

Prognostic value of platelet/lymphocyte ratio and CAMI-STEMI score for major adverse cardiac events in patients with acute ST segment elevation myocardial infarction after percutaneous coronary intervention

A prospective observational study

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Abstract

The aim of this study was to investigate the predictive value of the platelet-to-lymphocyte ratio (PLR) and the China Acute Myocardial Infarction registry-ST segment elevation myocardial infarction (CAMI-STEMI) score for major adverse cardiovascular events (MACE) in ST-segment elevation myocardial infarction (STEMI) patients undergoing percutaneous coronary intervention (PCI) within 6 months.

We enrolled STEMI patients who received emergency PCI in the First Hospital of Lianyungang from January 2016 to December 2019. The clinical characteristics of the patients, the PLR, and the CAMI-STEMI score were recorded. The MACE included heart failure, nonfatal re-infarction, recurrent angina pain, re-hospitalization for cardiovascular-related illness, repeat PCI, coronary artery bypass grafting, and all-cause mortality. According to the incidence of MACE during the follow-up the patients were divided into the MACE group (96 cases, 24.8%) and the non-MACE group (291 cases, 75.2%).

The PLR, 147.62 (121.13–205.20) in MACE group, was 111.19 (90.23–146.42) in the non-MACE group in comparison, the PLR was higher in MACE group than that in non-MACE group (P < .01). Multivariate regression analysis showed that PLR (odds ratio (OR)=1.007, 95% confidence interval (CI) 1.002–1.012, P < .01) and CAMI-STEMI score (OR=1.575, 95% CI: 1.311–1.892, P < .01) were independent predictors of MACE. Besides, I-BIL was also an independent predictor of MACE (OR=1.007, 95% CI: 1.011–1.146, P = .021). Reciever-operating characteristic curve showed that the area under curve of PLR was 0.704 (95%CI 0.644–0.763, P < .001). The cutoff value was 112.6, the sensitivity and specificity were 84.4% and 51.9%, respectively. PLR and CAMI-STEMI scores were independent risk factors of MACE after PCI in STEMI patients.

Abbreviations: ASE = American Society of Echocardiography, CAMI-STEMI = China Acute Myocardial Infarction registry-ST segment elevation myocardial infarction, GRACE = Global Registration of Acute Coronary Syndromes Events = indirect bilirubin, K = potassium, LVEF = left ventricular ejection fraction, LY % = lymphocyte ratio, LY = lymphocyte count, MACE = major adverse cardiovascular events, MONO = monocyte, N = sodium ion concentration, PCI = percutaneous coronary intervention, PLR = platelet-to-lymphocyte ratio, PLT = platelet, ROC = receiver-operating characteristic, WBC = white blood cell.

Keywords: major adverse cardiovascular events (MACE), platelet-to-lymphocyte ratio (PLR), prognosis

1. Introduction

Coronary heart disease is the leading cause of morbidity and mortality worldwide. The common pathophysiologic substrate is atherosclerosis which starts at childhood and develops throughout life. In ST elevation myocardial infarction (STEMI) patients, percutaneous coronary intervention (PCI) is crucial to improve myocardial savage and prevent reperfusion injury.^[1] Although there are a myriad of cardiovascular risk prediction

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models and risk factors that are being targeted by advanced therapies, MACE may still occurred after PCI unfortunately. Platelet/lymphocyte ratio (PLR), an inexpensive and easily available indicator, has emerged as a potential inflammatory marker of mortality in patients with STEMI.^[2] At the 2017 European Society of Cardiology, Yang et al developed the China Acute Myocardial Infarction registry-ST Elevation Myocardial Infarction (CAMI-STEMI) score.^[3] The CAMI-STEMI score can predict mortality among Chinese STEMI patients,^[4] with similar performance to the well-established Thrombolysis in Myocardial Infarction score and the Global Registration of Acute Coronary Syndromes Events (GRACE) score, while relying solely on simple variables. PLR can be used as a prognostic marker in various cardiovascular conditions including coronary artery disease^[5] and infarct-related artery patency in STEMI before primary PCI.^[6] However, the prognostic role of PLR and CAMI-STEMI score on the prognosis of MACE in STEMI after PCI remains in dispute. In this study we explore the diagnostic value of PLR and CAMI-STEMI scores in STEMI patients after PCI.

2. Materials and methods

This study is a prospective observational study. We selected 387 patients with STEMI who received PCI at the First People's Hospital of Lianyungang from January 2016 to December 2019. The inclusion criteria was as follows, patients with STEMI who were diagnosed based on the guidelines for the diagnosis and treatment of acute ST segment elevation myocardial infarction in 2019 (China). We excluded patients with cardiogenic shock, cardiac arrest, infection, major surgery, trauma, bleeding, acute or chronic congestive heart failure, aortic dissection, myocarditis, endocarditis, hypertrophic cardiomyopathy, scleroderma, severe infection, fever, acute pulmonary embolism, stroke, respiratory failure, heart surgery, and tumor over the past 3 months; we also excluded patients with no complete clinical data or on drug therapy potentially affecting coagulation.^[5] This study was approved by the ethical committee of the First People's Hospital of Lianyungang, and all patients signed informed consent.

2.1. Patient characteristics

All patients were followed up by a cardiovascular physician over the phone, outpatient visit, and clinical endpoints for all subjects were obtained. Major adverse cardiovascular events (MACE) has been defined by various authors since mid-1990 to include an overlapping range of adverse events.^[7] The MACE included heart failure, non-fatal re-infarction, recurrent angina pain, rehospitalization for cardiovascular-related illness, repeat percutaneous coronary intervention (PCI), coronary artery bypass grafting, and all-cause mortality.^[8] The endpoint was the MACE during the follow-up period (6 months after discharge).

The CAMI-STEMI score composed of 7 indicators published by the European Society of Cardiology in 2017: female (1 point), anterior wall infarction (1 point), systolic blood pressure \leq 115 mmHg (2 points), age \geq 70 years (2 points), heart rate \geq 100 beats/ min (2 points), Killip class >grade I (2 points) and cardiac arrest (4 points).^[6]

All patients were divided into MACE group and non-MACE group based on the 6-month follow-up results. Each patient's clinical baseline data were collected, which included blood cell count, renal function panel, electrolyte, liver function panel, cardiac biomarkers, cardiac Doppler ultrasound, and coronary angiography.

2.2. Research method

All patients were given a loading dose of aspirin (300 mg), clopidogrel (300 mg), or ticagrelor (180 mg) before PCI. At least two cardiology interventional doctors performed PCI. Only the criminal vessels were treated during emergency PCI, and other narrow blood vessels were treated after 1 week.

2.3. Echocardiographic methods

Echocardiographic studies were performed in accordance with American Society of Echocardiography (ASE) guidelines. On the day after PCI (before discharge), images were obtained using a standard ultrasound machine (GE Healthcare, Little Chalfont, United Kingdom) with a 1.5 MHz probe in standard parasternal and apical views. The pulsation, valve structure, blood flow and thickness of ventricular septum were carefully and continuously monitored for at least 3 cycles. Each measurement was performed by the same analyst for all participants and were averaged over 3 cycles. Left ventricle volumes and LVEF were obtained from apical 2- and 4-chamber views and derived according to the modified biplane Simpson's rule.

2.4. Statistical analysis

Analysis was performed using SPSS software, version 22.0 (SPSS, Inc., Chicago, IL). Categorical variables were expressed as frequencies with percentages, and χ^2 test was used for comparing differences in clinical parameters, nonparametric tests were used when data did not meet normality. A receiver-operating characteristic (ROC) curve was constructed, and an area under the curve was calculated to detect the cutoff value of PLR for detecting mortality and complications. Multivariate logistic regression analysis was performed to identify independent predictors of mortality and the difference was considered significant when P < .05.

3. Results

3.1. Comparison of CAMI-STEMI scores

Baseline clinical data were presented in Table 1. The total 387 STEMI patients were divided into MACE group (96 cases, accounting for 24.8%) and non-MACE group (291 cases, accounting for 73.2%). The CAMI-STEMI score was shown in Table 1: there were statistically significant differences in age, systolic blood pressure, heart rate, Killip class and cardiac arrest between the 2 groups (P < .05). However, there were no statistically significant differences in sex and anterior myocardial infarction (P > .05).

3.2. Baseline characteristics

Baseline characteristics of patients in MACE and non-MACE group are summarized in Table 2. The patients were 71 and 67 years of age in MACE and non-MACE group, respectively. The PLR level of MACE group was 147.62 (121.13–205.20), which was higher than that of non-MACE group (111.19 [90.23–146.42]) (P<.01), and there were statistically significant differ-

Table 1

| Comparison of CAMI-STEMI scores. | | | | | | | | |
|----------------------------------|--------------------|-------------|---|----------------------------|------------------------|--------------------|----------------------------|----------|
| | Female, no. (%) | | | systolic blood pressure | Heart rate /min | Killip class | Cardiac arrest, no. (%) | |
| | No. | С | Anterior myocardial infarction, no. (%) | Age (≥70 y), no. (%) | (≤115mmHg), No. (%) | (≥100), No. (%) | (>Level I), no. (%) | |
| MACE group | 96 | 31 (32.29) | 41 (42.70) | 54 (56.25) | 17 (17.70) | 17 (17.70) | 66 (68.75) | 4 (4.16) |
| Non-MACE group | 291 | 102 (35.05) | 102 (35.05) | 117 (40.20) | 28 (9.62) | 24 (8.24) | 263 (90.37) | 1 (0.34) |
| χ^2 value | | 0.244 | 1.817 | 7.534 | 4.593 | 6.822 | 26.502 | 8.273 |
| Ρ | | .622 | .178 | .006 | .032 | .009 | <.01 | .004 |

ences in age, PLR, lymphocyte ratio, lymphocyte count, sodium ion concentration (N), and CAMI-STEMI score between MACE group and non-MACE group (P < .05). There were no significant differences in hypertension, diabetes mellitus, previous stents implantation, body mass index, white blood cell, platelet, monocyte (%) [MONO,(%)], MONO, potassium (K), total bile acid, total bilirubin , indirect bilirubin (I-BIL), glucose, creatinine, total triglycerides, total cholesterol, low-density lipoprotein cholesterol (LD.

3.3. Cornary angiography data, medications, and clinical procedural

Patients in MACE group more frequently implanted stents and at the meantime implanted more stents than non-MACE group (P < .05) (Table 3), whereas there were no significant differences with regard to usage of aspirins, statins, IIb/IIIa receptor antagonists, crime vessel location (P > .05).

3.4. Cardiac doppler ultrasound in MACE and non-MACE group

As shown in Table 4, according to the results of Doppler ultrasound, there were statistically significant differences in LVEF and ventricular segmental motion abnormalities (P < .05) in the MACE group and non-MACE group, but there were no statistical differences between left ventricle and ventricular septal.

3.5. Univariate and multivariate analysis

As is presented in Table 5, univariate analysis showed that PLR was an independent predictor of MACE in STEMI patients after PCI (odds ratio [OR] 1.009; 95% confidence interval [CI] 1.005~1.013; P < .01). Multivariate analysis showed that CAMI-STEMI score was an independent risk factor of MACE incidence in STEMI patients after PCI (OR 1.575; 95% CI 1.311~1.892; P < .01). The Cox regression model included MONO%, I-BIL, CAMI-STEMI, score and PLR.

Table 2

Baseline characteristics of patients in MACE and non-MACE group.

| Variable | MACE group (n=96) | Non-MACE group (n=291) | Р |
|-------------------------------------|-----------------------|------------------------|------|
| Age, y, median (range) | 71 (63~78) | 67 (59~75) | .003 |
| Hypertension | 72 (75) | 211 (72.5) | .633 |
| Diabetes mellitus | 33 (34.3) | 74 (25.4) | .089 |
| Previous stents implantation | 32 (33.3) | 74 (25.42) | .132 |
| BMI, kg/m ²)(IQR) | 24.22 (22.81~26.25) | 24.83 (22.49~26.89) | .394 |
| PLR (IQR) | 147.62 (121.13~205.2) | 111.19 (90.23~146.42) | <.01 |
| WBC, 10 ⁹ cells/L (IQR) | 6.43 (5.41~7.62) | 6.32 (5.33~7.85) | .957 |
| HB, g/L (IQR) | 134 (124~146) | 139 (127~148) | .142 |
| PLT, 10 ⁹ cells/L (IQR) | 196 (165~233) | 189 (159~224) | .079 |
| LY (%), % (IQR) | 20.4 (15.84~27.37) | 26.3 (20.9~30.8) | <.01 |
| MONO (%), % (IQR) | 6.05 (4.72~7.75) | 5.6 (4.6~6.9) | .151 |
| LY, 10 ⁹ cells/L (IQR) | 1.33 (1~1.64) | 1.64 (1.23~2.05) | <.01 |
| MONO, 10 ⁹ cells/L (IQR) | 0.39 (0.29~0.46) | 0.37 (0.28~0.48) | .376 |
| K, mmol/L (IQR) | 3.92 (3.74~4.28) | 3.95 (3.74~4.2) | .643 |
| N, mmol/L (IQR) | 140.1 (138~141) | 140.6 (138.8~142.1) | .047 |
| TBA, μmol/L (IQR) | 4.75 (2.9~7.4) | 4 (2.6~7) | .304 |
| T-BIL, µmol/L (IQR) | 10.6 (8.72~15.12) | 10.8 (8~13.8) | .446 |
| I-BIL, µmol/L (IQR) | 7.4 (5.8~10.7) | 7.4 (5.4~9.9) | .319 |
| Glucose, mmol/L (IQR) | 5.76 (5.02~7.08) | 5.74 (5.07~7.05) | .643 |
| CR, μmol/L (IQR) | 92 (76~107) | 85 (71~102) | .089 |
| TG, mmol/L (IQR) | 1.3 (0.98~1.39) | 1.39 (1.02~2.18) | .296 |
| TC, mmol/L (IQR) | 3.8 (3.06~4.69) | 3.96 (3.25~4.99) | .288 |
| LDL-C, mmol/L (IQR) | 2.32 (1.69~2.88) | 2.37 (1.77~3.06) | .356 |
| CAMI-STEMI score (IQR) | 3 (2~5) | 2 (1~3) | <.01 |

Data are presented as median (IQR) or n (%). BMI=body mass index, CR=creatinine, HB=hemoglobin, I-BIL=indirect bilirubin, IQR = interquartile range, K=potassium, LDL-C=low-density lipoprotein cholesterol, LY=lymphocyte, MONO=monocyte, N=sodium, PLT=platelet, TBA=total bile acid, T-BIL=total bilirubin, TC=total cholesterol, TG=total triglycerides, WBC=white blood cell.

| Table 3 | | |
|------------|----------------|-------------|
| Medication | s and clinical | procedural. |

| Variable | MACE group (n=96) | Non-MACE group (n=291) | Р | |
|-------------------------------|----------------------|---------------------------|------|--|
| Aspirins | 89 (92.70) | 274 (94.15) | .61 | |
| Statins | 83 (86.45) | 235 (85.76) | .20 | |
| IIb/IIIa Receptor antagonists | 46 (47.91) | 118 (40.54) | .20 | |
| Stents implanted | 88 (91.66) | 243 (83.50) | .04 | |
| crime vessel Location | | 0.86 | | |
| LM | 3 (3.12) | 7 (2.40) | | |
| LAD | 43 (44.79) | 137 (47.07) | | |
| LCX | 19 (19.79) | 64 (21.99) | | |
| RCA | 31 (32.29) | 83 (28.52) | | |
| No. of stents implanted | 1.5 ± 0.8 | 1.1 ± 0.6 | <.05 | |

Data are presented as mean \pm standard deviation or n (%). LAD = left anterior descending, LCX = left circumflex branch, LM = left main coronary artery, RCA = right coronary artery.

3.6. ROC curve analysis

To obtain the optimal cutoff value of PLR, we performed ROC curve analysis. As showed in Figure 1, the cutoff value of the PLR for patients with MACE after PCI was 112.6 (area under the curve=0.704, 95% CI=0.644-0.763, Se=84.4%, Sp=51.9%).

4. Discussion

The main finding is that after controlling for the effects of different coronary artery lesions on MACE, PLR and CAMI-STEMI scores independently predicts MACE at long-term follow-up in patients with STEMI undergoing PCI. Platelets and inflammatory cells play a pivotal role in the evolution and pathogenesis of acute myocardial infarction and therosclerosis.^[9] Platelets are well-known components of hemostatic system, which was found to be involved in the pathogenesis of various inflammatory diseases recently. The role of inflammation in the prediction of CAD has also been investigated extensively.^[10] The lymphocyte count is inversely correlated with inflammation. PLR as an index contains both information on platelets and lymphocyte counts, therefore, the combination of increased platelet counts and low levels of lymphocytes can be an indispensable biomarker to predict the severity of inflammation. STEMI poses a serious threat to human life, earlier studies have showed that high PLR is significantly correlated with MACE, LVEF value,^[11] diameter of stent implantation,^[12] Killip grade in patients^[13] with AMI; however, few studies have been conducted for STEMI patients in particular. The CAMI-STEMI score is a practical, simple risk stratification scoring system which does not require blood tests and medical history. In Chinese STEMI patients, the predictive accuracy of mortality is similar to that obtained by Thrombolysis in Myocardial Infarction score and

| Table 4 | |
|------------|-------------------|
| Cardiac Do | ppler ultrasound. |

| MACE group (n=96) | Non-MACE group (n=291) | Р |
|----------------------|--|--|
| 4.74 (4.21–5.18) | 4.70 (4.32-4.94) | .25 |
| 1.09 (0.98-1.21) | 1.06 (0.98-1.18) | .24 |
| 0.58 (0.43-0.68) | 0.67 (0.61-0.72) | <.01 |
| 26 (27.08) | 48 (16.49) | .02 |
| | MACE group (n = 96) 4.74 (4.21-5.18) 1.09 (0.98-1.21) 0.58 (0.43-0.68) 26 (27.08) | MACE group (n = 96) Non-MACE group (n = 291) 4.74 (4.21-5.18) 4.70 (4.32-4.94) 1.09 (0.98-1.21) 1.06 (0.98-1.18) 0.58 (0.43-0.68) 0.67 (0.61-0.72) 26 (27.08) 48 (16.49) |

Data are presented as median (IQR) or n (%). IVS = interventricular septum, LV = left ventricle, LVEF = left ventricular ejection fraction.

GRACE score. Many studies have shown that CAMI-STEMI score is an independent predictor of MACE in patients with acute coronary syndrome.^[14,15]

Previous study showed that patients with PLR > 171 exhibited more severe coronary artery stenosis (OR 2.393; 95% CI 1.394-4.108; P=.002) and worse prognoses,^[16] PLR was closely associated with the severity of CAD, high PLR was an independent predictor of future cardiovascular disease in a Chinese Han population. Gary T found that PLR can be regarded as a novel marker for critical limb ischemia in patients with peripheral arterial occlusive disease; higher PLR may reflect enhanced thrombocyte activation and a prothrombotic state. Studies of Azab et al showed that PLR levels can reflect the inflammation and hypercoagulability of patients with acute coronary syndromes; PLR is a significant independent predictor of long-term mortality after NSTEMI.^[17] Compared with either lymphocyte or platelet counts, PLR was more stable, which was less frequently influenced by many physiological and pathological changes. Besides, PLR represents 2 inversely related predictors of immune pathways. The present data is in accordance with most current studies, in our study we illustrated that PLR level is positively correlated with age, ventricular segmental motion abnormality and negatively correlated with sodium ion concentration, LVEF; therefore, age, ventricular segmental motion abnormality, and LVEF value may all affect the prognosis of STEMI patients. In addition, this study found that PLR is correlated with the occurrence of MACE after PCI in STEMI patients, patients with PLR >112.6 more frequently occurred MACE, the sensitivity and specificity are 84.4% and 51.9% respectively. Early identification of the risks of STEM patients is of great significance to improve prognosis in STEMI patients after PCI.

We are aware of the limitations of this study. First, the prospective nature of this analysis that may have introduced potential bias and confounding factors, overall patients came from the First People's Hospital of Lianyungang. Secondly, the number of sample is relatively small and it is not a standard randomized controlled trial. Thirdly, Only PLR was collected for

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Univariate and multivariate analysis and predictors for MACE.

| Variable | Univariate an | alysis | | Multivariate analysis | | |
|------------------|---------------|-------------|------|-----------------------|-------------|------|
| | OR | 95% CI | Р | OR | 95%CI | Р |
| MONO% | 1.103 | 1.005~1.211 | .039 | _ | _ | _ |
| I-BIL | 1.052 | 1.006~1.101 | .027 | 1.077 | 1.011~1.146 | .021 |
| CAMI-STEMI score | 1.574 | 1.361~1.820 | <.01 | 1.575 | 1.311~1.892 | <.01 |
| PLR | 1.009 | 1.005~1.013 | <.01 | 1.007 | 1.002~1.012 | .003 |

Data are presented as median (IQR) or n (%). 95%CI = 95% confidence interval, I-BIL = indirect bilirubin, MONO = Monocyte, OR = odds ratio, PLR = platelet-to-lymphocyte ratio.



Figure 1. ROC curve analysis for PLR. The area under the curve of the PLR was 0.704 (95% CI=0.644–0.763), the cutoff value of the PLR for patients with MACE after PCI was 112.6 (Se=84.4%, Sp=51.9%). PLR = platelet-to-lymphocyte ratio, ROC = receiver-operating characteristics.

the first time on admission, and no dynamic monitoring was performed. We did not include other proinflammatory proteins (C-reactive protein, tumor necrosis factor alpha, interleukin-1, and interleukin-6) into the study. In the last, long-term follow-up was not conducted, and larger, multicenter prospective study is needed to evaluate the prognosis of patients with STEMI.

In summary, PLR is independently associated with MACE in patients with STEMI undergoing PCI, high PLR may be a simple and easily obtainable marker of the severity of MACE. CAMI-STEMI score is also an independent predictor of MACE in patients with STEMI after PCI, PLR and CAMI-STEMI score can used to identify high-risk patients early, and provide predictive value for the occurrence of MACE in patients with STEMI after PCI.

Author contributions

Data curation: Zhongxing Peng.

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Methodology: Zhongxing Peng.

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