

## Risk Factors for Long-term Major Adverse Cardiovascular Events and Predictive Value of Risk Scoring Systems in Patients with ST-segment Elevation Myocardial Infarction after Percutaneous Coronary Intervention: A Postprint Study

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### Abstract

**Background:** Patients with ST-segment elevation myocardial infarction (STEMI) have a high risk of long-term major adverse cardiovascular events (MACEs) after percutaneous coronary intervention (PCI). Guidelines emphasize that accurate early risk stratification is of significant importance for the management of MACEs after PCI in STEMI patients. Currently, commonly utilized risk scoring systems include the Age, Creatinine, and Ejection Fraction (ACEF) score, Thrombolysis in Myocardial Infarction (TIMI) score, Zwolle score, Primary Angioplasty in Myocardial Infarction (PAMI) score, and Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications (CADILLAC) score. However, which risk scoring system is more applicable for predicting long-term prognosis in STEMI patients undergoing PCI remains undetermined. **Objective:** To analyze the risk factors for long-term MACEs after PCI in Chinese STEMI patients and to compare the predictive value of the five currently commonly used risk scoring systems (ACEF, TIMI, Zwolle, PAMI, CADILLAC) for the risk of long-term MACEs occurrence. **Methods:** A retrospective cohort of 687 STEMI patients who successfully underwent primary PCI in the Department of Cardiology, Gansu Provincial People's Hospital from June 2016 to June 2020 was selected as the study population. General patient information, laboratory, and imaging examination results were collected. All enrolled patients were assessed using the ACEF, TIMI, Zwolle, PAMI, and CADILLAC risk scoring systems. Patients were followed up via telephone and outpatient review after discharge on an annual basis until August 2023, with the primary endpoint being the occurrence of MACEs during the follow-up period. Multivariate Logistic regression analysis

was employed to investigate the influencing factors of long-term MACEs after PCI in STEMI patients. Receiver operating characteristic (ROC) curves for diagnosing MACEs were plotted for different risk scoring systems, and the areas under the ROC curves (AUC) were compared using the Delong test. Results: Among 687 STEMI patients who underwent PCI, 44 patients were excluded due to excessive missing baseline data during follow-up, resulting in a final cohort of 643 patients with a median follow-up duration of 37 (25, 49) months. By the conclusion of follow-up, 134 patients had experienced MACEs, yielding an incidence rate of 20.8%, comprising 36 cases (26.9%) of all-cause mortality, 19 cases (14.2%) of cardiac mortality, 33 cases (24.6%) of recurrent myocardial infarction, 61 cases (45.5%) of recurrent angina, and 12 cases (8.9%) of recurrent heart failure. Statistically significant differences were observed between the MACEs and non-MACEs groups in age, length of hospital stay, Killip class, brain natriuretic peptide precursor, fibrinogen, anemia, left ventricular ejection fraction, estimated glomerular filtration rate, serum creatinine, and valvular regurgitation ( $P < 0.05$ ). Multivariate Logistic regression analysis revealed that prolonged length of hospital stay (OR=1.071, 95%CI=1.012~1.134,  $P=0.018$ ), elevated serum creatinine (OR=1.018, 95%CI=1.006~1.030,  $P=0.003$ ), and increased fibrinogen (OR=1.226, 95%CI=1.066~1.409,  $P=0.004$ ) were independent risk factors for MACEs, whereas increased left ventricular ejection fraction (OR=0.980, 95%CI=0.960~1.000,  $P=0.045$ ), mild regurgitation (OR=0.377, 95%CI=0.051~0.938,  $P=0.036$ ), and moderate regurgitation (OR=0.164, 95%CI=0.051~0.522,  $P=0.002$ ) were protective factors. The ACEF, TIMI, Zwolle, PAMI, and CADILLAC risk scoring system scores were all significantly higher in the MACEs group compared to the non-MACEs group ( $P < 0.05$ ). ROC curves were constructed for the five risk scoring systems to predict long-term MACEs after PCI in STEMI patients, and no statistically significant difference was found in the predictive value among the five risk scoring systems for long-term MACEs after PCI in STEMI patients ( $P > 0.05$ ). Conclusion: Length of hospital stay, serum creatinine level, fibrinogen, left ventricular ejection fraction, and valvular regurgitation status are risk factors influencing the occurrence of long-term MACEs after PCI in STEMI patients. The five risk scoring systems (ACEF, TIMI, Zwolle, PAMI, CADILLAC) can all predict the occurrence of long-term MACEs after PCI in STEMI patients, but the CADILLAC score is recommended based on considerations of discrimination and sensitivity.

## Full Text

# Risk Factors and Predictive Value of Risk Scoring Systems for Long-Term Major Adverse Cardiovascular Events in Patients with ST-Segment Elevation Myocardial Infarction Following Percutaneous Coronary Intervention

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## Abstract

**Background:** Patients with ST-segment elevation myocardial infarction (STEMI) undergoing percutaneous coronary intervention (PCI) face a substantial risk of long-term major adverse cardiovascular events (MACEs). Clinical guidelines emphasize that accurate early risk stratification is crucial for managing post-PCI MACEs in STEMI patients. Commonly used risk scoring systems include the Age, Creatinine, and Ejection Fraction (ACEF) score, Thrombolysis in Myocardial Infarction (TIMI) score, Zwolle score, Primary Angioplasty in Myocardial Infarction (PAMI) score, and Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications (CADILLAC) score. However, which of these systems is most suitable for predicting long-term outcomes in STEMI patients after PCI remains inconclusive.

**Objective:** This study aimed to analyze the risk factors for long-term MACEs following PCI in Chinese STEMI patients and to compare the predictive value of five commonly used risk scoring systems—ACEF, TIMI, Zwolle, PAMI, and CADILLAC—for long-term MACEs risk.

**Methods:** We retrospectively selected 687 STEMI patients who underwent their first successful PCI in the Department of Cardiology at Gansu Provincial People's Hospital between June 2016 and June 2020. Patient demographics, laboratory results, and imaging findings were collected, and all patients were scored using the ACEF, TIMI, Zwolle, PAMI, and CADILLAC risk scoring systems. Patients were followed up annually via telephone and outpatient clinic visits until August 2023, with primary documentation of MACEs occurrence during follow-up. Multivariable logistic regression analysis was used to identify

factors influencing long-term MACEs after PCI. Receiver operating characteristic (ROC) curves were plotted for each risk scoring system, and areas under the curve (AUC) were compared using the DeLong test.

**Results:** Among 687 patients who underwent PCI, 643 were included in the final analysis after excluding 44 with excessive missing data. The median follow-up duration was 37 months (interquartile range: 25–49 months). By follow-up completion, 134 patients (20.8%) had experienced MACEs. Multivariable analysis identified prolonged hospital stay, elevated creatinine, and increased fibrinogen as independent risk factors, while higher LVEF and mild-to-moderate valvular regurgitation were protective. All five risk scores were significantly higher in the MACEs group (all  $P < 0.05$ ). ROC curve analysis showed no statistically significant differences in predictive value among the five scoring systems for long-term MACEs after PCI ( $P > 0.05$ ).

**Conclusion:** Hospital stay duration, serum creatinine, fibrinogen, LVEF, and valvular regurgitation status are significant factors affecting long-term MACEs occurrence after PCI in STEMI patients. While all five risk scoring systems—ACEF, TIMI, Zwolle, PAMI, and CADILLAC—can predict long-term MACEs, the CADILLAC score is recommended based on its discriminative ability and sensitivity.

**Keywords:** ST-segment elevation myocardial infarction; percutaneous coronary intervention; major adverse cardiovascular events; risk factors; risk scoring

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## Introduction

ST-segment elevation myocardial infarction (STEMI) is a rapidly progressing condition with high mortality and disability rates and poor prognosis, representing a common type of myocardial infarction in clinical practice. Percutaneous coronary intervention (PCI) is recommended as the preferred treatment for STEMI patients during the acute phase. However, STEMI patients still face a series of adverse events after PCI, particularly major adverse cardiovascular events (MACEs), with reported incidence rates as high as 27%. The 2019 Guidelines for the Diagnosis and Treatment of Acute ST-Segment Elevation Myocardial Infarction emphasize that accurate early risk stratification is essential for managing MACEs in STEMI patients post-PCI.

Currently, commonly used risk scoring systems for predicting MACEs after PCI include the Age, Creatinine, and Ejection Fraction (ACEF) score, Thrombolysis in Myocardial Infarction (TIMI) score, Zwolle score, Primary Angioplasty in Myocardial Infarction (PAMI) score, and Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications (CADILLAC) score. The ACEF score primarily predicts 30-day mortality and myocardial infarction risk. The TIMI score focuses on clinical risk factor assessment for predicting one-year mortality. The Zwolle score serves as an auxiliary tool for predicting 30-day

MACEs to identify low-risk patients suitable for early discharge. The PAMI score predicts six-month mortality, while the CADILLAC score predicts one-year mortality.

Existing research has primarily used these systems to predict short-term MACEs, with few studies evaluating long-term outcomes and limited large-scale data directly comparing multiple scoring systems. Consequently, which system best predicts long-term prognosis in STEMI patients after PCI remains undetermined. Assessing long-term prognosis is crucial for healthcare providers to evaluate treatment efficacy and manage post-discharge care. Therefore, this study utilized clinical data from STEMI patients who underwent PCI at Gansu Provincial People's Hospital to analyze risk factors for long-term MACEs and compare the predictive value of ACEF, TIMI, Zwolle, PAMI, and CADILLAC scoring systems.

## Methods

**Study Population** We retrospectively selected 687 STEMI patients who underwent their first successful PCI in the Department of Cardiology at Gansu Provincial People's Hospital between June 2016 and June 2020. Inclusion criteria were: (1) diagnosis of STEMI according to the Fourth Universal Definition of Myocardial Infarction guidelines; (2) PCI treatment; (3) age  $\geq 18$  years; (4) hospital stay  $>48$  hours with complete medical records. Exclusion criteria included: (1) heart failure, severe valvular heart disease, or cardiomyopathy at admission; severe hepatic or renal insufficiency; (2) other severe physical diseases or severe cognitive impairment; (3) other surgical procedures during the same admission; (4) inability to complete follow-up; (5) refusal to provide informed consent or non-compliance. The study was approved by the Ethics Committee of the School of Nursing, Lanzhou University (LZUHLXY20210017), and all participants provided informed consent.

**Data Collection Basic Information:** We collected data on age, sex, height, weight, systolic blood pressure, diastolic blood pressure, heart rate, medical history (hypertension, diabetes, dyslipidemia, stroke), smoking status, alcohol consumption, Killip class, hospital stay duration, and time to myocardial ischemia.

**Laboratory and Imaging Examinations:** (1) Blood samples were collected immediately after admission, including fasting glucose, glycated hemoglobin, white blood cell count, neutrophil count, lymphocyte count, hemoglobin, creatine kinase, creatine kinase-MB, troponin, aspartate aminotransferase, alanine aminotransferase, serum creatinine, total cholesterol, triglycerides, high-density lipoprotein, low-density lipoprotein, NT-proBNP, fibrinogen, prothrombin time, and estimated glomerular filtration rate (eGFR).  $eGFR < 90 \text{ mL} \cdot \text{min}^{-1} \cdot (1.73 \text{ m}^2)^{-1}$  was considered abnormal. (2) Imaging examinations included admission echocardiography and coronary angiography.

**Scoring Criteria:** All patients were scored using the ACEF, TIMI, Zwolle,

PAMI, and CADILLAC risk scoring systems upon enrollment. The evaluation indicators for each system are shown in Table 1 .

**Definitions and Diagnostic Criteria:** (1) Diagnostic criteria for hypertension, dyslipidemia, diabetes, and stroke followed the Expert Consensus on Core Data Elements and Definitions for Stroke Clinical Diagnosis and Disease Management. (2) Smoking was defined as  $\geq 1$  cigarette daily for  $>6$  months. (3) Alcohol consumption was defined as  $\geq 1$  drink weekly for  $\geq 1$  year. (4) Anemia was defined as hemoglobin  $<120$  g/L in men and  $<110$  g/L in women. (5) Valvular regurgitation was classified according to the Expert Consensus on Standardized Echocardiographic Examination of Adult Valvular Heart Disease in China. (6) TIMI flow grade: grades 0-1 were defined as no flow, grade 2 as slow flow, and grade 3 as normal flow. (7) Normal cardiac chamber size was defined as left atrial diameter 24-36 mm, left ventricular end-diastolic diameter 37-55 mm, right atrial diameter 33-41 mm, and right ventricular end-diastolic diameter 14-25 mm.

**Follow-up and Grouping:** Patients were followed up annually via telephone and outpatient clinic visits until August 2023, with primary documentation of MACEs occurrence. MACEs included cardiac death, recurrent myocardial infarction, recurrent angina, recurrent heart failure, repeat revascularization, and all-cause death. Patients were divided into MACEs and non-MACEs groups based on follow-up outcomes. Exclusion criterion: patients with  $>10$  missing data points in their basic information were excluded.

**Statistical Analysis** Data were analyzed using SPSS 26.0. Non-normally distributed continuous variables were expressed as median (P25, P75) and compared using non-parametric tests. Categorical variables were expressed as frequencies and percentages and compared using  $\chi^2$  tests. Variables with significant differences in univariate analysis were entered into multivariable logistic regression analysis. ROC curves were plotted for each risk scoring system, and AUCs were compared using the DeLong test. Statistical significance was set at  $P<0.05$ .

## Results

**Follow-up Outcomes** Among 687 patients who underwent PCI, 44 were excluded due to excessive missing data, leaving 643 patients for analysis. The median follow-up duration was 37 months (interquartile range: 25-49 months). By follow-up completion, 134 patients had experienced MACEs, yielding an incidence rate of 20.8%. These events comprised 36 cases (26.9%) of all-cause death, 19 cases (14.2%) of cardiac death, 33 cases (24.6%) of recurrent myocardial infarction, 61 cases (45.5%) of recurrent angina, and 12 cases (8.9%) of recurrent heart failure.

**Comparison of Baseline Characteristics** The MACEs and non-MACEs groups showed significant differences in age, hospital stay duration, Killip class,

NT-proBNP, fibrinogen, anemia, LVEF, eGFR, serum creatinine, and valvular regurgitation (all  $P < 0.05$ ). No significant differences were observed in sex, hypertension, diabetes, dyslipidemia, stroke, smoking, alcohol consumption, time to ischemia  $> 4$  hours, height, weight, blood pressure, heart rate, glycosylated hemoglobin, fasting glucose, white blood cell count, neutrophil count, lymphocyte count, high-density lipoprotein, low-density lipoprotein, liver enzymes, homocysteine, troponin, lactate dehydrogenase peak, creatine kinase peak, creatine kinase-MB, prothrombin time, activated partial thromboplastin time, number of stents, normal cardiac chamber size ratio, ventricular aneurysm, TIMI flow grade, myocardial infarction location, or number of diseased vessels (all  $P > 0.05$ ) (Table 2).

**Multivariable Logistic Regression Analysis** Using MACEs occurrence as the dependent variable (yes=1, no=0) and variables with significant univariate differences as independent variables, multivariable logistic regression revealed that prolonged hospital stay (OR=1.071, 95%CI=1.012-1.134,  $P=0.018$ ), elevated creatinine (OR=1.018, 95%CI=1.006-1.030,  $P=0.003$ ), and increased fibrinogen (OR=1.226, 95%CI=1.066-1.409,  $P=0.004$ ) were independent risk factors for MACEs. Conversely, higher LVEF (OR=0.980, 95%CI=0.960-1.000,  $P=0.045$ ), mild regurgitation (OR=0.377, 95%CI=0.051-0.938,  $P=0.036$ ), and moderate regurgitation (OR=0.164, 95%CI=0.051-0.522,  $P=0.002$ ) were protective factors (Table 3).

**Comparison of Risk Scores Between Groups** The MACEs group had significantly higher scores than the non-MACEs group for all five risk scoring systems: ACEF, TIMI, Zwolle, PAMI, and CADILLAC (all  $P < 0.05$ ) (Table 4).

**Predictive Value of Risk Scoring Systems** ROC curves for the five risk scoring systems predicting long-term MACEs after PCI showed no statistically significant differences in predictive value among the systems ( $P > 0.05$ ) (Table 5, Table 6, Figure 1 [Figure 1: see original paper]).

## Discussion

The widespread application of PCI technology has significantly reduced mortality in STEMI patients. However, MACEs occurrence remains a major contributor to long-term high mortality rates. Studies show that MACEs incidence after discharge exceeds that of the early postoperative period, with out-of-hospital mortality higher than in-hospital mortality. Reported MACEs rates at 30 days, 1 year, and 3 years post-PCI are 6.7%, 20%, and 26.2%, respectively. Our median follow-up of 37 months with 134 MACEs cases (20.8% incidence) aligns with previous reports. Given the high incidence of long-term MACEs, identifying risk factors is essential for prevention. Early recognition enables personalized interventions to improve outcomes.

Our findings indicate that hospital stay duration significantly affects long-term MACEs. Prolonged hospitalization typically reflects greater comorbidity burden and disease severity, leading to poorer prognosis and higher MACEs risk. Reduced LVEF emerged as a risk factor, consistent with evidence that STEMI patients with LVEF <40% have increased long-term MACEs risk due to reduced cardiac output, myocardial ischemia, and heightened thrombotic risk. Elevated fibrinogen also increased MACEs risk, expanding its clinical utility beyond reflecting coronary lesion severity. Abnormal creatinine levels represented another risk factor, as renal dysfunction causes calcium-phosphate metabolism disorders and endothelial dysfunction, increasing cardiovascular risk. Compared to mild or moderate regurgitation, severe regurgitation predisposed patients to long-term MACEs by altering cardiac structure and intracardiac pressures, causing myocardial hypoxia and functional impairment. Previous studies reported higher 1-year mortality in STEMI patients with ischemic mitral regurgitation. Therefore, timely revascularization and postoperative rehabilitation are essential.

Validated risk scoring systems including ACEF, TIMI, Zwolle, PAMI, and CADILLAC can predict MACEs after PCI. However, direct comparisons are limited due to varying outcome measures and follow-up durations. SIMONA et al. compared CADILLAC, PAMI, TIMI, and Zwolle scores, demonstrating different predictive values at 30 days, 1 year, 2 years, and 3 years. Our study provides the first large-scale comparison for long-term MACEs prediction in Chinese STEMI patients. All five systems predicted long-term MACEs, with CADILLAC showing the highest sensitivity, TIMI the best specificity, and CADILLAC the optimal discriminative ability.

Age is a common predictor across all five systems, though it was not an independent risk factor in our study, possibly due to the older age distribution of our cohort. Age thresholds vary across systems: TIMI and CADILLAC use  $\geq 65$  years, Zwolle adds 2 points for age  $\geq 60$ , and PAMI considers age  $>65$  as a risk factor with greater weight for age  $>75$ . However, with STEMI incidence trending younger, 35-year-old and younger patients have 20% MACEs rates, yet remain underrepresented in scoring systems.

CADILLAC incorporates echocardiographic and coronary angiography data with dynamic laboratory values and objective indicators (e.g., Killip class, eGFR, anemia) that evolve with disease progression, offering high discriminative ability and operability. Guo et al. demonstrated CADILLAC's strong predictive value for 28-day mortality in acute myocardial infarction with cardiogenic shock. In our study, CADILLAC similarly outperformed other systems for long-term MACEs prediction with an AUC of 0.595, showing optimal discrimination and sensitivity, though specificity was lower.

TIMI and Zwolle include time-to-treatment  $>4$  hours as an evaluation component, but treatment delay depends on both hospital capability and patient presentation time. Studies show high rates of delayed presentation in China associated with older age, lack of insurance, and lower education levels, poten-

tially limiting these scores' predictive value in Chinese populations. TIMI and PAMI scores, while convenient, lack coronary angiography data. TIMI' s time component relies on patient recall, introducing bias. Their static predictors (e.g., medical history) reflect lifestyle factors present in many patients without MACEs, limiting their discriminative power for long-term outcomes. In our study, TIMI showed high specificity but lower discrimination and sensitivity compared to other systems.

ACEF' s three predictors are all objective: LVEF from echocardiography (non-invasive, low-cost, recommended by guidelines), serum creatinine (dynamic), and age. ACEF includes two of our identified risk factors (LVEF and creatinine) and demonstrated stable sensitivity and specificity for long-term MACEs prediction.

This study has limitations: (1) Some patients may have recall bias regarding MACEs timing or symptoms due to long post-PCI duration or advanced age, suggesting need for more frequent follow-up; (2) Single-center design limits generalizability, requiring multi-center validation; (3) Limited variables were included, omitting potentially relevant factors like ECG ST-segment changes or blood type.

In conclusion, ACEF, TIMI, Zwolle, PAMI, and CADILLAC scores can all assess long-term MACEs risk in STEMI patients post-PCI. However, considering discriminative ability and sensitivity, TIMI, PAMI, Zwolle, and ACEF show moderate predictive value for long-term MACEs, while CADILLAC is recommended.

**Author Contributions:** Guoli Zhang, Rongrong Zhao, Fanghong Yan, and Lin Han were responsible for conceptualization and design. Fanghong Yan conducted feasibility analysis. Guoli Zhang, Rongrong Zhao, Guotian Peng, Ruiyi Sun, and Pengyu Qiao collected data. Guoli Zhang performed data analysis and drafted the manuscript. Fanghong Yan and Rongrong Zhao revised the manuscript. Lin Han supervised study design, funding, writing, quality control, and takes overall responsibility for the article.

**Conflicts of Interest:** None declared.

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*Note: Figure translations are in progress. See original paper for figures.*

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