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ORIGINAL RESEARCH

Significance of Multiple Lymphocyte-to-C-Reactive Protein Ratios in Predicting Long-Term Major Cardiovascular Adverse Events in Emergency Percutaneous Coronary Intervention Patients with ST-Segment Elevation Myocardial Infarction

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Aim: The high morbidity and mortality associated with ST-segment elevation myocardial infarction (STEMI) are an urgent concern. This study aimed to investigate the ratio of lymphocyte count to C-reactive protein ratio (LCR) in multiple measurements in the perioperative period, exploring dynamic changes as the best predictor of major adverse cardiovascular events (MACE) in STEMI patients.

Methods: We enrolled 205 STEMI patients, conducting blood counts at admission, 24 hours post-percutaneous coronary intervention (PCI), and at discharge. Cox proportional risk models evaluated factors independently associated with STEMI prognosis. The receiver operating characteristic (ROC) curve and the De-Long test determined the best predictor. Kaplan–Meier analysis assessed the prognostic value of LCR for STEMI patients. Statistical differences and correlations between LCR at 24 hours post-PCI and cardiovascular disease risk factors were also analyzed.

Results: Gensini score (HR, 1.015; 95% CI, 1.007–1.022; $P < 0.001$), total stent length (HR, 1.015; 95% CI, 1.002–1.029; $P=0.025$), lipoprotein (a) (HR, 1.001; 95% CI, 1.000–1.002; $P=0.043$), LCR at admission (HR, 0.995; 95% CI, 0.989–1.000; $P=0.002$), and LCR at 24 hours post-PCI (HR, 0.587; 95% CI, 0.486–0.708; $P < 0.001$) were independent risk factors for long-term STEMI prognosis after PCI. LCR at admission (cut-off value, 2.252; 95% CI, 0.040–0.768; $P < 0.001$) and LCR at 24 hours post-PCI (cut-off value, 2.252; 95% CI, 0.831–0.924; $P < 0.001$) effectively predicted MACEs occurrence, with the latter exhibiting a superior predictive effect ($P<0.001$). Kaplan-Meier analysis revealed that patients with LCR at admission ≤ 50.29 and LCR at 24 hours post-PCI ≤ 2.25 had significantly higher risks of developing MACEs (Log-rank $P < 0.0001$).

Conclusion: LCR at 24 hours post-PCI may be a superior marker for long-term MACE prediction in STEMI patients, serving as the best predictor for distant MACE occurrence.

Keywords: lymphocyte, C-reactive protein, major cardiovascular adverse events, percutaneous coronary intervention, ST-segment elevation myocardial infarction

Introduction

Cardiovascular diseases are now a leading global cause of death, significantly impacting human health and quality of life.[1] The genesis and progression of coronary artery disease involve factors such as atherosclerosis from abnormal lipid metabolism and immune dysregulation.[2] In regions with limited medical resources or low-middle income, the incidence and prevalence of coronary artery disease are notably high.[3] ST-segment elevation myocardial infarction (STEMI)

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progresses swiftly, demanding immediate attention. Its pathogenesis primarily stems from early coronary atherosclerosis and subsequent occlusion due to vulnerable plaque rupture and thrombosis, significantly affecting patient prognosis[4] Emergency percutaneous coronary intervention (PCI) stands out as the preferred reperfusion method for STEMI patients, substantially reducing major adverse cardiovascular events (MACEs).[4,5] Despite timely PCI, some patients still experience MACEs post-surgery, leading to a grim prognosis.[6] Consequently, early identification of patients prone to MACEs and delivering targeted medical care holds paramount importance.

Scientific studies have established the pivotal role of the inflammatory immune response in the onset and progression of coronary artery disease, closely influencing the clinical prognosis of patients.[7–9] Lymphocytes, integral to specific immune pathways, signify a reduced count as a cardiovascular event risk. Myocardial infarction-induced lymphocytonia, considered a severe reaction, may correlate with heightened inflammatory mediator release.[10] Serum C-reactive protein (CRP), a classical inflammatory activity indicator, primarily contributes to acute myocardial infarction by activating complement and inducing vascular endothelial dysfunction. CRP predicts cardiovascular events in stable patients with angina pectoris, serving as a marker for atherosclerotic plaque vulnerability and coronary artery disease activity.[11,12] Nevertheless, the individual variability of lymphocyte counts and CRP levels, influenced by multiple factors, impairs their specificity, resulting in limited predictive value for long-term MACEs.

Previous studies have identified the preoperative lymphocyte-to-CRP ratio (LCR) as a promising marker for predicting outcomes in colorectal cancer surgery and tumors. It serves as a clinically feasible prognostic marker for nutritional inflammation in gastric cancer patients and as a novel prognostic indicator for those with resectable gallbladder cancer.[13–15] In our prior investigation, we determined that preoperative LCR is a reliable biomarker for predicting both in-hospital and long-term adverse prognoses in STEMI patients undergoing emergency PCI. Its predictive efficacy surpassed that of traditional inflammatory markers, namely neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and CRP-to-lymphocyte ratio (CAR).[16] Emergency PCI stands out as the primary treatment strategy for STEMI patients. However, assessing prognosis based solely on preoperative LCR overlooks the impact of emergency PCI on long-term MACEs, posing certain limitations. Therefore, this retrospective study was designed to explore the predictive value of LCR levels and fluctuations in STEMI patients before emergency PCI, 24 hours post-PCI, and at three time-points before discharge. The aim is to discern their relevance to long-term MACEs in STEMI patients, providing precise strategies for the prolonged management of STEMI patients.

Methods

Patients

We included STEMI-diagnosed patients who underwent emergency PCI at the Department of Cardiology, Wuxi Clinical College of Anhui Medical University, from September 2020 to September 2021. STEMI diagnosis followed the fourth General Rule of Myocardial Infarction (2018):[17] considering: (1) chest pain lasting more than 10 minutes, (2) characteristic ECG changes during emergency admission, and (3) elevated myocardial injury markers.

Exclusion criteria comprised: (1) severe renal insufficiency, chronic or acute inflammatory diseases, hematological diseases, malignant tumors, or allergy to contrast agents/anticoagulants; (2) incomplete clinical data; (3) in-hospital deaths; (4) loss to follow-up within 1 year post-discharge; and (5) history of coronary stent implantation or coronary artery bypass grafting for unstable angina pectoris.

Data Collection

Clinical and lab data, encompassing age, sex, smoking, hypertension, diabetes, BMI, heart rate, Killip class, DtoB time, length of stay, and post-discharge meds (ACE inhibitors/angiotensin receptor antagonists, beta-blockers, calcium channel blockers, diuretics, nitrates), were collected. Blood biochemistry covered heart rate, myoglobin, glucose, peak troponin I, hemoglobin, albumin, CRP, total cholesterol, triglycerides, HDL/LDL cholesterol, serum creatinine, lipoprotein (a), and serum uric acid. Coagulation system function indexes (fibrinogen, D-dimer) and blood routine indexes (neutrophils, lymphocytes, monocytes) were also examined.

STEMI patients received a loading dose of aspirin (300mg) and ticagrelor (180mg) prior to emergency PCI surgery. Two interventional cardiologists performed PCI and recorded the intraoperative information. Coronary angiography (CAG) was performed by standard Judkins method,[18] assessing severity of coronary artery disease using the Gensini score.[19] Myocardial infarction sites (left main branch, left anterior descending branch, left circumflex branch, right coronary artery), number of diseased vessels (degree of coronary artery stenosis ≥ 50%),[20] length and diameter of implanted stent, coronary artery internal diameter and flow after emergency PCI were monitored. Patients were divided into normal flow group and no reflow group according to TIMI grade: normal flow group: TIMI grade 3; No reflow group: TIMI grade ≤ 2.[21] STEMI patients underwent bedside Doppler echocardiography within 48 hours post-PCI to record left ventricular end-diastolic diameter (LVDd) and left ventricular ejection fraction (LVEF) at admission. Peripheral artery ultrasonography before discharge checked for carotid plaques. Discharged patients received aspirin enteric-coated tablets and ticagrelor antiplatelet therapy without contraindications.

Lymphocyte counts and CRP levels were collected at admission, 24 hours post-PCI, and three points before discharge. The corresponding LCR values were calculated using the formula: LCR = (lymphocyte count [10^9/L] / CRP [μg/L]) × 100. Fluctuations in LCR values during hospitalization were analyzed by calculating the differences at the three time points.

Definition of MACEs and Follow-Up

For STEMI patients undergoing emergency PCI, we recorded 1-year post-discharge MACEs, such as cardiogenic death, heart failure, unstable angina pectoris post-stent implantation, and myocardial infarction recurrence. A cardiovascular physician collected follow-up data by reviewing electronic records, either inpatient or outpatient. Patients not returning for review within 1 year were contacted by phone for endpoint event information.

Statistical Analysis

Statistical analysis utilized SPSS (version 26.0; SPSS Inc., Chicago, IL, USA), MedCalc, and Graphpad Prism 9.4.1. The normality of data was assessed with the Kolmogorov–Smirnov test. Normally distributed continuous variables were presented as means ± standard deviations and compared using Student's *t*-test. Skewed continuous variables were expressed as median (IQR, 25th–75th percentile) and compared using the Mann–Whitney *U*-test. Categorical variables, presented as frequencies (percentages), were compared using the chi-square test and Fisher's exact test.

Cox regression identified risk factors for MACEs post-emergency PCI in STEMI patients. Variables with $P < 0.05$ entered multivariate Cox regression using forward and backward likelihood ratio methods. Pearson correlation assessed normal variable correlations; Spearman correlation analyzed skewed variable correlations. ROC curves evaluated LCR values at different time points for predicting STEMI patient prognosis after emergency PCI. Cut-off values, sensitivity, specificity, risk ratio (HR), and 95% CIs were calculated. The DeLong test compared predictive efficacy differences.

Patients, categorized by LCR cut-off, underwent Kaplan–Meier analysis and Log rank tests for non-MACE survival rates, plotted on survival curves. All tests were two-tailed, and $P < 0.05$ indicated statistical significance.

Results

Demographic Information of STEMI Patients

A total of 205 STEMI patients who underwent emergency PCI were included in this study based on predefined criteria. Patients were categorized into MACE and non-MACE groups based on events occurring within 1 year post-surgery. The results revealed a higher proportion of MACEs among patients with a history of diabetes mellitus (P=0.016), Killip class ≥ II ($P < 0.001$), no-reflow (P=0.002), ≥ 2 diseased arteries (P=0.007), and mitral regurgitation (P=0.002) compared to that in the non-MACE group. Additionally, the MACE group exhibited elevated levels of myoglobin (P=0.024), glucose (P=0.008), fibrinogen ($P < 0.001$), D-dimer ($P < 0.001$), and lipoprotein (a) (P=0.001), as well as increased total stent length (P=0.049) and Gensini score ($P < 0.001$). Conversely, the MACE group had significantly lower LVEF ($P < 0.001$), LCR at admission ($P < 0.001$), LCR at 24 hours post-PCI ($P < 0.001$), LCR at discharge ($P < 0.001$), LCR (admission-24 hours post-PCI) ($P < 0.001$), and LCR (discharge - 24 hours post-PCI) ($P < 0.001$) compared to the corresponding parameters in the non-MACE group (Table 1).

Table 1 Basic Clinical Characteristics Between MACE and Non-MACE Groups in STEMI Patients

Basic Clinical Characteristics	All, n=205	MACE group, n=86	Non-MACE group, n=119	*P* -value[b]
Demographics				
Age, years	63.00 (52.00, 69.00)	64.00 (55.75, 72.00)	61.00 (50.00, 76.00)	0.056
Male sex, n (%)	173 (84.40)	70 (81.40)	103 (86.60)	0.315
Smoking, n (%)	133 (64.90)	54 (62.80)	79 (66.40)	0.595
Hypertension, n (%)	126 (61.50)	56 (65.10)	70 (58.80)	0.361
Diabetes mellitus, n (%)	43 (21.00)	25 (29.10)	18 (15.10)	0.016
BMI (kg/m^2)	24.22 (22.84, 25.60)	24.16 (22.49, 25.26)	24.45 (23.03, 26.12)	0.072
Killip classification ≥ II, n (%)	67 (32.70)	43 (50.00)	24 (20.20)	<0.001
Time from pain to balloon (min)	106.00 (73.50, 146.50)	108.00 (70.50, 147.50)	140.00 (76.00, 143.00)	0.919
In-hospital day	11.00 (10.00, 13.50)	12.00 (9.75, 15.25)	11.00 (10.00, 13.00)	0.076
Prior medications				
Beta-blocker, n (%)	161 (78.50)	64 (74.40)	97 (81.50)	0.222
ACEI/ARBs, n (%)	104 (500)	45 (52.30)	59 (49.60)	0.698
CCB, n (%)	20 (9.80)	5 (5.80)	12 (10.10)	0.274
Diuretic, n (%)	68 (33.20)	34 (30.50)	34 (28.60)	0.100
Nitrate, n (%)	71 (34.60)	34 (39.50)	37 (31.10)	0.210
Laboratory parameters				
Heart rate (/min)	70.00 (66.00, 85.00)	70.00 (63.50, 86.00)	70.00 (68.00, 84.00)	0.639
Myoglobin (ng/dL)	96.50 (42.47, 305.03)	145.10 (53.41, 311.81)	95.42 (30.00, 287.70)	0.024
Glucose (mmol/L)	6.06 (5.23, 8.36)	6.81 (5.41, 10.62)	5.87 (5.10, 7.48)	0.008
Troponin I peak (ng/dL)	11.78 (3.37, 34.17)	12.88 (4.57, 40.96)	11.78 (2.65, 29.47)	0.146
Hemoglobin (g/L)	140.00 (129.00, 148.00)	140.00 (125.75, 149.25)	140.00 (130.00, 147.00)	0.883
Albumin (g/L)	36.84±3.89	36.55±4.55	37.05±3.35	0.359[a]
Total cholesterol (mmol/L)	4.50 (3.86, 5.09)	4.42 (3.87, 5.12)	4.53 (3.83, 4.86)	0.269
Triglyceride (mmol/L)	1.52 (1.09, 2.04)	1.51 (1.08, 2.06)	1.52 (1.07, 2.03)	0.578
HDL cholesterol (mmol/L)	1.09 (0.93, 1.23)	1.08 (0.93, 1.18)	1.09 (0.92, 1.27)	0.434
LDL cholesterol (mmol/L)	2.64 (2.20, 3.00)	2.56 (2.19, 2.98)	2.64 (2.20, 3.07)	0.513
Serum creatinine (μmol/L)	75.00 (63.50, 88.00)	77.00 (62.00, 105.00)	73.00 (64.00, 84.00)	0.077
Fibrinogen (g/L)	3.11 (2.55, 3.79)	3.49 (2.80, 3.90)	2.87 (2.48, 3.52)	<0.001
D-dimer (mg/L)	0.41 (0.27, 0.81)	0.57 (0.31, 1.04)	0.37 (0.23, 0.54)	<0.001
Lipoprotein (a) (mg/L)	97.00 (55.00, 189.55)	128.50 (76.35, 251.00)	85.00 (42.00, 158.30)	0.001
Uric acid (μmol/L)	368.00 (291.50, 453.00)	394.00 (282.75, 510.25)	359.00 (294.00, 428.00)	0.076
Carotid artery calcification, n (%)	94 (45.90)	34 (39.50)	60 (50.40)	0.123
LVEF (%)	59.00 (57.00, 61.00)	58.00 (53.75, 60.00)	60.00 (58.00, 61.00)	<0.001
LVDd (mm)	46.00 (43.00, 49.00)	46.00 (44.00, 49.00)	46.00 (42.00, 49.00)	0.115
Mitral regurgitation, n (%)	108 (52.70)	56 (65.10)	52 (43.70)	0.002
Localization of MI, n (%)				
Left main coronary artery, n (%)	9 (4.40)	6 (7.00)	3 (2.50)	0.234
Left anterior descending artery, n (%)	105 (51.20)	40 (46.50)	65 (54.60)	0.252
Left circumflex artery, n (%)	28 (13.70)	12 (14.00)	16 (13.40)	0.917
Right coronary artery, n (%)	63 (30.70)	28 (32.60)	35 (29.40)	0.630
Angiographic characteristics				
Number of diseased arteries ≥ 2, n (%)	136 (66.30)	66 (76.70)	70 (58.80)	0.007
Mean stent diameter (mm)	3.00 (2.75, 3.25)	3.00 (2.75, 3.50)	3.00 (2.75, 3.25)	0.366
Total stent length (mm)	36.00 (27.00, 52.00)	36.00 (28.00, 58.25)	36.00 (24.00, 47.00)	0.049
No-reflow, n (%)	41 (20.00)	26 (30.20)	15 (12.60)	0.002
Gemini score	64.00 (42.50, 87.00)	80.00 (51.50, 99.50)	54.00 (40.00, 80.00)	<0.001
Inflammation indicators				
LCR at admission	27.03 (8.29, 60.59)	17.65 (4.86, 31.64)	49.66 (13.96, 91.88)	<0.001
LCR at 24 hours post-PCI	2.64 (1.34, 5.43)	1.16 (0.68, 2.25)	4.73 (2.52, 8.36)	<0.001
LCR at discharge	25.85 (9.29, 71.18)	12.94 (5.22, 36.56)	42.31 (15.39, 88.64)	<0.001

(*Continued*)

Table 1 (Continued).

Basic Clinical Characteristics	All, n=205	MACE group, n=86	Non-MACE group, n=119	*P* -value[b]
LCR (admission-24 hours post-PCI)	23.65 (6.62, 55.79)	15.47 (3.91, 29.57)	35.70 (9.80, 82.88)	<0.001
LCR (discharge – 24 hours post-PCI)	21.88 (6.21, 66.45)	11.61 (3.68, 36.11)	34.57 (12.37, 75.50)	<0.001
LCR (discharge - at admission)	0.87 (−24.64, 26.57)	0.82 (−16.06, 18.33)	2.17 (−45.91, 29.50)	0.280

Notes: [a]Unpaired Student's *t*-test. [b]Mann–Whitney *U*-test and chi-square/Fisher's exact test.

Abbreviations: MACEs, major adverse cardiovascular events; BMI, body mass index; ACEI/ARBs, angiotensinogen converting enzyme inhibitor/angiotensinogen receptor blockers; CCB, calcium channel blocker; HDL cholesterol, high-density lipoprotein cholesterol; LDL cholesterol, low-density lipoprotein cholesterol; LVEF, left ventricular ejection fraction; LVDd, Left ventricular end diastolic diameter; LCR, lymphocyte to C-reactive protein ratio; PCI, percutaneous coronary intervention.

Univariate and Multivariate Cox Regression Analysis

Variables with $P < 0.05$ in Table 1 underwent univariate Cox regression analysis (Table 2). Following the univariate analysis, multivariate Cox regression was performed, adjusting for confounding factors using forward and backward likelihood ratio methods (Table 3). The forward method identified Gensini score (HR, 1.016; 95% CI, 1.009–1.024; $P < 0.001$), total stent length (HR, 1.017; 95% CI, 1.003–1.031; P=0.016), lipoprotein (a) (HR, 1.011; 95% CI, 1.000–1.002; P=0.032), and LCR 24 hours post-PCI (HR, 0.559; 95% CI, 0.465–0.672; $P < 0.001$) as independent risk factors for long-term prognosis in patients with STEMI post-PCI. The backward method revealed Gensini score (HR, 1.015; 95% CI, 1.007–1.022; $P < 0.001$), total stent length (HR, 1.015; 95% CI, 1.002–1.029; P=0.025), lipoprotein (a) (HR, 1.001; 95% CI, 1.000–1.002; P=0.043), LCR at admission (HR, 0.995; 95% CI, 0.989–1.000; P=0.002), and LCR at 24 hours post-PCI (HR, 0.587; 95% CI, 0.486–0.708; $P < 0.001$) as independent risk factors for long-term prognosis in patients with STEMI post-PCI.

Table 2 Univariate Cox Proportional Hazard Regression Analysis of MACEs Occurrence Within 1 Year of Hospital Discharge in Patients with STEMI After PCI

	Univariate Analysis			
	P-value	HR	95% CI	
Gensini score	<0.001	1.020	1.013	1.027
Diabetes mellitus, n (%)	0.016	1.770	1.111	2.821
Killip classification ≥ II, n (%)	<0.001	2.758	1.803	4.219
Myoglobin (ng/dL)	0.005	1.000	1.000	1.001
Lipoprotein (a) (mg/L)	0.006	1.001	1.000	1.002
Glucose (mmol/L)	<0.001	1.109	1.047	1.174
D-dimer (mg/L)	0.002	1.428	1141	1.788
Fibrinogen (g/L)	<0.001	1.322	1.138	1.535
LVEF (%)	<0.001	0.944	0.916	0.974
No-reflow, n (%)	0.002	2.085	1.315	3.309
Mitral regurgitation, n(%)	0.003	1.978	1.269	3.084
Number of diseased arteries ≥ 2, n (%)	0.006	2.017	1.223	3.328
Total stent length (mm)	0.014	1.015	1.003	1.027
LCR at admission	<0.001	0.987	0.980	0.994
LCR at 24 hours post-PCI	0.001	0.535	0.444	0.644
LCR at discharge	0.071	0.998	0.995	1.000
LCR (admission-24 hours post-PCI)	<0.001	0.990	0.984	0.996

Abbreviations: MACEs, major adverse cardiac events; PCI, percutaneous coronary intervention; LVEF, left ventricular ejection fraction; LCR, lymphocyte-to-C-reactive protein ratio; HR, hazard ratio; CI, confidence interval.

Table 3 Multivariable Cox Proportional Hazard Regression Analysis of MACEs Occurrence Within 1 Year of Hospital Discharge in Patients with STEMI After PCI

Multivariable Analysis								
	Forward Likelihood Ratio				Backward Likelihood Ratio			
	P-value	HR	95% CI		*P*-value	HR	95% CI	
Gensini score	<0.001	1.016	1.009	1.024	<0.001	1.015	1.007	1.022
Total stent length (mm)	0.016	1.017	1.003	1.031	0.025	1.015	1.002	1.029
Lipoprotein (a) (mg/L)	0.032	1.001	1.000	1.002	0.043	1.001	1.000	1.002
LCR at admission					0.044	0.995	0.989	1.000
LCR at 24 hours post-PCI	<0.001	0.559	0.465	0.672	<0.001	0.587	0.486	0.708

Abbreviations: LCR, lymphocyte-to-C-reactive protein ratio; HR, hazard ratio; CI, confidence interval.

ROC Curve Evaluated the Performance of LCR at Admission and LCR at 24 Hours Post-PCI in Predicting MACEs

The Receiver Operating Characteristic (ROC) curves were employed to assess the LCR at admission and 24 hours post-PCI in predicting MACEs. The Area Under the Curve (AUC) for LCR at admission in predicting MACEs was 0.707 (95% CI: 0.640–0.768, $P<0.001$). The optimal cutoff value was 50.286, with a sensitivity of 74.00% and a specificity of 82.40% (Figure 1A). For the LCR 24 hours post-PCI in predicting MACEs, the AUC was 0.883 (95% CI: 0.831–0.924, $P<0.001$). The optimal cutoff value was 2.252, with a sensitivity of 76.70% and a specificity of 82.40% (Figure 1B). These findings suggest that both LCR at admission and 24 hours post-PCI serve as robust predictors of MACEs.

Subsequently, the DeLong test was employed to compare the ROC curves of LCR at admission and 24 hours post-PCI in predicting MACEs. The results indicated a significantly superior predictive effect for LCR 24 hours post-PCI ($P<0.001$). Building upon these findings, we further explored the impact of LCR 24 hours post-PCI on the clinical prognosis of STEMI patients.

Prognostic Value of LCR at Admission and 24 Hours Post-PCI for STEMI Patients

According to the optimal cut-off value of LCR at admission obtained from the previous ROC curve, patients were categorized into two groups: LCR at admission > 50.29 and LCR at admission ≤ 50.29. Similarly, based on the optimal cut-off value of LCR at 24 hours post-PCI, patients were grouped into LCR at 24 hours post-PCI > 2.25 and LCR at 24 hours post-PCI ≤ 2.25. Kaplan-Meier analysis (Figure 2) revealed that patients with LCR at admission ≤ 50.29 had a significantly higher risk of developing MACEs compared to those in patients with LCR at admission > 50.29 (Log-rank

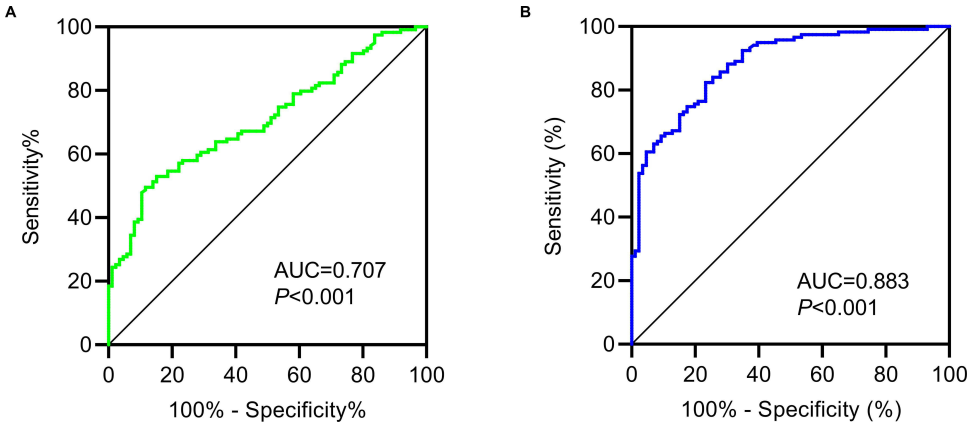

Figure 1 Receiver operating characteristic (ROC) curves. (**A**) ROC curve of LCR at admission in predicting MACEs; (**B**) ROC curve of LCR 24 hours post-PCI in predicting MACEs.

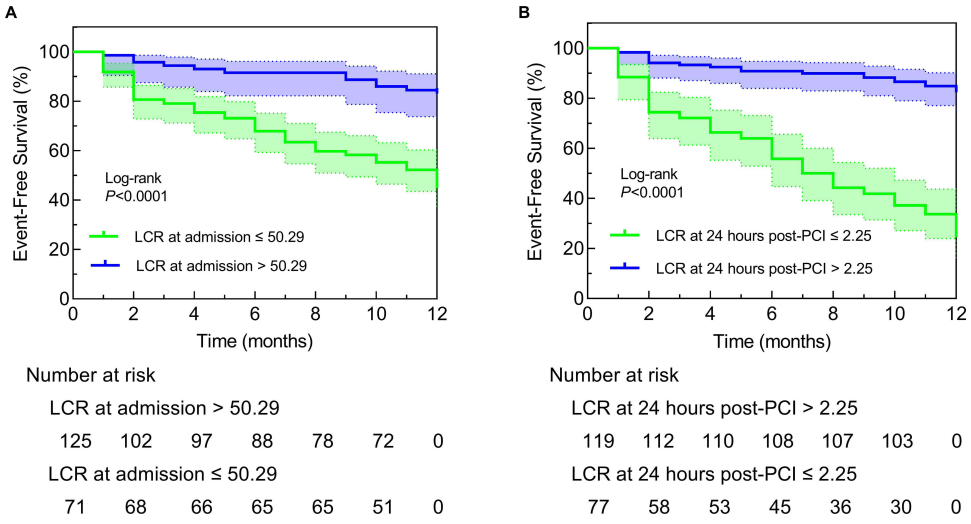

Figure 2 Kaplan–Meier survival analysis. (**A**) Patients with low LCR values at admission (LCR at admission ≤ 50.29) had a much higher risk of MACEs compared to that in patients with a high value (LCR at admission > 50.29); (**B**) Patients with a low value of LCR at 24 hours post-PCI (LCR at 24 hours post-PCI ≤ 2.25) had a much higher risk of MACEs compared to that in patients with a high value (LCR at 24 hours post-PCI > 2.25).

$P < 0.0001$). Additionally, patients with LCR at 24 hours post-PCI ≤ 2.25 exhibited a significantly higher risk of MACEs compared to those in patients with LCR at 24 hours post-PCI > 2.25 (Log-rank $P < 0.0001$).

To further investigate the prognostic value of LCR at admission and 24 hours post-PCI for MACEs in STEMI patients, we assessed its impact on cardiac death, heart failure, unstable angina pectoris after stenting, and non-fatal myocardial infarction. Kaplan–Meier analysis (Figure 3) revealed that patients with LCR at admission ≤ 50.29 faced a significantly higher risk of cardiac death compared to those in patients with LCR at admission > 50.29 (Log-rank $P < 0.0012$). The risk of cardiac death remained significantly higher in patients with LCR at 24 hours post-PCI ≤ 2.25 compared to those in patients with LCR at 24 hours post-PCI > 2.25 (Log-rank $P < 0.0001$). Patients exhibiting LCR at admission ≤ 50.29 also had a significantly higher risk of heart failure than compared to that in patients with LCR at admission > 50.29 (Log-rank P=0.0039). Similarly, patients with LCR at 24 hours post-PCI ≤ 2.25 faced a significantly

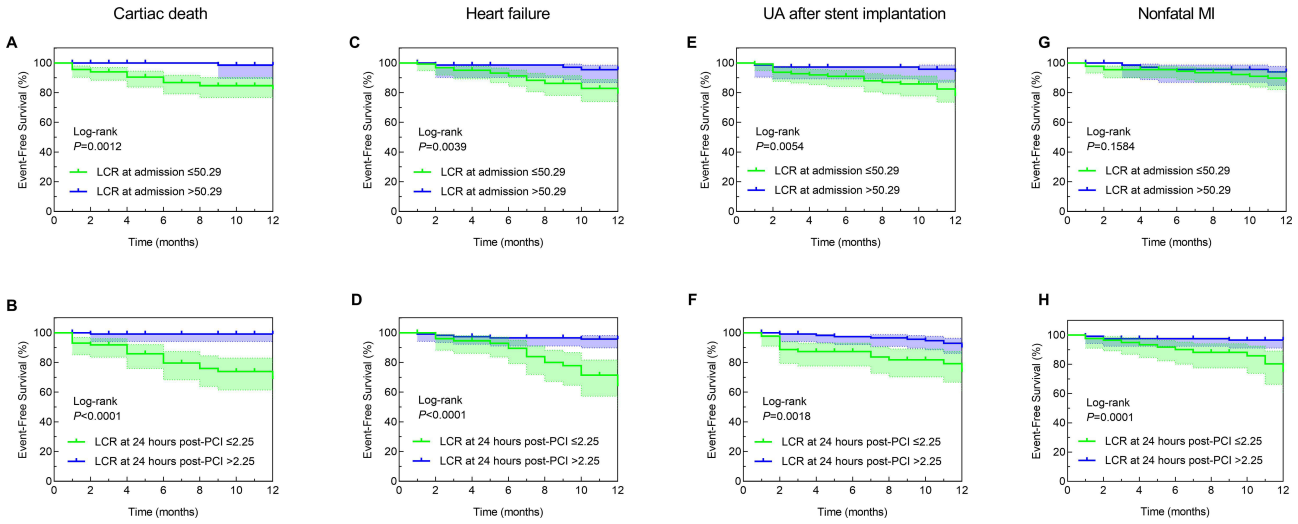

Figure 3 Kaplan–Meier survival analysis. (**A**) LCR at admission predicts the risk of cardiac death in STEMI patients; (**B**) LCR at 24 hours post-PCI predicts the risk of cardiac death in STEMI patients; (**C**) LCR at admission predicts the risk of heart failure in STEMI patients; (**D**) LCR at 24 hours post-PCI predicts the risk of heart failure in STEMI patients; (**E**) LCR at admission predicts the risk of unstable angina pectoris after stenting in STEMI patients; (**F**) LCR at 24 hours post-PCI predicts the risk of unstable angina pectoris after stenting in STEMI patients; (**G**) LCR at admission predicts the risk of non-fatal myocardial infarction in STEMI patients; (**H**) LCR at 24 hours post-PCI predicts the risk of non-fatal myocardial infarction in STEMI patients.

Abbreviations: UA, unstable angina; MI, myocardial infarction; LCR, lymphocyte-to-C-reactive protein ratio; PCI, percutaneous coronary intervention.

higher risk of heart failure compared to those in patients with LCR at 24 hours post-PCI > 2.25 (Log-rank $P < 0.0001$). The risk of unstable angina pectoris after stenting was significantly elevated in patients with LCR at admission ≤ 50.29 compared to those in patients with LCR at admission > 50.29 (Log-rank P=0.0054). Similarly, the risk of unstable angina pectoris after stenting was significantly higher in patients with LCR at 24 hours post-PCI ≤ 2.25 compared to that in patients with LCR at 24 hours post-PCI > 2.25 (Log-rank P=0.0018). No significant difference in the risk of non-fatal myocardial infarction was observed between patients with LCR at admission ≤ 50.29 and those with LCR at admission > 50.29 (Log-rank P=0.1584). However, the risk of non-fatal myocardial infarction in patients with LCR at 24 hours post-PCI ≤ 2.25 was significantly higher compared to that in patients with LCR at 24 hours post-PCI > 2.25 (Log-rank $P <$ 0.0001).

Correlation Between LCR at 24 Hours Post-PCI and Gensini Score, TIMI Flow, and Mitral Regurgitation

Spearman correlation analysis was employed to explore the relationship between the Gensini scores of 205 patients with STEMI and LCR at 24 hours post-PCI. The results revealed a negative correlation between the Gensini score ($r_s = -0.200$, $P = 0.004$) and LCR at 24 hours post-PCI (Figure 4A). Additionally, STEMI patients were categorized into a reflow group (TIMI = 3) and a no-reflow group (TIMI ≤ 2) based on TIMI flow post-PCI. The LCR at 24 hours post-PCI was significantly different between the two groups ($P = 0.035$) (Figure 4B). Furthermore, STEMI patients were stratified into a mitral regurgitation group and a non-mitral regurgitation group, depending on whether mitral regurgitation occurred post-PCI during hospitalization. The results demonstrated a significant difference in LCR at 24 hours post-PCI between the two groups ($P = 0.002$) (Figure 4C).

Correlation of LCR at 24 Hours Post-PCI with Other Traditional Cardiovascular Risk Factors

We conducted an analysis to examine the relationship between LCR 24 hours post-PCI and traditional cardiovascular risk factors, including Lp(a), D-dimer, fibrinogen, LVEF, diabetes mellitus, Killip class, and the number of diseased arteries (Figures 5 and 6). The results indicated that Lp(a) ($r_s = -0.214$, $P = 0.002$), D-dimer ($r_s = -0.359$, $P < 0.001$), and fibrinogen ($r_s = -0.281$, $P < 0.001$) negatively correlated with LCR 24 hours post-PCI. LVEF showed a positive correlation with LCR 24 hours post-PCI ($r_s = 0.279$, $P < 0.001$). A significant difference was observed in LCR at 24 hours post-PCI between the diabetes mellitus group and the non-diabetes mellitus group ($P = 0.011$), Killip class ≥ II group and Killip class ≤ I group ($P < 0.001$), and the group with the number of diseased arteries ≥ 2 and the group with the number of diseased arteries ≤ 1 ($P = 0.039$). The diabetes mellitus group exhibited a lower level of LCR at 24 hours post-PCI compared to that in the non-diabetes mellitus group. Similarly, the Killip class ≥ II group had a lower level of LCR at 24 hours post-PCI compared to in patients the Killip class ≤ I group, and the group with the number of diseased

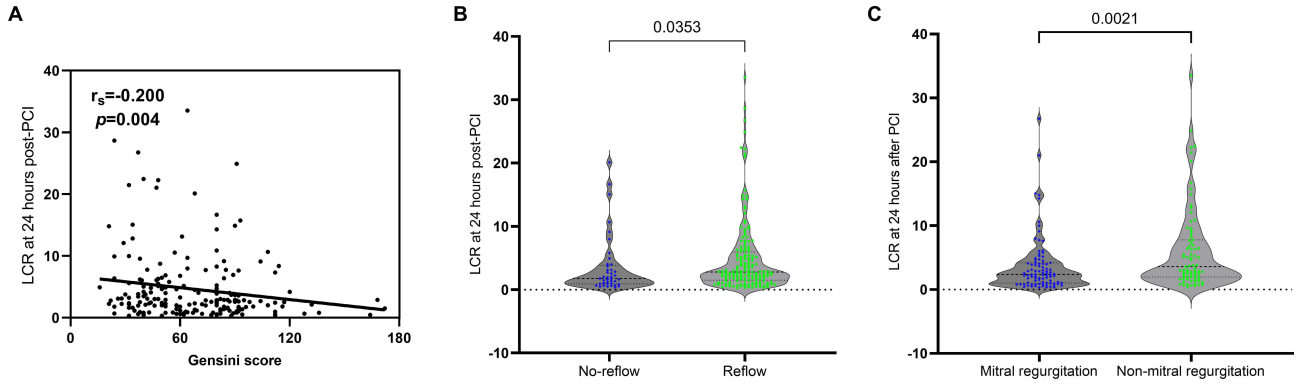

Figure 4 Correlation of LCR at 24 hours post-PCI with Gensini score, TIMI flow, and mitral regurgitation. (**A**) Spearman correlation analysis between Gensini score and LCR at 24 hours post-PCI; (**B**) The no-reflow group had a lower level of LCR at 24 hours post-PCI compared to that in the reflow group; (**C**) The mitral regurgitation group had a lower level of LCR at 24 hours post-PCI compared to that in the non-mitral regurgitation group.

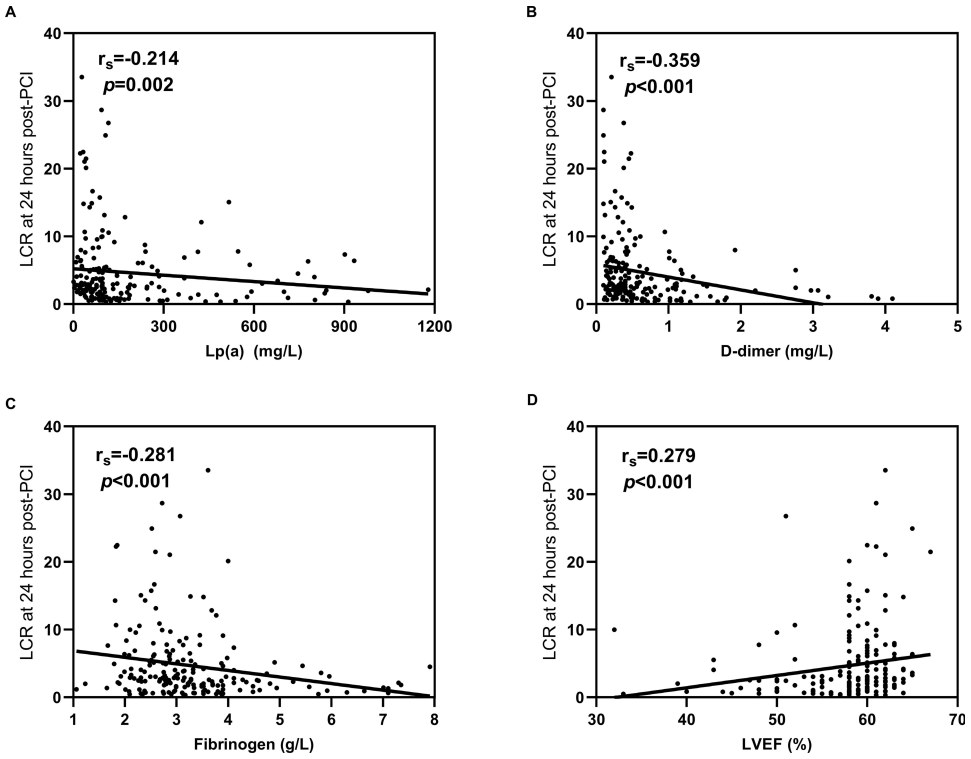

Figure 5 Correlation of LCR at 24 hours post-PCI with Lp(a), D-dimer, fibrinogen and LVEF. (**A**) Spearman correlation analysis between Lp(a) and LCR at 24 hours post-PCI; (**B**) Spearman correlation analysis between D-dimer and LCR at 24 hours post-PCI; (**C**) Spearman correlation analysis between fibrinogen and LCR at 24 hours post-PCI; (**D**) Spearman correlation analysis between LVEF and LCR at 24 hours post-PCI.

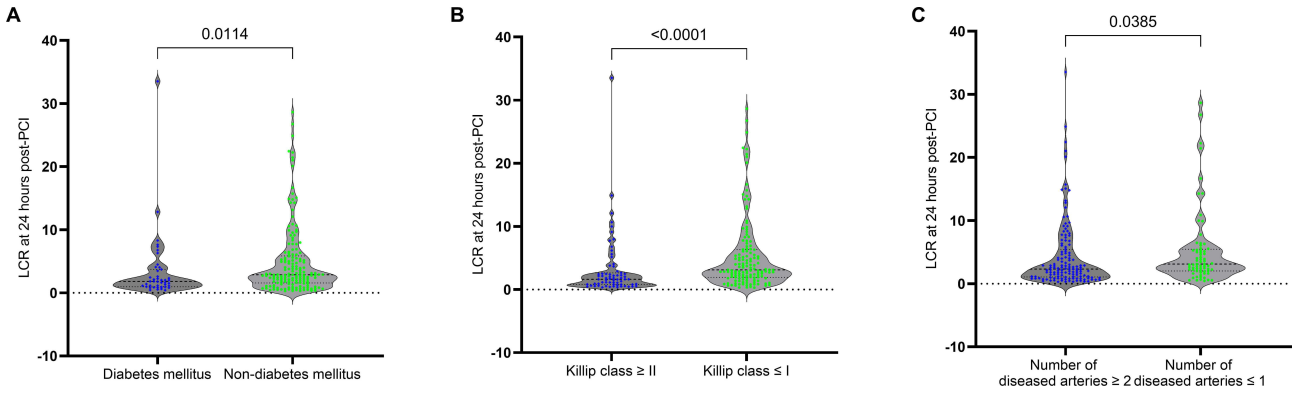

Figure 6 Correlation of LCR at 24 hours post-PCI with diabetes mellitus, Killip class, and number of diseased arteries. (**A**) The diabetes mellitus group had a lower level of LCR at 24 hours post-PCI compared to that in the non-diabetes mellitus group; (**B**) The Killip class ≥ II group had a lower level of LCR at 24 hours post-PCI compared to that in the Killip class ≤ I group; (**C**) The number of diseased arteries ≥ 2 group had a lower level of LCR at 24 hours post-PCI compared to that in the number of diseased arteries ≤ 1 group.

arteries ≥ 2 had a lower level of LCR at 24 hours post-PCI compared to that in the group with the number of diseased arteries ≤ 1.

Discussion

In this study, we retrospectively analyzed the routine examination results of STEMI patients at three time points during the hospitalization period. We subsequently followed up on long-term MACEs and examined the relationship between LCR at different time intervals and the occurrence of MACEs. Our results revealed that LCR at admission and 24 hours post-PCI were independent risk factors for MACEs, aligning with previous findings.[16] Furthermore, we identified that the

optimal cut-off value of LCR at 24 hours post-PCI (> 2.25) served as a superior predictor of MACEs compared to the optimal cut-off value of LCR at admission (> 50.29). These findings offer a more convenient and accurate approach to assessing the long-term prognosis of patients with STEMI after PCI, providing new insights into the evaluation of individualized treatment strategies upon patient discharge.

According to the ROC curve analysis, we determined the optimal cutoff values for LCR at admission and LCR 24 hours post-PCI. We then categorized them into high- and low-level groups based on these cutoff values. Kaplan–Meier analysis of these two groups led us to the conclusion that both LCR at admission and LCR 24 hours post-PCI exhibit a strong long-term predictive effect on the occurrence of MACEs. The primary MACEs considered were cardiogenic death, heart failure, unstable angina pectoris following stent implantation, and nonfatal myocardial infarction. Further Kaplan–Meier analysis revealed that LCR at admission and 24 hours post-PCI had a robust long-term predictive effect on cardiac death, heart failure, and unstable angina pectoris following stenting. However, for the extended prediction of nonfatal myocardial infarction, only LCR at 24 hours post-PCI demonstrated a significant long-term predictive effect. In summary, the long-term predictive efficacy of LCR at 24 hours post-PCI surpassed that of LCR at admission.

We further observed that 24 hours post-PCI, the LCR correlated with traditional cardiovascular risk factors, including the Gensini score, Lp(a), D-dimer, fibrinogen, LVEF, diabetes mellitus, TIMI flow, Killip class, and the number of vascular lesions. These conventional cardiovascular risk factors have all been confirmed as contributors to the occurrence of MACEs.[10,14,22–27] While there are limited studies on LCR as a relatively new biomarker for predicting MACEs, our research affirms that the LCR 24 hours post-PCI is associated with traditional cardiovascular risk factors and consistently predicts long-term MACEs.

Our study revealed that the LCR at 24 hours post-PCI serves as a robust predictor of long-term MACEs. We inferred that a higher Gensini score correlates with more severe coronary artery lesions. When blood vessels are blocked, individuals with elevated Gensini scores exhibit a weaker compensatory capacity and a heightened inflammatory reaction in the body. The complexity of the coronary artery is closely linked to emergency interventional treatment, operation time, and operation difficulty. Patients with high Gensini scores may necessitate more extended surgery time, encounter more challenging procedures, and experience heightened sympathetic transition excitation. The LCR is determined by two indicators: lymphocyte count and CRP. Inflammatory aggravation and an increase in catecholamine and cortisol levels, particularly under stress, contribute to increased lymphocyte apoptosis and a decrease in peripheral blood lymphocyte count. Prior studies have demonstrated that reduced peripheral blood lymphocyte counts are associated with the progression of atherosclerosis, impaired coronary microcirculation, and major cardiac events in patients with acute chest pain. CRP, as the most representative inflammatory marker, not only reflects the inflammatory response of the body but also participates in the pathogenesis of acute myocardial infarction through complement activation and the influence of vascular endothelial dysfunction. Consequently, it can be inferred that patients with higher Gensini scores will exhibit a lower LCR 24 hours post-PCI. Thus, LCR 24 hours post-PCI can comprehensively reflect the varying degrees of inflammation caused by different Gensini scores, offering superior long-term prediction efficacy.

Similarly, concerning TIMI flow, the LCR 24 hours post-PCI reflects the inflammatory response in patients who have undergone emergency PCI. Emergency PCI stands out as the most crucial treatment option for STEMI patients. Active intraoperative prevention and swift, accurate treatment of non-reflow lead to markedly different patient outcomes. We posit that LCR assessed 24 hours post-PCI reflects real-world outcomes influenced by TIMI flow changes and holds superior prognostic value.

Mitral regurgitation arises from restricted valve motion, dysfunction, reduced left ventricular force, and systolic dyssynchronization due to papillary muscle displacement. Its occurrence following acute myocardial infarction tends to worsen long-term prognosis.[28] Our study revealed that the LCR level 24 hours post-PCI was lower in the group with mitral regurgitation post-PCI compared to that in the group without regurgitation. This sheds new light on the pathophysiological mechanisms contributing to the development of mitral regurgitation.

Limitations of the Study

Our study had certain limitations. First, it was a single-center retrospective study with a small sample size and a relatively short follow-up time. Large-scale data from multiple centers are essential to validate the accuracy of the results. Second,

while this study demonstrated that STEMI patients with a low LCR at admission and LCR at 24 hours post-PCI had a poor prognosis, it remains unclear whether other confounding factors, such as anti-inflammatory therapy, may impact their outcomes. Addressing this uncertainty necessitates a multicenter, large-sample prospective study. Finally, given the retrospective nature of our analysis, the data were acquired at admission, 24 hours post-PCI, and at three time points before discharge. The fluctuations in LCR and the identification of its lowest point demand a more precise experimental design and comprehensive research.

Conclusion

This retrospective study analyzed the lymphocyte count to CRP ratio in patients with STEMI at multiple time points, spanning from admission to PCI to discharge. The study compared the fluctuations in this ratio to comprehensively determine its predictive effect on MACEs occurring within one year after PCI. The findings suggest that the lymphocyte count to CRP ratio 24 hours post-PCI may serve as the most reliable predictor of long-term MACEs in patients with STEMI after PCI. These results could guide clinicians in follow-up evaluations, optimizing management, and improving the overall quality of life for these patients.

Data Sharing Statement

Data from this study are available from the corresponding author upon request.

Ethical Approval and Informed Consent

The study adhered to the Declaration of Helsinki, approved by the Ethics Committee of Wuxi Clinical College, Anhui Medical University (ethics approval number: 20240105). Informed consent requirement was waived due to the retrospective nature of the study. At the time of the patient's visit, we notify them of the Patient Information Confidentiality Statement and make sure their privacy is sufficiently protected in order to maintain the confidentiality of patient information.

Author Contributions

Each author contributed significantly to the work reported, whether it was in the form of ideation, study design, execution, data acquisition, analysis, and interpretation, or in all of these areas; they all helped draft, revise, or critically evaluate the article; they all approved the final version that was submitted for publication; they all agreed on the journal to which the article was submitted; and they all agreed to take responsibility for the work in its entirety.

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Disclosure

The authors report no conflicts of interest in this work.

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