5.30)	5.30 (3.37–5.30)	0.002
GGT/Albumin ratio	9.83 (1.1–62.4)	4.91 (0.8–140.9)	< 0.001

Data are presented as mean ± standard deviation (SD), median (minimum-maximum), or number (percentage), as appropriate. No-reflow was defined as final Thrombolysis in Myocardial Infarction (TIMI) flow grade ≤ 2. LVEF: left ventricular ejection fraction; WBC: white blood cell count; AST: aspartate aminotransferase; ALT: alanine aminotransferase; BNP: B-type natriuretic peptide; GGT: gamma-glutamyl transferase; CRP: C-reactive protein. p values < 0.05 were considered statistically significant; ns indicates non-significant.

The no-reflow group showed higher WBC, AST, ALT, BNP, GGT, and CRP values, along with lower hemoglobin, lymphocyte, and albumin levels. GAR was also greater in this group [9.83 (1.1–62.4) vs. 4.91 (0.8–140.9), p < 0.001]. Platelet count, sodium, potassium, neutrophil count, monocyte count, creatinine, and uric acid showed no statistically significant between-group differences.

In the univariable models (Table 2), WBC count, CAR, GAR, age, and LVEF reached statistical significance; lymphocyte count did not. The estimated odds ratios were 1.058 for GAR (95% CI: 1.016–1.101, p = 0.006) and 1.076 for CAR (95% CI: 1.025–1.130, p = 0.003).

Table 2
Univariable logistic regression analysis for predictors of no-reflow

Variable	**OR**	**95% CI**	**p value**
WBC	1.101	1.012–1.199	0.026
Lymphocyte	0.614	0.356–1.059	0.079
CAR	1.076	1.025–1.130	0.003
GGT/Albumin ratio	1.058	1.016–1.101	0.006
Age	1.004	1.00005–1.00797	0.047
LVEF	0.99	0.98–0.99	< 0.001

OR: odds ratio; CI: confidence interval; WBC: white blood cell count; CAR: C-reactive protein-to-albumin ratio; LVEF: left ventricular ejection fraction.

After simultaneous adjustment (Table 3), LVEF, GAR, and CAR continued to meet the significance criterion. For each 1% increment in LVEF, the odds of no-reflow decreased (OR: 0.936, 95% CI: 0.898–0.975, p = 0.002). The adjusted estimates were OR 1.054 for GAR (95% CI: 1.012–1.097, p < 0.001) and OR 1.007 for CAR (95% CI: 1.002–1.017, p = 0.011). Neither age nor WBC count was significant in this model.

Table 3
Multivariable logistic regression analysis for predictors of no-reflow

Variable	OR	95% CI	p value
Age (per year)	1.036	0.997–1.077	0.072
LVEF (per 1% increase)	0.936	0.898–0.975	0.002
GGT/Albumin ratio	1.054	1.012–1.097	< 0.001
WBC (×10³/μL)	1.000	0.989–1.012	0.944
CRP/Albumin ratio	1.007	1.002–1.017	0.011

OR: odds ratio; CI: confidence interval; LVEF: left ventricular ejection fraction; WBC: white blood cell count; GGT: gamma-glutamyl transferase; CRP: C-reactive protein. p values < 0.05 were considered statistically significant; ns indicates non-significant.

Receiver operating characteristic analysis produced an AUC of 0.748 for GAR (95% CI: 0.645–0.852, p < 0.001; Fig. 1).

Discussion

Three findings summarize this analysis. First, GAR values were higher when final angiographic flow met the no-reflow definition. Second, the relationship between GAR and no-reflow persisted in the multivariable model, in which LVEF and CAR were also significant. Third, no-reflow was documented in 31 of 241 patients (12.9%).

PCI frequently restores flow in the epicardial culprit vessel, yet microvascular reperfusion can remain incomplete. This distinction explains why angiographic patency and tissue-level recovery do not always coincide. Across the risk strata examined by Xie et al., no-reflow frequencies ranged from 6.1% to 34% in 834 patients with ACS [9]. The rate observed in our cohort falls within that interval.

The heterogeneous biology of no-reflow is consistent with its variable clinical presentation. Distal migration of thrombus or plaque during angioplasty can obstruct the microcirculation, particularly early in ST-elevation myocardial infarction (STEMI) [10]. At the same time, prolonged ischemia followed by reperfusion may damage both myocardium and the microvascular bed more extensively than embolization alone [11]. Associations reported for total ischemic duration, proximal lesion location, and stent length further indicate that both patient characteristics and procedural factors contribute to the final flow result [12].

Inflammatory activity provides a plausible link between the measured biomarkers and coronary microvascular injury. CRP has been related to the burden of coronary artery disease (CAD), recurrent cardiovascular events, and mortality in stable CAD and ACS [13]. He et al. described a correlation between circulating GGT and CRP in CAD [8], and higher admission GGT has been linked to long-term mortality and major adverse cardiac events after STEMI [16]. Albumin adds a different dimension: lower

concentrations have been associated with in-hospital outcomes, in-stent restenosis, greater angiographic CAD severity, and no-reflow after PCI [14, 15, 17].

The direction of our findings is also biologically coherent. Higher GGT often accompanies systemic inflammation, metabolic syndrome, oxidative stress, and an unfavorable cardiometabolic profile [18]. Experimental observations indicate that GGT may facilitate reactive oxygen species generation within atherosclerotic plaques, thereby contributing to plaque progression and instability [19–21]. Albumin may oppose platelet aggregation through prostaglandin D_2 formation [22]; conversely, low albumin can increase blood viscosity through lysophosphatidylcholine and may impair endothelial function [23]. In our cohort, the combination of higher GGT and lower albumin translated into a higher GAR among patients with no-reflow. The adjusted association suggests that GAR conveys information not fully represented by the other variables included in the model.

Conclusion

In this cohort of patients with ACS undergoing PCI, admission GAR differed according to final angiographic flow and retained statistical significance after adjustment. GAR is obtainable from routine laboratory measurements and may serve as an additional marker when evaluating no-reflow, although confirmation in larger prospective cohorts is required.

Limitations

Interpretation of these results should account for the modest cohort size and the absence of several potential determinants of no-reflow from the dataset. In addition, reperfusion was classified by visual angiographic assessment rather than by coronary flow reserve, contrast echocardiography, or cardiac magnetic resonance imaging.

Declarations

Presentation

Not presented.

Ethics approval and consent to participate

The study protocol was approved by the Ankara Etlik City Hospital Scientific Research Evaluation and Ethics Committee (approval number: AEŞH-BADEK2-2026-395). The requirement for informed consent was waived by the ethics committee due to the retrospective design of the study. The study was conducted in accordance with the Declaration of Helsinki.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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No funding was received for this study.

Author Contribution

Authors' contributionsOA contributed to conceptualization, study design, data collection, analysis, and manuscript drafting. MA contributed to data collection, methodology, and manuscript revision. CT contributed to data collection and literature review. SB contributed to angiographic assessment and manuscript revision. MD contributed to supervision and critical revision of the manuscript. All authors read and approved the final manuscript.

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Not applicable.

Data Availability

The datasets used and/or analyzed during the current study are not publicly available due to institutional and privacy restrictions but are available from the corresponding author on reasonable request.

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Figures

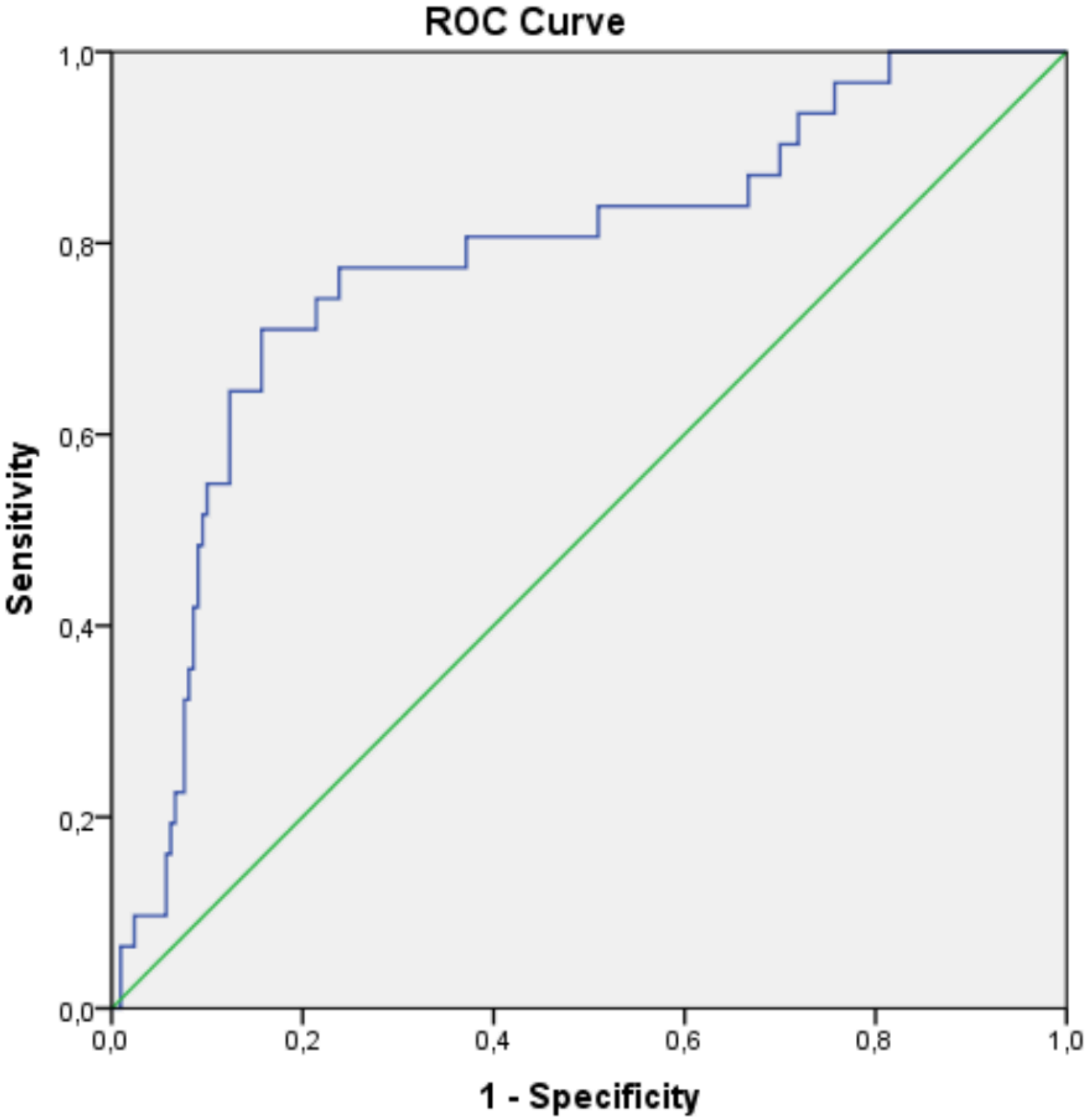


Figure 1

Receiver operating characteristic (ROC) curve of the gamma-glutamyl transferase-to-albumin (GGT/albumin) ratio for no-reflow. The area under the curve was 0.748 (95% CI 0.645-0.852, p<0.001).