BMJ Open

A nomogram for the prediction of in-hospital mortality in patients with acute ST-elevation myocardial infarction after primary percutaneous coronary intervention

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2021-056101
Article Type:	Original research
Date Submitted by the Author:	06-Aug-2021
Complete List of Authors:	Wang, Yudan; Hebei Medical University, School of Graduate; Hebei General Hospital, Department of Cardiology Center Gao, Man; Hebei Medical University, School of Graduate Jia, Shengqi; Hebei Medical University, School of Graduate Zheng, Shihang; Hebei North University, School of Graduate Wang, Jiaqi; Hebei North University, School of Graduate Dang, Yi; Hebei General Hospital, Department of Cardiology Center Li, Yingxiao; Hebei General Hospital, Department of Cardiology Center Qi, Xiaoyong; Hebei Medical University, School of Graduate; Hebei General Hospital, Department of Cardiology Center
Keywords:	Coronary intervention < CARDIOLOGY, Coronary heart disease < CARDIOLOGY, Myocardial infarction < CARDIOLOGY

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

A nomogram for the prediction of in-hospital mortality in patients with acute ST-elevation myocardial infarction after primary percutaneous coronary intervention

Running title: Nomogram for STEMI in-hospital mortality after PCI

Yudan Wang[1,2], Man Gao[1], Shengqi Jia[1], Shihang Zheng[3], Jiaqi Wang[3], Yi Dang[2], Yingxiao Li[2], Xiaoyong Qi[1,2,*]

[1]School of Graduate, Hebei Medical University, Shijiazhuang, Hebei Province, People's Republic of China

[2]Department of Cardiology Center, Hebei General Hospital, Shijiazhuang, Hebei Province, People's Republic of China

[3]School of Graduate, Hebei North University, Zhangjiakou, Hebei Province, People's Republic of China

[*]**Corresponding Author**

Xiaoyong Qi

School of Graduate, Hebei Medical University, Shijiazhuang, Hebei Province, People's Republic of China

Department of Cardiology Center, Hebei General Hospital, No. 348, Heping West Road, Shijiazhuang 050051, Hebei Province, People's Republic of China

E-mail address: hbghqxy@126.com

Word count: 2720

ABSTRACT

Objectives: To establish a clinical prognostic nomogram for predicting in-hospital mortality after primary percutaneous coronary intervention (PCI) among patients with ST-elevation myocardial infarction (STEMI).

Design: Retrospective, multicenter, observational study.

Setting: Thirty-nine hospitals in Hebei Province.

Participants: Patients with STEMI who underwent PCI from January 2018 to December 2019.

Interventions: A multivariable logistic regression model was used to identify the factors associated with in-hospital mortality. Then, they were incorporated into a nomogram. The performance of the nomogram was evaluated by the discrimination, calibration, and clinical usefulness.

Primary and secondary outcome measures: The outcome was the factors associated with in-hospital mortality.

Results: This study included 855 patients, among whom 223 died in hospital. Age, Body Mass Index (BMI), systolic pressure on admission, hemoglobin, random blood glucose on admission, ejection fraction after PCI, use aspirin before admission, long lesions, thrombolysis in myocardial infarction (TIMI) flow grade, and neutrophils/lymphocytes ratio (N/L ratio) were independently associated with in-hospital mortality (all $P<0.05$). In the training set, the nomogram showed a C-index of 0.947, goodness-of-fit of 0.683, and area under the receiver operating characteristic curve (AUC) of 0.947 (95%CI=0.927-0.967). In the testing set, the C-index was 0.891, goodness-of-fit was 0.462, and AUC was 0.891 (95%CI=0.844-0.939). The results indicate that the nomogram had good

discrimination and good prediction accuracy and could achieve a good net benefit.

Conclusions: A nomogram that provides an individual prediction of in-hospital mortality for patients with STEMI after PCI in a Chinese population was established and validated.

Keywords: nomogram; ST-elevated myocardial infarction; percutaneous coronary intervention; in-hospital mortality

ARTICLE SUMMARY

- This study included 39 tertiary centers and 855 patients, including 223 (26.1%) who met the outcome.
- The data were obtained retrospectively, which can lead to less reliable information.
- Other potential risk factors in our study, such as LVEF before PCI, could not be included in the analyses.

INTRODUCTION

ST-segment elevation myocardial infarction (STEMI), a type of coronary artery disease (CAD), is a common clinical emergency and critical illness [1]. STEMI is most often caused by plaque rupture of an atherosclerotic lesion in the affected (culprit) coronary artery followed by total occlusion of the vessel lumen with a thrombus [2, 3]. Common risk factors for CAD, including STEMI, are tobacco abuse, dyslipidemias, hypertension, diabetes mellitus, and a family history of CAD [4]. Myocardial infarction is the main cause of global morbidity, mortality, and major cardiovascular events (MACEs), representing 15% of the annual deaths worldwide [5]. In recent years, with the diagnosis and treatment guidelines, the continuous standardization of the treatment of STEMI, the increasing evidence of determinants of patient prognosis, and the continuous development of emerging technologies have contributed to a reduction in mortality; still, mortality seems to have plateaued [3].

Primary percutaneous coronary intervention (PCI) has become the preferred reperfusion strategy in patients with STEMI according to the current clinical guidelines for STEMI in the United States and Europe [6, 7]. Nevertheless, even if such patients receive timely PCI and/or appropriate antiplatelet drugs, the prognosis is still poor, and a substantial number of patients still die in-hospital after PCI. About 6% of STEMI patients die in the hospital [3, 8, 9]. Therefore, there is still room for improving the short-term outcomes after PCI.

Various studies examined the risk factors of short- and long-term mortality of STEMI patients after PCI [10-12]. Guidelines encourage the use of clinical scores such as the thrombolysis in myocardial infarction (TIMI) or The Global Registry of Acute Coronary Events (GRACE) for STEMI to assess early- and long-term risk [6, 7, 13]. Several

biomarkers have been reported to confer independent prognostic information after STEMI, including Cardiac Troponin (cTn), Brain Natriuretic Peptide (BNP), amino-terminal pro-Brain Natriuretic Peptide (NT-proBNP), and D-dimer [14-17]. Unfortunately, these studies often exclude patients with advanced age, liver or kidney dysfunction, and other comorbidities and complications. Therefore, the generalizability of those studies is limited, and it is difficult to summarize and reflect the real-world treatment situation comprehensively.

Therefore, the objective of this study was to develop a clinical nomogram for predicting in-hospital mortality of patients with STEMI after PCI. The results could provide clinical guidance and improve the outcome of STEMI patients.

PATIENTS AND METHODS

Study design and patients

This multicenter, retrospective, observational study included STEMI patients treated with PCI at 39 PCI hospitals in Hebei Province from January 2018 to December 2019. The training set patients enrolled from January 2018 to December 2018 and the testing set patients enrolled from January 2019 to December 2019.

All patients met the diagnostic criteria of acute STEMI based on their symptoms and/or ECG, myocardial damage markers and other test results and underwent primary PCI according to the 2017 ESC guidelines for the management of STEMI [6], namely with persistent chest discomfort or other symptoms suggestive of ischemia and ST-segment elevation in at least two contiguous leads. Patients with non-ST segment myocardial infarction (NSTEMI) or unstable angina or STEMI patients who did not undergo PCI were excluded.

The study was approved by the Ethics Committees of Hebei General Hospital as the lead center and the ethics committee of each participating hospital. The requirement for informed consent was waived by the committee. The study was conducted according to the tenets of the Declaration of Helsinki for Medical Research Involving Human Subjects and Good Clinical Practice.

Patient and Public Involvement

Patients or the public were not involved in the design or reporting or dissemination plans of our research as this study is a retrospective, observational study. Patients were involved in the conduct of the trial by sharing medical records during the visits.

Data collection

Demographics (age, sex, and BMI), medical history (hypertension, diabetes mellitus, atrial fibrillation (AF), hypertension and family history of coronary artery disease (CAD), stroke, renal failure, and peripheral artery disease), angiographic characteristics and information of cardiac procedures (disease condition, TIMI flow grade, number and length of stents, use of intra-aortic balloon pump (IABP), use of temporary pacemaker, use of ventilator, and whether there was no-reflow, coronary perforation, and cardiac arrest), medications on admission (antiplatelet agents, β-blockers, nitrate, angiotensin-converting enzyme inhibitors (ACEI), angiotensin receptor blockers (ARB), and statin), biochemical markers (N/L ratio), hematocrit (HCT), hemoglobin (HGB), platelets (PLT), and random blood glucose on admission), and left ventricular ejection fraction (LVEF) after PCI were extracted from the medical charts. All treatments were according to the current guidelines.

Nomogram construction

Demographics, medical history, vital signs before and after PCI, and auxiliary examinations were evaluated using univariable logistic regression. Variables with $P<0.05$ in the univariable logistic analyses were included for multivariable logistic analysis and nomogram construction. Receiver operator characteristic (ROC) curve analysis was used to quantify the prediction performance of the nomogram. A calibration curve was used to evaluate the calibration of the nomogram, and its goodness of fit was assessed using the Hosmer-Lemeshow test. Finally, the clinical usefulness of the nomogram was accessed using a decision curve analysis (DCA).

Statistical analysis

Statistical analyses were performed using R version 4.0.3 (R Foundation for Statistical Computing) with RStudio (version 1.3.959; RStudio, Auckland, New Zealand). R packages used in this study were rms, reader, tableone, pROC, ResourceSelection, and rmda. The predictive accuracy of the nomogram was measured using the C-statistic (Bootstrap method, 1000 times). Calibration was evaluated using the Hosmer-Lemeshow statistic. Categorical variables were presented as frequencies with percentages, normally distributed continuous variables as means ± SD, and other data as medians with interquartile ranges (IQRs). Categorical variables were compared using the chi-square test or Fisher's test if the expected cell count was <5. Student's t-test was used to compare normally distributed continuous variables. Otherwise, the Mann-Whitney U-test was used. The significance level was set at 0.05, and two-sided tests were used.

RESULTS

Characteristics of the patients

The whole study population consisted of 855 patients diagnosed with STEMI and who underwent PCI, including 396 in the training set (132 (33.3%) dead patients and 264 (66.7%) survivors) and 459 (91 (19.8%) dead patients, and 368 (80.2%) survivors) in the test set (Figure 1). The clinical characteristics, including demographic, medical history, angiographic characteristics, and information of cardiac procedures, medications, and biochemical markers, are summarized in Table 1. The patients who died in the hospital were older (69.8±10.2 vs. 60.2±12.6 years, P<0.01), more likely to be women (32.7% vs. 21.5%, P<0.01), and more had complications like hypertension, AF, and hyperlipidemia.

Nomogram construction

According to the multivariable logistic analysis, the 10 variables were found to meet the threshold of P<0.05. Age (OR=1.069, 95% CI=1.048-1.092, P=0.049), BMI (OR=0.55, 95% CI=0.31=0.87, P=0.019), SBP on admission (OR=0.92, 95% CI=0.86-0.97, P=0.009), HGB (OR=0.85, 95% CI=0.73-0.97, P=0.017), random blood glucose on admission (OR=1.53, 95% CI=1.13-2.21, P=0.011), EF after PCI (OR=0.89, 95% CI=0.80-0.97, P=0.015), aspirin (OR=0.001, 95% CI=0.009-0.04, P=0.001), N/L ratio (OR=1.34, 95% CI=1.12-1.69, P=0.004), long lesions (OR=2.00, 95% CI=1.310-3.084, P<0.001), and TIMI flow grade (OR=2.15, 95% CI=1.242-3.900, P=0.008) were independently associated with in-hospital mortality after PCI of STEMI (Table 2). The nomogram is shown in Figure 2. The formula for calculating the total point of the nomogram is 15.5628+0.0320×age-0.2991×BMI-0.0184×SBP-0.0331×HGB+0.3663×random blood

glucose on admission-0.1188×LVEF after PCI-4.7705×aspirin+0.0521×N/L ratio-2.4688×long leisions+5.1018×TIMI flow grade.

Evaluation of the nomogram

In the training set, the C-index was 0.947, indicating that the prediction model was valuable in clinical practice (Figure 3a). The value of goodness-of-fit was 0.683, indicating a good prediction accuracy. The ROC curve is shown in Figure 4a (AUC=0.947, 95% CI: 0.927-0.967). Figure 5a shows the DCA curve for the training set, indicating that the nomogram had a high overall net benefit in predicting in-hospital mortality after PCI treatment.

In the testing set, the C-index was 0.891. Figure 3b shows the calibration curve, and the value of goodness-of-fit was 0.462. The ROC curve is shown in Figure 4b (AUC=0.891, 95% CI: 0.844-0.939). The DCA curve is shown in Figure 5b. The results of the testing set indicate that the nomogram had good discrimination and good prediction accuracy and could achieve a good net benefit.

DISCUSSION

In this study, a relatively accurate clinical nomogram was constructed, which demonstrated adequate discrimination and calibration power to provide an individualized estimation for the in-hospital mortality in STEMI patients after PCI. For the construction of the nomogram, 10 significant predictors were screened by multivariable logistic analysis.

In this study, men with STEMI overall experienced a lower unadjusted in-hospital mortality than women (OR=0.503, 95%CI: 0.320-0.792), but the difference y became non-significant after multivariable adjustments. Age was an independent risk factor of STEMI patients, in accordance with other analyses of STEMI patients and underlining the high-risk profile of elderly patients, as they usually present with more risk factors and comorbidities than younger patients [18, 19]. High mortality in the older patients might also result from end-organ dysfunction, competing risks might also offset the benefits from reperfusion, such that successful outcomes are more dependent on overall health issues. In accordance with previous studies [8, 10, 12, 19-23], predictors for a worse clinical outcome are associated with age, such as the higher prevalence of renal insufficiency, lower LVEF, and longer delay times. Therefore, for older patients, some authors have also questioned the benefit of reperfusion therapy [20]. This point is of great importance as Medina et al. [24] reported that patients undergoing primary PCI or thrombolysis had lower in-hospital mortality compared with the no reperfusion strategy.

The present study showed that a lower BMI was an independent risk factor for in-hospital death. The previous view is that obesity increases insulin resistance, worsens plasma lipid profiles, and increases arterial blood pressure, and thus has adverse effects on patients with CAD through the indirect effects of other risk factors (such as hypertension, impaired

glucose tolerance, and hyperinsulinemia) [25]. Therefore, obese patients demonstrate greater adverse left ventricle (LV) remodeling and more impaired LV deformation after STEMI compared with those similar infarct characteristics but normal BMI [21, 26]. Interestingly, on the other hand, some studies have shown the so-called "obesity paradox", whereby obesity is related to better clinical outcomes [23, 25, 27, 28], consistent with the present study. Fukuoka et al. [29] reported that this phenomenon is only observed in elderly patients, not in younger patients, so the influence of BMI on risk factors for death might vary with age. Nevertheless, obesity is currently recognized as a risk factor for the long-term prognosis of patients with CAD, and it is worth recommending maintaining BMI at a normal level [29].

As a key factor in the inflammatory response, neutrophils play an irreplaceable role in STEMI. Lymphocytes reflect the body's stress level. Acute stress has been shown to regulate the immune response of lymphocytes and reduce the number of peripheral blood lymphocytes. The smaller the value, the higher the body's stress level. Therefore, the N/L ratio is an index for systemic inflammatory status and usually increases after STEMI [30-32]. Pan et al. [33] demonstrated the independent association between increased N/L ratio and short-term mortality in STEMI patients after PCI. The predictive value of the N/L ratio may be based on the following reasons. Stimulated neutrophils release superoxide radicals, proteolytic enzymes, and arachidonic acid metabolites that increase the infarct size and lead to cardiac electrical instability by damaging endothelial cells, activating coagulation cascade, aggregation of leukocytic cells, and plugging the micro-arteries [34]. These actions will participate in the extension of the areas of myocardial infarction, impaired epicardial and microvascular perfusion, no-reflow/slow flow during PCI, decreased

ejection fraction (LVEF), and post-infarction death [35-37].

The acute phase of STEMI leads to insulin resistance, glucose intolerance, and hyperglycemia. The elevated levels of cytokines, growth hormone, glucagon, and cortisol result in increased hepatic glucose production. Hepatic glycogenolysis is further enhanced by catecholamines that also inhibit glycogenesis and stimulate the release of free fatty acids (FFAs). High concentrations of FFAs will increase myocardial oxygen requirement, reduce myocardial activity and contractility, impair calcium homeostasis and increase the production of free radicals, leading to an increased risk of myocardial damage and arrhythmias [38-41]. Thus, acute hyperglycemia is associated with adverse metabolic effects that might contribute to a poor outcome. Previous studies reported that higher admission glucose was strongly correlated with larger infarct size, lower LVEF, and increased mortality risk in patients with and without diabetes [22, 42]. Exercise training, dietary modifications, and medical intervention might reduce the mortality risk in such patients. Intervention in the hospital, such as tight glycemic control during early PCI or at least within 24 h after STEMI, is also beneficial [43, 44].

Lower admission HGB was associated with higher in-hospital mortality when analyzed as a continuous variable (OR=0.966, 95%CI: 0.954-0.978). The time from onset of precordial pain to coronary angiography in patients with AMI is inversely proportional to the drop in HGB concentration [45]. HGB levels and inflammation are closely related; in patients with inflammation, an abundance of hepcidin leads to poor uptake of iron from the gastrointestinal tract, iron sequestration in macrophages, little iron recycling to the erythron for red-cell production, and microcytic anemia, and this process is termed inflammatory block [46].

Because of the important role of platelets in thrombus formation, the present study showed that prior aspirin use could reduce in-hospital mortality of STEMI patients after PCI, as supported by earlier clinical trials [47, 48]. Weidmann et al. [48] provided evidence suggesting that pre-existing treatment with aspirin favorably affected the clinical presentation, infarct size, and degree of inflammation of patients with STEMI. Yonetsu et al. [49] reported that aspirin inhibits platelet aggregation and therefore reduces the probability of an occluding clot on top of a ruptured plaque and, conversely, the occurrence of STEMI. Despite these proven benefits, some studies revealed the existence of an "aspirin paradox", namely that prior aspirin use may predispose to worse outcomes than those not previously taking aspirin, such as recurrent MI and ischemic events [50, 51].

Previous studies indicated that lesion length is associated with long-term adverse events after PCI and is an important risk factor for restenosis and stent thrombosis [52-54]. A longer lesion, with its greater plaque burden, is conceived to provide a major source of smooth muscle cells that will then proliferate to form neointima. Atherosclerotic plaques have often been found to demonstrate an increased expression of isoforms characteristic of activated smooth muscle cells that are not present in normal vasculature [55]. Still, there are few studies on lesion length and in-hospital mortality, and further studies are still necessary. Preprocedural reperfusion might have a prognostic value [56]. A strong relationship exists between preprocedural TIMI flow grade and infarct size and predischarge LVEF [57]. SBP is a critical factor, and hypotension was associated with a decrease in survival [58].

A nomogram is a simple and intuitive representation of a mathematical model that allows calculating clinical scores [59]. In addition, to be of clinical usefulness in a routine setting,

the nomogram must contain variables assessed in the routine clinical setting, which is the case with the nomogram developed here. The results indicate that the nomogram had good discrimination and good prediction accuracy and could achieve good net benefit. Another nomogram based on other variables (left main coronary artery disease, grading of thrombus, TIMI classification, slow flow, use of IABP, use of β-blocker, use of ACEI/ARB, symptom-to-door time, symptom-to-balloon time, syntax score, LVEF, and CK-MB peak) also showed a high AUC for in-hospital mortality of patients with STEMI after PCI [60]. Nevertheless, since the two nomograms were obtained in different study populations, the two nomograms should be compared within the same study.

Some study limitations should be mentioned. This study has limitations that are inherent to retrospective observational studies. The data were obtained retrospectively, which can lead to less reliable information. As the ischemic time is shortened as much as possible, patients whose symptoms and/or ECG can be diagnosed are directly treated with PCI. Therefore, other potential risk factors in our study, such as LVEF before PCI, could not be included in the analyses. Further studies are still necessary to confirm the performance of the clinical nomogram in future investigations.

In conclusion, a nomogram to predict in-hospital mortality in patients with STEMI after PCI was developed and validated in Hebei, China. The nomogram showed a satisfactory performance, with a C-index of 0.948. Thus, this nomogram might be a precisely individualized predictive tool for prognosis. Still, additional studies are needed to determine whether it can be applied to other populations before its implementation in clinical practice.

Acknowledgements

We acknowledge the members of the heart team at the participating centers for their efforts in collecting clinical data and ensuring the accuracy and completeness of the data. We thank the study participants and patient advisers for accepting to be part of the study for working tirelessly to make this work a reality.

Funding

None.

Competing Interests

The authors of this work have nothing to disclose.

Ethical standards disclosure

The study was approved by the Ethics Committees of Hebei General Hospital as the lead center and the ethics committee of each participating hospital (No. 202144). The requirement for informed consent was waived by the committee. The study was conducted according to the tenets of the Declaration of Helsinki for Medical Research Involving Human Subjects and Good Clinical Practice.

Authors' contribution

Yudan Wang, Man Gao and Shihang Zheng carried out the studies, participated in collecting data, and drafted the manuscript. Yudan Wang, Yi Dang and Xiaoyong Qi performed the statistical analysis and participated in its design. Shengqi Jia, Jiaqi Wang

and Yingxiao Li helped to draft the manuscript. All authors read and approved the final manuscript.

Data sharing statement

All data generated or analyzed during this study are included in this published article.

REFERENCES

1. O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation* 2013;127:e362-425.
2. Trost JC, Lange RA. Treatment of acute coronary syndrome: part 2: ST-segment elevation myocardial infarction. *Crit Care Med* 2012;40:1939-45.
3. Vogel B, Claessen BE, Arnold SV, et al. ST-segment elevation myocardial infarction. *Nature reviews Disease primers* 2019;5:39.
4. Authors/Task Force M, Piepoli MF, Hoes AW, et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts): Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). *Eur J Prev Cardiol* 2016;23:NP1-NP96.
5. Jayaraj JC, Davatyan K, Subramanian SS, et al. Epidemiology of Myocardial Infarction. In: Pamkucu B, editor. Myocardial Infarction. London: IntechOpen; 2018.
6. Ibanez B, James S, Agewall S, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J* 2018;39:119-77.

7. O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2013;61:e78-e140.
8. Li J, Li X, Wang Q, et al. ST-segment elevation myocardial infarction in China from 2001 to 2011 (the China PEACE-Retrospective Acute Myocardial Infarction Study): a retrospective analysis of hospital data. *Lancet* 2015;385:441-51.
9. Canto JG, Kiefe CI, Rogers WJ, et al. Number of coronary heart disease risk factors and mortality in patients with first myocardial infarction. *JAMA* 2011;306:2120-7.
10. Cenko E, Yoon J, Kedev S, et al. Sex Differences in Outcomes After STEMI: Effect Modification by Treatment Strategy and Age. *JAMA Intern Med* 2018;178:632-9.
11. Mehta SR, Wood DA, Storey RF, et al. Complete Revascularization with Multivessel PCI for Myocardial Infarction. *N Engl J Med* 2019;381:1411-21.
12. Scholz KH, Maier SKG, Maier LS, et al. Impact of treatment delay on mortality in ST-segment elevation myocardial infarction (STEMI) patients presenting with and without haemodynamic instability: results from the German prospective, multicentre FITT-STEMI trial. *Eur Heart J* 2018;39:1065-74.
13. Levine GN, Bates ER, Bittl JA, et al. 2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines: An Update of the 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention, 2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery, 2012

ACC/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the Diagnosis and Management of Patients With Stable Ischemic Heart Disease, 2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction, 2014 AHA/ACC Guideline for the Management of Patients With Non-ST-Elevation Acute Coronary Syndromes, and 2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery. *Circulation* 2016;134:e123-55.

14. Ottani F, Galvani M, Nicolini FA, et al. Elevated cardiac troponin levels predict the risk of adverse outcome in patients with acute coronary syndromes. *Am Heart J* 2000;140:917-27.
15. Sun T, Wang L, Zhang Y. Prognostic value of B-type natriuretic peptide in patients with acute coronary syndromes. *Arch Med Res* 2006;37:502-5.
16. Jaberg L, Toggweiler S, Puck M, et al. Prognostic value of N-terminal pro-B-type natriuretic peptide in patients with acute coronary syndromes undergoing left main percutaneous coronary intervention. *Circ J* 2011;75:2648-53.
17. Yu T, Jiao Y, Song J, et al. Hospital mortality in acute coronary syndrome: adjustment of GRACE score by D-dimer enables a more accurate prediction in a prospective cohort study. *BMC Cardiovasc Disord* 2019;19:252.
18. Forman DE, Chen AY, Wiviott SD, et al. Comparison of outcomes in patients aged <75, 75 to 84, and ≥ 85 years with ST-elevation myocardial infarction (from the ACTION Registry-GWTG). *Am J Cardiol* 2010;106:1382-8.
19. Rathod KS, Jones DA, Gallagher S, et al. Atypical risk factor profile and excellent long-term outcomes of young patients treated with primary percutaneous coronary

intervention for ST-elevation myocardial infarction. *Eur Heart J Acute Cardiovasc Care* 2016;5:23-32.

20. Haller PM, Jäger B, Farhan S, et al. Impact of age on short- and long-term mortality of patients with ST-elevation myocardial infarction in the VIENNA STEMI network. *Wien Klin Wochenschr* 2018;130:172-81.
21. Payvar S, Kim S, Rao SV, et al. In-hospital outcomes of percutaneous coronary interventions in extremely obese and normal-weight patients: findings from the NCDR (National Cardiovascular Data Registry). *J Am Coll Cardiol* 2013;62:692-6.
22. Planer D, Witzenbichler B, Guagliumi G, et al. Impact of hyperglycemia in patients with ST-segment elevation myocardial infarction undergoing percutaneous coronary intervention: the HORIZONS-AMI trial. *Int J Cardiol* 2013;167:2572-9.
23. Samanta R, Narayan A, Kovoor P, et al. Influence of BMI on Short and Long-Term Outcomes in Patients With STEMI and LV Dysfunction. *Heart Lung Circ* 2020;29:361-7.
24. Medina HM, Cannon CP, Fonarow GC, et al. Reperfusion strategies and quality of care in 5339 patients age 80 years or older presenting with ST-elevation myocardial infarction: analysis from get with the guidelines-coronary artery disease. *Clin Cardiol* 2012;35:632-40.
25. Lavie CJ, De Schutter A, Milani RV. Healthy obese versus unhealthy lean: the obesity paradox. *Nat Rev Endocrinol* 2015;11:55-62.
26. Winzap P, Davies A, Klingenberg R, et al. Diabetes and baseline glucose are associated with inflammation, left ventricular function and short- and long-term outcome in acute coronary syndromes: role of the novel biomarker Cyr 61.

Cardiovasc Diabetol 2019;18:142.

27. Samanta R, Pouliopoulos J, Kumar S, et al. Influence of BMI on inducible ventricular tachycardia and mortality in patients with myocardial infarction and left ventricular dysfunction: The obesity paradox. *Int J Cardiol* 2018;265:148-54.
28. Lavie CJ, Milani RV, Ventura HO. Obesity and cardiovascular disease: risk factor, paradox, and impact of weight loss. *J Am Coll Cardiol* 2009;53:1925-32.
29. Fukuoka S, Kurita T, Dohi K, et al. Untangling the obesity paradox in patients with acute myocardial infarction after primary percutaneous coronary intervention (detail analysis by age). *Int J Cardiol* 2019;289:12-8.
30. Ayça B, Akın F, Celik O, et al. Neutrophil to Lymphocyte Ratio is Related to Stent Thrombosis and High Mortality in Patients With Acute Myocardial Infarction. *Angiology* 2015;66:545-52.
31. Machado GP, Araujo GN, Carpes CK, et al. Comparison of neutrophil-to-lymphocyte ratio and mean platelet volume in the prediction of adverse events after primary percutaneous coronary intervention in patients with ST-elevation myocardial infarction. *Atherosclerosis* 2018;274:212-7.
32. Arbel Y, Shacham Y, Ziv-Baran T, et al. Higher neutrophil/lymphocyte ratio is related to lower ejection fraction and higher long-term all-cause mortality in ST-elevation myocardial infarction patients. *Can J Cardiol* 2014;30:1177-82.
33. Pan W, Zhao D, Zhang C, et al. Application of neutrophil/lymphocyte ratio in predicting coronary blood flow and mortality in patients with ST-elevation myocardial infarction undergoing percutaneous coronary intervention. *J Cardiol* 2015;66:9-14.
34. Sen N, Afsar B, Ozcan F, et al. The neutrophil to lymphocyte ratio was associated

with impaired myocardial perfusion and long term adverse outcome in patients with ST-elevated myocardial infarction undergoing primary coronary intervention. *Atherosclerosis* 2013;228:203-10.

35. Kaya MG, Akpek M, Lam YY, et al. Prognostic value of neutrophil/lymphocyte ratio in patients with ST-elevated myocardial infarction undergoing primary coronary intervention: a prospective, multicenter study. *Int J Cardiol* 2013;168:1154-9.
36. Kirtane AJ, Bui A, Murphy SA, et al. Association of peripheral neutrophilia with adverse angiographic outcomes in ST-elevation myocardial infarction. *Am J Cardiol* 2004;93:532-6.
37. Sheridan FM, Cole PG, Ramage D. Leukocyte adhesion to the coronary microvasculature during ischemia and reperfusion in an in vivo canine model. *Circulation* 1996;93:1784-7.
38. Dandona P, Chaudhuri A, Ghanim H, et al. Insulin as an anti-inflammatory and antiatherogenic modulator. *J Am Coll Cardiol* 2009;53:S14-20.
39. Devos P, Chioléro R, Van den Berghe G, et al. Glucose, insulin and myocardial ischaemia. *Curr Opin Clin Nutr Metab Care* 2006;9:131-9.
40. Young LH, Renfu Y, Russell R, et al. Low-flow ischemia leads to translocation of canine heart GLUT-4 and GLUT-1 glucose transporters to the sarcolemma in vivo. *Circulation* 1997;95:415-22.
41. Khani S, Tayek JA. Cortisol increases gluconeogenesis in humans: its role in the metabolic syndrome. *Clin Sci (Lond)* 2001;101:739-47.
42. Timmer JR, van der Horst IC, Ottervanger JP, et al. Prognostic value of admission glucose in non-diabetic patients with myocardial infarction. *Am Heart J*

2004;148:399-404.

43. Buchanan TA, Xiang AH, Peters RK, et al. Preservation of pancreatic beta-cell function and prevention of type 2 diabetes by pharmacological treatment of insulin resistance in high-risk hispanic women. *Diabetes* 2002;51:2796-803.
44. Marfella R, Sasso FC, Siniscalchi M, et al. Peri-procedural tight glycemic control during early percutaneous coronary intervention is associated with a lower rate of in-stent restenosis in patients with acute ST-elevation myocardial infarction. *J Clin Endocrinol Metab* 2012;97:2862-71.
45. Shacham Y, Leshem-Rubinow E, Ben-Assa E, et al. Lower admission hemoglobin levels are associated with longer symptom duration in acute ST-elevation myocardial infarction. *Clin Cardiol* 2014;37:73-7.
46. Keel SB, Abkowitz JL. The microcytic red cell and the anemia of inflammation. *N Engl J Med* 2009;361:1904-6.
47. Brener SJ, Mehran R, Lansky AJ, et al. Pretreatment with aspirin in acute coronary syndromes: Lessons from the ACUITY and HORIZONS-AMI trials. *Eur Heart J Acute Cardiovasc Care* 2016;5:449-54.
48. Weidmann L, Obeid S, Mach F, et al. Pre-existing treatment with aspirin or statins influences clinical presentation, infarct size and inflammation in patients with de novo acute coronary syndromes. *Int J Cardiol* 2019;275:171-8.
49. Yonetsu T, Lee T, Murai T, et al. Association Between Prior Aspirin Use and Morphological Features of Culprit Lesions at First Presentation of Acute Coronary Syndrome Assessed by Optical Coherence Tomography. *Circ J* 2017;81:511-9.
50. Lancaster GI, Lancaster CJ, Radley D, et al. Prior aspirin use in unstable angina

predisposes to higher risk: the aspirin paradox. *Int J Cardiol* 2001;80:201-7.

51. Lancaster GI, Jain H, Zarich SW. The role of aspirin resistance in the treatment of acute coronary syndromes. *Clin Cardiol* 2008;31:11-7.
52. Claessen BE, Smits PC, Kereiakes DJ, et al. Impact of lesion length and vessel size on clinical outcomes after percutaneous coronary intervention with everolimus- versus paclitaxel-eluting stents pooled analysis from the SPIRIT (Clinical Evaluation of the XIENCE V Everolimus Eluting Coronary Stent System) and COMPARE (Second-generation everolimus-eluting and paclitaxel-eluting stents in real-life practice) Randomized Trials. *JACC Cardiovasc Interv* 2011;4:1209-15.
53. Kastrati A, Elezi S, Dirschinger J, et al. Influence of lesion length on restenosis after coronary stent placement. *Am J Cardiol* 1999;83:1617-22.
54. Choi IJ, Koh YS, Lim S, et al. Impact of the stent length on long-term clinical outcomes following newer-generation drug-eluting stent implantation. *Am J Cardiol* 2014;113:457-64.
55. Leclerc G, Isner JM, Kearney M, et al. Evidence implicating nonmuscle myosin in restenosis. Use of in situ hybridization to analyze human vascular lesions obtained by directional atherectomy. *Circulation* 1992;85:543-53.
56. Brodie BR, Stuckey TD, Hansen C, et al. Benefit of coronary reperfusion before intervention on outcomes after primary angioplasty for acute myocardial infarction. *Am J Cardiol* 2000;85:13-8.
57. De Luca G, Ernst N, Zijlstra F, et al. Preprocedural TIMI flow and mortality in patients with acute myocardial infarction treated by primary angioplasty. *J Am Coll Cardiol* 2004;43:1363-7.

58. Lee KL, Woodlief LH, Topol EJ, et al. Predictors of 30-day mortality in the era of reperfusion for acute myocardial infarction. Results from an international trial of 41,021 patients. GUSTO-I Investigators. *Circulation* 1995;91:1659-68.

59. Shariat SF, Karakiewicz PI, Godoy G, et al. Use of nomograms for predictions of outcome in patients with advanced bladder cancer. *Ther Adv Urol* 2009;1:13-26.

60. Gao N, Qi X, Dang Y, et al. Establishment and validation of a risk model for prediction of in-hospital mortality in patients with acute ST-elevation myocardial infarction after primary PCI. *BMC Cardiovasc Disord* 2020;20:513.

Table 1 Clinical characteristics of the patients used to construct the nomogram

Variables	Training set			Testing set		
	Survival (n=264)	In-hospital mortality (n=132)	P	Survival (n=368)	In-hospital mortality (n=91)	P
Age (years) (mean ±SD)	60.3±12.9	69.3±9.8	<0.001	59.8±12.4	74.4±9.6	0.249
Male (n (%))	202 (76.5)	82 (62.1)	0.004	294 (79.9)	58 (63.7)	0.001
BMI (kg/m^2)	26.0 (25.4, 26.0)	24.9 (24.9, 24.9)	<0.001	25.5±3.0	25.3 (23.4, 27.5)	0.953
Cardiac arrest (n (%))	6 (2.3)	4 (3.0)	0.910	6 (1.6)	2 (2.2)	0.711
Cardiogenic shock before admission (n (%))	6 (2.3)	28 (21.2)	<0.001	15 (4.1)	15 (16.5)	<0.001
Use of temporary pacemaker before admission (n (%))	0	3 (2.3)	0.065	2 (0.5)	2 (2.2)	0.128
Ventilator support before admission (n (%))	1 (0.4)	5 (3.8)	0.029	2 (0.5)	5 (5.5)	0.001
CPR before admission (n (%))	5 (1.9)	7 (5.3)	0.12	0	5 (5.5)	<0.001

SBP on admission (median (IQR))	133 (114, 149)	118 (100, 140)	<0.001	129±25	121 (107, 135)	0.003
DBP on admission (median (IQR))	82 (72, 92)	73 (62, 82)	<0.001	80±15	76±16	0.011
Heart rate on admission (median (IQR))	76 (64, 89)	80 (66, 96)	0.025	78±17	79±18	0.613
Fatal arrhythmia before admission (n (%))	15 (5.7)	6 (4.5)	0.812	12 (3.3)	8 (8.8)	0.021
Total ischemic time (min (median (IQR)))	153.5 (95.3, 249.5)	360.0 (193.8, 420.0)	<0.001	190.0 (126.5, 282.8)	218.0 (125.3, 374.8)	0.042
Killip class 3-4 (n (%))	95 (36.0)	37 (28.0)	0.142	66 (17.9)	53 (58.2)	<0.001
Past medical history						
Hypertension (n (%))	137 (51.9)	74 (56.1)	0.499	38 (10.3)	35 (38.5)	<0.001
DM (n (%))	49 (18.6)	47 (35.6)	<0.001	84 (22.8)	20 (22.0)	0.863
Hyperlipidemia (n (%))	12 (4.5)	27 (20.5)	<0.001	23 (6.3)	18 (19.8)	<0.001

Previous PCI (n (%))	8 (3.0)	10 (7.6)	0.073	17 (4.6)	6 (6.6)	0.440
Previous CABG (n (%))	0	1 (0.8)	0.723	0	1 (1.1)	0.044
CAD (n (%))	17 (6.4)	28 (21.2)	<0.001	20 (5.4)	20 (22.0)	<0.001
AF (n (%))	1 (0.4)	10 (7.6)	<0.001	3 (0.8)	10 (11.0)	<0.001
HF (n (%))	3 (1.1)	1 (0.8)	0.722	18 (4.9)	7 (7.7)	0.292
Renal insufficiency (n (%))	1 (0.4)	61 (46.2)	<0.001	1 (0.3)	12 (13.2)	<0.001
History of cerebrovascular disease (n (%))	40 (15.2)	24 (18.2)	0.530	60 (16.3)	12 (13.2)	0.464
Peripheral vascular disease (n (%))	5 (1.9)	4 (3.0)	0.721	3 (0.8)	2 (2.2)	0.255
History of bleeding (n (%))	1 (0.4)	1 (0.8)	>0.999	6 (1.6)	1 (1.1)	0.711
Family history of CAD (n (%))	28 (10.6)	16 (11.1)	0.875	62 (16.8)	6 (6.6)	0.014
Angiographic characteristics						
Number of stents (median (IQR))	1 (1, 1)	1 (0, 1)	<0.001	1 (1, 1)	1 (1, 1)	0.067

Long lesions (n (%))	178 (67.4)	67 (50.8)	0.002	131 (35.6)	63 (69.2)	<0.001
Thrombus aspiration (n (%))	92 (34.8)	31 (23.5)	0.029	205 (55.7)	16 (17.6)	<0.001
Residual stenosis (n (%))	2 (0.8)	10 (7.6)	0.001	4 (1.1)	6 (6.6)	0.001
Use temporary pacemaker (n (%))	4 (1.5)	18 (13.6)	<0.001	2 (0.5)	7 (7.7)	<0.001
IABP (n (%))	4 (1.5)	15 (11.4)	<0.001	4 (1.1)	11 (12.1)	<0.001
Respirator support (n (%))	1 (0.4)	19 (14.4)	<0.001	2 (0.5)	11 (12.1)	<0.001
Pericardial aspiration (n (%))	0	3 (2.3)	0.065	0	3 (3.3)	<0.001
No flow (n (%))	48 (18.2)	50 (37.9)	<0.001	55 (14.9)	29 (31.9)	<0.001
Coronary perforation (n (%))	0	5 (3.8)	0.001	1 (0.3)	1 (1.1)	0.283
Dissection (n (%))	0	3 (2.3)	0.065	0	5 (5.5)	<0.001
Pericardial tamponade (n (%))	0	9 (6.8)	<0.001	0	2 (2.2)	0.004
Acute HF (n (%))	22 (8.3)	33 (25.0)	<0.001	30 (7.7)	22 (24.2)	<0.001
Bleeding (n (%))	0	2 (1.5)	0.210	3 (0.8)	3 (3.3)	0.062
Cardiac arrest (n (%))	1 (0.4)	23 (17.4)	<0.001	6 (1.6)	8 (8.8)	<0.001

Recurrent MI (n (%))	1 (0.4)	15 (11.4)	<0.001	2 (0.5)	5 (5.5)	0.001
Stent thrombosis (n (%))	6 (2.3)	2 (1.5)	0.900	13 (3.5)	1 (1.1)	0.227
Type B2-C (n (%))	213 (80.7)	96 (72.7)	0.094	230 (62.5)	47 (51.6)	0.058
TIMI flow grade 0-1 before PCI (n (%))	197 (74.6)	114 (86.4)	0.011	274 (74.5)	65 (71.4)	0.556
LAD (n (%))	85 (32.2)	64 (48.5)	0.002	177 (48.1)	32 (35.2)	0.027
Biochemical markers						
Hyperkalemia (n (%))	3 (1.1)	33 (25.0)	<0.001	11 (3.0)	19 (20.9)	<0.001
Hyponatremia (n (%))	12 (4.5)	19 (14.4)	0.001	31 (8.4)	6 (6.6)	0.566
Anemia (n (%))	12 (4.5)	14 (10.6)	0.022	21 (5.7)	19 (20.9)	<0.001
N/L ratio (median (IQR))	4.70 (2.68, 7.87)	8.54 (3.19, 11.46)	<0.001	5.08 (3.65, 9.46)	6.02 (7.95, 8.73)	0.107
HCT, % (median (IQR))	41.8 (38.0, 44.6)	38.5 (36.8, 41.3)	<0.001	41.1±5.7	41.0 (38.2, 44.6)	0.790
HGB, g/L (median (IQR))	142.0 (129.0, 155.0)	129.0 (119.0, 137.3)	<0.001	139.5±1.7	127.3±1.2	0.286
PLT, $\times 10^9$/L (median (IQR))	224.0 (186.0, 269.0)	227.0 (194.8, 246.3)	0.554	229.0 (191.0, 274.0)	224.0 (182.0, 259.3)	0.301

Random blood glucose on admission, mmol/L (median (IQR))	5.95 (5.02, 7.44)	9.81 (8.60, 9.81)	<0.001	6.13 (5.05, 9.35)	6.15 (5.15, 8.07)	0.668
EF after PCI, % (median (IQR))	54.0 (47.8, 59.0)	43.0 (38.0, 48.5)	<0.001	56 (49, 61)	55 (47, 60)	0.584
Medication list on admission						
Aspirin	262 (99.2)	117 (88.6)	<0.001	332 (90.2)	72 (79.1)	0.004
Ticagrelor/clopidogrel	262 (99.2)	131 (99.2)	>0.999	332 (90.2)	86 (94.5)	0.199
ACEI/ARB	100 (37.9)	33 (25.0)	0.014	18 (4.9)	7 (7.7)	0.292
β-Blocker	66 (25.0)	26 (19.7)	0.239	29 (7.9)	8 (8.9)	0.753
Statin	130 (49.2)	5 8(43.9)	0.319	181 (49.2)	25 (27.5)	<0.001

BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; DM: diabetes mellitus; PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft; CAD: coronary atherosclerotic heart disease; AF: atrial fibrillation; HF: heart failure; IABP: intra-aortic balloon pump; MI: myocardial infarction; LAD: left anterior descending branch; N/L ratio: neutrophils/lymphocytes ratio; HCT: hematocrit; HGB: hemoglobin; PLT: platelets; EF: ejection fraction; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker.

Table 2 Variables selected as predictors for the nomogram according to the multivariable logistic analysis

Variables	P	OR	95% CI	
			Low	High
Age	0.049	1.07	1.05	1.09
BMI	0.019	0.55	0.31	0.87
SBP on admission	0.009	0.92	0.86	0.97
HGB	0.017	0.85	0.73	0.97
Random blood glucose on admission	0.011	1.53	1.13	2.21
EF after PCI	0.015	0.89	0.80	0.97
Use aspirin before admission	0.001	0.01	0.009	0.04
N/L ratio	0.004	1.34	1.12	1.69
Long lesions	<0.001	2.00	1.31	3.08
TIMI flow grade 0-1 before PCI	0.008	2.15	1.24	3.90

OR: odds ratio; CI: confidence interval; BMI: body mass index; SBP: systolic blood pressure; HGB: hemoglobin; EF: ejection fraction; PCI: percutaneous coronary intervention; N/L ratio: neutrophils/lymphocytes ratio; TIMI: thrombolysis in myocardial infarction.

Figure legends

Figure 1. Flowchart illustrating the process of patient selection.

Figure 2. The nomogram for the prediction of in-hospital mortality in patients with acute ST-elevation myocardial infarction after primary PCI. BMI: body mass index; SBP: systolic blood pressure; HGB: hemoglobin; EF: ejection fraction; N/L ratio: neutrophils/lymphocytes ratio.

Figure 3. The calibration curves of the nomogram for the training set (A) and the testing set (B).

Figure 4. The received operating characteristics (ROC) curves of the nomogram for the training set (A) and the testing set (B).

Figure 5. The decision curve analysis (DCA) for the risk model for the training set (A) and the testing set (B).

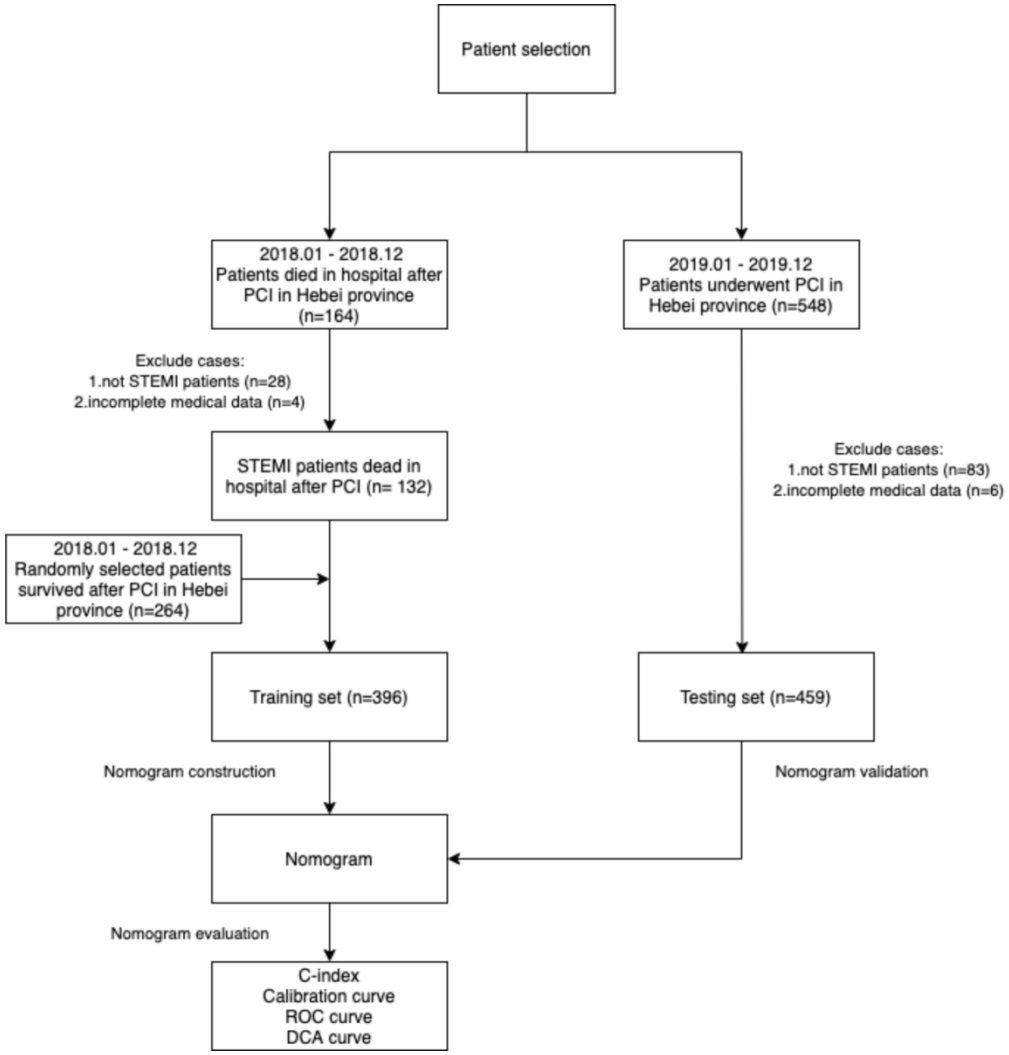

Figure 1. Flowchart illustrating the process of patient selection.

170x177mm (300 x 300 DPI)

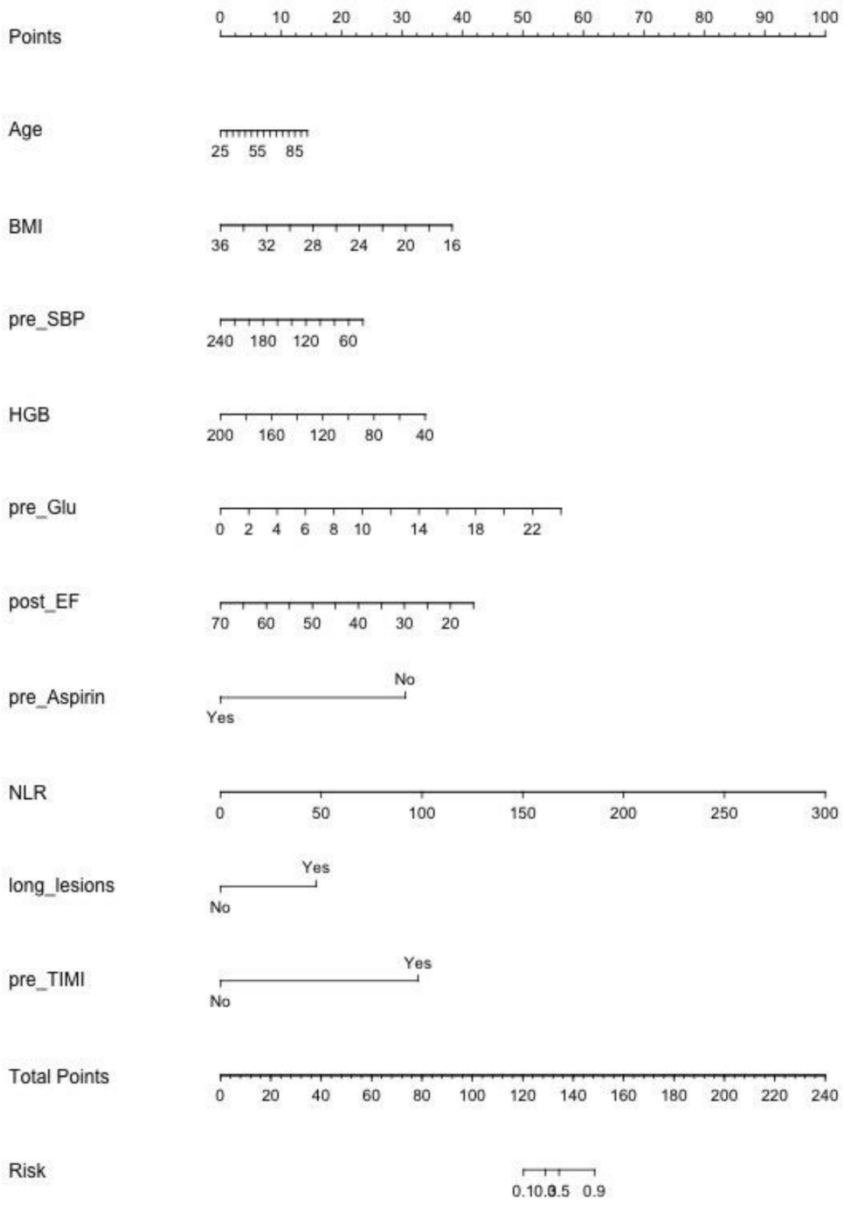

Figure 2. The nomogram for the prediction of in-hospital mortality in patients with acute ST-elevation myocardial infarction after primary PCI. BMI: body mass index; SBP: systolic blood pressure; HGB: hemoglobin; EF: ejection fraction; N/L ratio: neutrophils/lymphocytes ratio.

170x242mm (300 x 300 DPI)

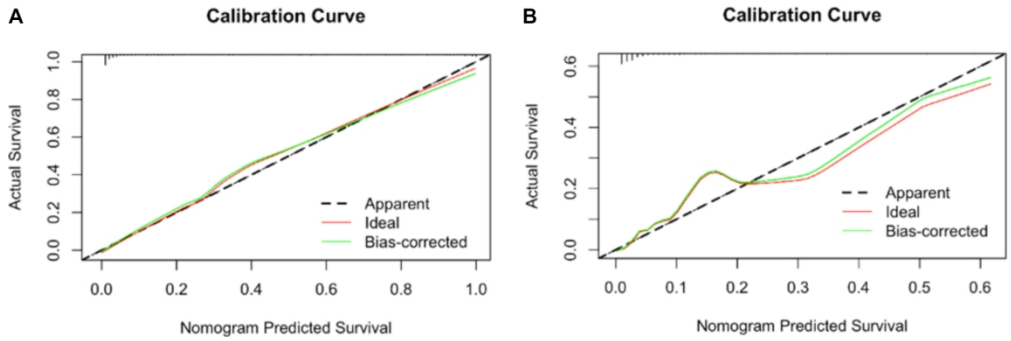

Figure 3. The calibration curves of the nomogram for the training set (A) and the testing set (B).

170x56mm (300 x 300 DPI)

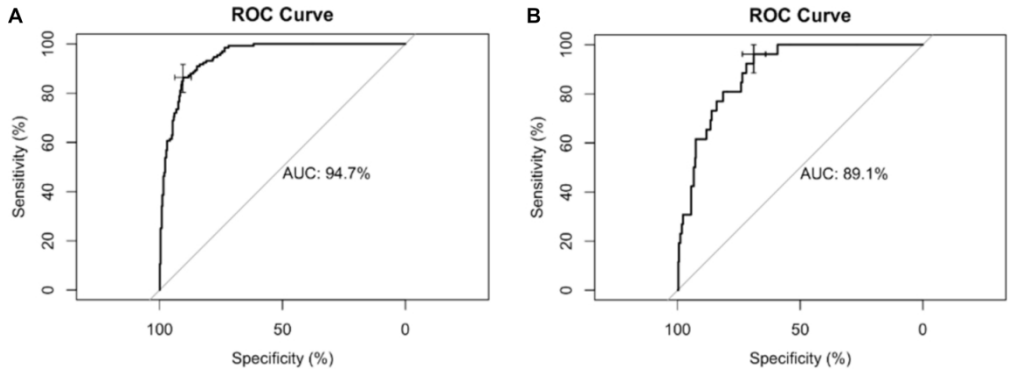

Figure 4. The received operating characteristics (ROC) curves of the nomogram for the training set (A) and the testing set (B).

170x61mm (300 x 300 DPI)

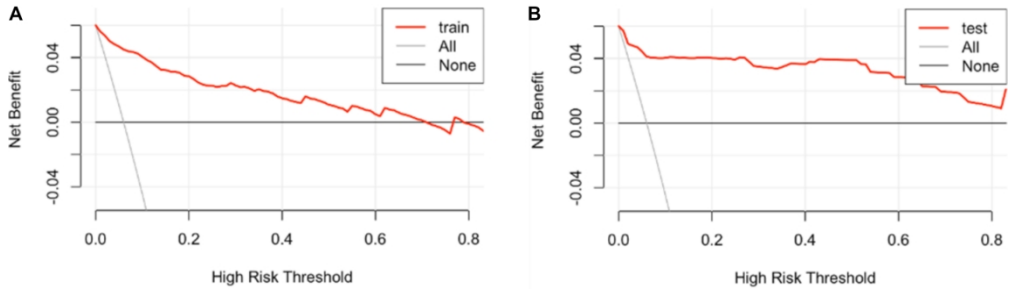

Figure 5. The decision curve analysis (DCA) for the risk model for the training set (A) and the testing set (B).

170x48mm (300 x 300 DPI)

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any pre-specified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	9
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15
Generalisability	21	Discuss the generalisability (external validity) of the study results	15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

A nomogram for the prediction of in-hospital mortality in patients with acute ST-elevation myocardial infarction after primary percutaneous coronary intervention: a multicentre, retrospective, observation study in Hebei Province, China

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2021-056101.R1
Article Type:	Original research
Date Submitted by the Author:	30-Dec-2021
Complete List of Authors:	Wang, Yudan; Hebei Medical University, School of Graduate; Hebei General Hospital, Department of Cardiology Center Wang, Wenjing; Hebei General Hospital, Department of Cardiology Center Jia, Shengqi; Hebei Medical University, School of Graduate Gao, Man; Hebei Medical University, School of Graduate Zheng, Shihang; Hebei North University, School of Graduate Wang, Jiaqi; Hebei North University, School of Graduate Dang, Yi; Hebei General Hospital, Department of Cardiology Center Li, Yingxiao; Hebei General Hospital, Department of Cardiology Center Qi, Xiaoyong; Hebei Medical University, School of Graduate; Hebei General Hospital, Department of Cardiology Center
Primary Subject Heading:	Cardiovascular medicine
Secondary Subject Heading:	Cardiovascular medicine
Keywords:	Coronary intervention < CARDIOLOGY, Coronary heart disease < CARDIOLOGY, Myocardial infarction < CARDIOLOGY

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

A nomogram for the prediction of in-hospital mortality in patients with acute ST-elevation myocardial infarction after primary percutaneous coronary intervention: a multicentre, retrospective, observation study in Hebei Province, China

Running title: Nomogram for STEMI in-hospital mortality after PCI

Yudan Wang[1,2], Wenjing Wang[2], Shengqi Jia[1], Man Gao[1], Shihang Zheng[3], Jiaqi Wang[3], Yi Dang[2], Yingxiao Li[2], Xiaoyong Qi[1,2*]

[1]School of Graduate, Hebei Medical University, Shijiazhuang, Hebei Province, People's Republic of China

[2]Department of Cardiology Center, Hebei General Hospital, Shijiazhuang, Hebei Province, People's Republic of China

[3]School of Graduate, Hebei North University, Zhangjiakou, Hebei Province, People's Republic of China

[*]**Corresponding Author**

Xiaoyong Qi

School of Graduate, Hebei Medical University, Shijiazhuang, Hebei Province, People's Republic of China

Department of Cardiology Center, Hebei General Hospital, No. 348, Heping West Road, Shijiazhuang 050051, Hebei Province, People's Republic of China

E-mail address: hbghqxy@126.com

Word count: 3020

ABSTRACT

Objectives: To establish a clinical prognostic nomogram for predicting in-hospital mortality after primary percutaneous coronary intervention (PCI) among patients with ST-elevation myocardial infarction (STEMI).

Design: Retrospective, multicenter, observational study.

Setting: Thirty-nine hospitals in Hebei Province.

Participants: Patients with STEMI who underwent PCI from January 2018 to December 2019.

Interventions: A multivariable logistic regression model was used to identify the factors associated with in-hospital mortality. Then, they were incorporated into a nomogram. The performance of the nomogram was evaluated by the discrimination, calibration, and clinical usefulness.

Primary and secondary outcome measures: The outcome was the factors associated with in-hospital mortality.

Results: This study included 855 patients, among whom 223 died in hospital. Age, Body Mass Index (BMI), systolic pressure on admission, hemoglobin, random blood glucose on admission, ejection fraction after PCI, use aspirin before admission, long lesions, thrombolysis in myocardial infarction (TIMI) flow grade, and neutrophils/lymphocytes ratio (N/L ratio) were independently associated with in-hospital mortality (all $P<0.05$). In the training set, the nomogram showed a C-index of 0.947, goodness-of-fit of 0.683, and area under the receiver operating characteristic curve (AUC) of 0.947 (95%CI=0.927-0.967). In the testing set, the C-index was 0.891, goodness-of-fit was 0.462, and AUC was 0.891 (95%CI=0.844-0.939). The results indicate that the nomogram had good

discrimination and good prediction accuracy and could achieve a good net benefit.

Conclusions: A nomogram to predict in-hospital mortality in patients with STEMI after PCI was developed and validated in Hebei, China and showed a satisfactory performance

Keywords: nomogram; ST-elevated myocardial infarction; percutaneous coronary intervention; in-hospital mortality

Strengths and limitations of this study

- This is a multi-center study, included 39 tertiary centers and 855 patients, including more patients (223, 26.1%) who died in the hospital.
- The data were obtained retrospectively and some patients died during the PCI, which can lead to some missing information.
- Further prospective studies are still necessary to confirm the performance of the clinical applicability in future investigations and verify the practicality in ICU.

INTRODUCTION

ST-segment elevation myocardial infarction (STEMI), a type of coronary artery disease (CAD), is a common clinical emergency and critical illness [1]. STEMI is most often caused by plaque rupture of an atherosclerotic lesion in the affected (culprit) coronary artery followed by total occlusion of the vessel lumen with a thrombus [2 3]. Common risk factors for CAD, including STEMI, are tobacco abuse, dyslipidemias, hypertension, diabetes mellitus, and a family history of CAD [4]. Myocardial infarction is the main cause of global morbidity, mortality, and major cardiovascular events (MACEs), representing 15% of the annual deaths worldwide [5]. In recent years, with the diagnosis and treatment guidelines, the continuous standardization of the treatment of STEMI, the increasing evidence of determinants of patient prognosis, and the continuous development of emerging technologies have contributed to a reduction in mortality; still, mortality seems to have plateaued [3].

Primary percutaneous coronary intervention (PCI) has become the preferred reperfusion strategy in patients with STEMI according to the current clinical guidelines for STEMI in the United States and Europe [6 7]. Nevertheless, even if such patients receive timely PCI and/or appropriate antiplatelet drugs, the prognosis is still poor, and a substantial number of patients still die in-hospital after PCI. About 6% of STEMI patients die in the hospital [3 8 9]. Therefore, there is still room for improving the short-term outcomes after PCI.

Various studies examined the risk factors of short- and long-term mortality of STEMI patients after PCI [10-12]. Guidelines encourage the use of clinical scores such as the thrombolysis in myocardial infarction (TIMI) or The Global Registry of Acute Coronary Events (GRACE) for STEMI to assess early- and long-term risk [6 7 13]. Several biomarkers

have been reported to confer independent prognostic information after STEMI, including Cardiac Troponin (cTn), Brain Natriuretic Peptide (BNP), amino-terminal pro-Brain Natriuretic Peptide (NT-proBNP), and D-dimer [14-17]. Unfortunately, these studies often exclude patients with advanced age, liver or kidney dysfunction, and other comorbidities and complications. Therefore, the generalizability of those studies is limited, and it is difficult to summarize and reflect the real-world treatment situation comprehensively.

Therefore, the objective of this study was to develop a clinical nomogram for predicting in-hospital mortality of patients with STEMI after PCI. The results could provide clinical guidance and improve the outcome of STEMI patients.

PATIENTS AND METHODS

Study design and patients

This multicenter, retrospective, observational study included STEMI patients treated with PCI at 39 PCI hospitals in Hebei Province from January 2018 to December 2019. The cohort was divided into a training set and a time-independent validation set. The training set refers to the use of modeled data to verify the predictive effect of the model, while test set is to use another set of patients' data (namely external data) to verify the prediction accuracy of the model. The training set patients enrolled from January 2018 to December 2018 and the testing set patients enrolled from January 2019 to December 2019.

All patients met the diagnostic criteria of acute STEMI based on their symptoms and/or ECG, myocardial damage markers and other test results and underwent primary PCI according to the 2017 ESC guidelines for the management of STEMI [6], namely with persistent chest discomfort or other symptoms suggestive of ischemia and ST-segment elevation in at least two contiguous leads. Patients with non-ST segment myocardial infarction (NSTEMI) or unstable angina or STEMI patients who did not undergo PCI were excluded. Patients who were re-admitted to the hospital for revascularization of non-criminal vessels were also excluded. The treatment strategy after PCI of surviving patients is determined by the doctor in charge in accordance with relevant guidelines.

The study was approved by the Ethics Committees of Hebei General Hospital as the lead center and the ethics committee of each participating hospital. The requirement for informed consent was waived by the committee. The study was conducted according to the tenets of the Declaration of Helsinki for Medical Research Involving Human Subjects and Good Clinical Practice.

Patient and Public Involvement

Patients or the public were not involved in the design or reporting or dissemination plans of our research as this study is a retrospective, observational study.

Definitions

Long lesions was defined as the stenosis that has as ≥ 50% reduction and more than 20mm in luminal diameter[18].

Residual stenosis was defined as **>** 30% residual stenosis of the target lesion after PCI.

Bleeding was defined as a composite of major bleeding according to Bleeding Academic Research Consortium Definition for Bleeding (BARC) type 3 or 5, but was not related to coronary-artery bypass grafting (CABG)[19].

Data collection

Demographics (age, sex, and BMI), medical history (hypertension, diabetes mellitus, atrial fibrillation (AF), hyperlipidemia and family history of coronary artery disease (CAD), stroke, renal failure, and peripheral artery disease), angiographic characteristics and information of cardiac procedures (disease condition, TIMI flow grade, number of stents, use of intra-aortic balloon pump (IABP), use of temporary pacemaker, use of ventilator, and whether there was no-reflow, coronary perforation, and cardiac arrest), medications on admission (antiplatelet agents, β-blockers, nitrate, angiotensin-converting enzyme inhibitors (ACEI), angiotensin receptor blockers (ARB), and statin), biochemical markers (N/L ratio), hematocrit (HCT), hemoglobin (HGB), platelets (PLT), and random blood

glucose on admission), and left ventricular ejection fraction (LVEF) after PCI were extracted from the medical charts. All treatments were according to the current guidelines.

Nomogram construction

Demographics, medical history, vital signs before and after PCI, and auxiliary examinations were evaluated using univariable logistic regression. Variables with $P<0.05$ in the univariable logistic analyses were included for multivariable logistic analysis and nomogram construction. Receiver operator characteristic (ROC) curve analysis was used to quantify the prediction performance of the nomogram. A calibration curve was used to evaluate the calibration of the nomogram, and its goodness of fit was assessed using the Hosmer-Lemeshow test. Finally, the clinical usefulness of the nomogram was accessed using a decision curve analysis (DCA).

Statistical analysis

Statistical analyses were performed using R version 4.0.3 (R Foundation for Statistical Computing) with RStudio (version 1.3.959; RStudio, Auckland, New Zealand). R packages used in this study were rms, reader, tableone, pROC, ResourceSelection, and rmda. The predictive accuracy of the nomogram was measured using the C-statistic (Bootstrap method, 1000 times). Calibration was evaluated using the Hosmer-Lemeshow statistic. Categorical variables were presented as frequencies with percentages, normally distributed continuous variables as means ± SD, and other data as medians with interquartile ranges (IQRs). Categorical variables were compared using the chi-square test or Fisher's test if the expected cell count was <5. Student's t-test was used to compare normally distributed

continuous variables. Otherwise, the Mann-Whitney U-test was used. The significance level was set at 0.05, and two-sided tests were used.

RESULTS

Characteristics of the patients

The whole study population consisted of 855 patients diagnosed with STEMI and who underwent PCI, including 396 in the training set (132 (33.3%) dead patients and 264 (66.7%) survivors) and 459 (91 (19.8%) dead patients, and 368 (80.2%) survivors) in the test set (Figure 1). The clinical characteristics, including demographic, medical history, angiographic characteristics, and information of cardiac procedures, medications, and biochemical markers, are summarized in Table 1. The patients who died in the hospital were older (69.8±10.2 vs. 60.2±12.6 years, P<0.01), more likely to be women (32.7% vs. 21.5%, P<0.01), and more had complications like hypertension, AF, and hyperlipidemia. The hospital stay was 8.51±5.11 days in the training set and 8.32±4.70 days in the test set.

Nomogram construction

According to the multivariable logistic analysis, the 10 variables were found to meet the threshold of P<0.05. Age (OR=1.069, 95% CI=1.048-1.092, P=0.049), BMI (OR=0.55, 95% CI=0.31=0.87, P=0.019), SBP on admission (OR=0.92, 95% CI=0.86-0.97, P=0.009), HGB (OR=0.85, 95% CI=0.73-0.97, P=0.017), random blood glucose on admission (OR=1.53, 95% CI=1.13-2.21, P=0.011), EF after PCI (OR=0.89, 95% CI=0.80-0.97, P=0.015), aspirin (OR=0.001, 95% CI=0.009-0.04, P=0.001), N/L ratio (OR=1.34, 95% CI=1.12-1.69, P=0.004), long lesions (OR=2.00, 95% CI=1.310-3.084, P<0.001), and TIMI flow grade (OR=2.15, 95% CI=1.242-3.900, P=0.008) were independently associated with in-hospital mortality after PCI of STEMI (Table 2). The nomogram is shown in Figure 2. The formula for calculating the total point of the nomogram is

15.5628+0.0320×age-0.2991×BMI-0.0184×SBP-0.0331×HGB+0.3663×random blood glucose on admission-0.1188×LVEF after PCI-4.7705×aspirin+0.0521×N/L ratio-2.4688×long leisions+5.1018×TIMI flow grade.

Evaluation of the nomogram

In the training set, the C-index was 0.947, indicating that the prediction model was valuable in clinical practice (Figure 3a). The value of goodness-of-fit was 0.683, indicating a good prediction accuracy. The ROC curve is shown in Figure 4a (AUC=0.947, 95% CI: 0.927-0.967). Figure 5a shows the DCA curve for the training set, indicating that the nomogram had a high overall net benefit in predicting in-hospital mortality after PCI treatment.

In the testing set, the C-index was 0.891. Figure 3b shows the calibration curve, and the value of goodness-of-fit was 0.462. The ROC curve is shown in Figure 4b (AUC=0.891, 95% CI: 0.844-0.939). The DCA curve is shown in Figure 5b. The results of the testing set indicate that the nomogram had good discrimination and good prediction accuracy and could achieve a good net benefit.

DISCUSSION

In this study, a relatively accurate clinical nomogram was constructed, which demonstrated adequate discrimination and calibration power to provide an individualized estimation for the in-hospital mortality in STEMI patients after PCI. For the construction of the nomogram, 10 significant predictors were screened by multivariable logistic analysis.

In our study, age was an independent risk factor of STEMI patients, in accordance with other analyses of STEMI patients and underlining the high-risk profile of elderly patients, as they usually present with more risk factors and comorbidities than younger patients[20 21], such as the higher prevalence of renal insufficiency, lower LVEF. High mortality in the older patients might also result from end-organ dysfunction, competing risks might also offset the benefits from reperfusion, such that successful outcomes are more dependent on overall health issues. Therefore, for older patients, some authors have also questioned the benefit of reperfusion therapy[22].

The previous view is that obesity increases insulin resistance, worsens plasma lipid profiles, and increases arterial blood pressure, and thus has adverse effects on patients with CAD through the indirect effects of other risk factors (such as hypertension, impaired glucose tolerance, and hyperinsulinemia) [23]. Therefore, obese patients demonstrate greater adverse left ventricle (LV) remodeling and more impaired LV deformation after STEMI compared with those similar infarct characteristics but normal BMI [24 25]. Interestingly, some studies have shown the so-called “obesity paradox”, whereby obesity is related to better clinical outcomes [23 26-28], consistent with the present study. Fukuoka et al. [29] reported that this phenomenon is only observed in elderly patients, not in younger patients, so the influence of BMI on risk factors for death might vary with age. Nevertheless, obesity is currently

recognized as a risk factor for the long-term prognosis of patients with CAD, and it is worth recommending maintaining BMI at a normal level [29].

Acute stress has been shown to regulate the immune response of lymphocytes and reduce the number of peripheral blood lymphocytes. The smaller the value, the higher the body's stress level. Therefore, the N/L ratio, as an index for systemic inflammatory status and usually increases after STEMI [30-32]. Pan et al. [33] demonstrated the independent association between increased N/L ratio and short-term mortality in STEMI patients after PCI. The predictive value of the N/L ratio may be based on the following reasons. Stimulated neutrophils release superoxide radicals, proteolytic enzymes, and arachidonic acid metabolites that increase the infarct size and lead to cardiac electrical instability by damaging endothelial cells, activating coagulation cascade, aggregation of leukocytic cells, and plugging the micro-arteries [34]. These actions will participate in the extension of the areas of myocardial infarction, impaired epicardial and microvascular perfusion, no-reflow/slow flow during PCI, decreased LVEF, and post-infarction death [35-37].

The acute phase of STEMI leads to insulin resistance, glucose intolerance, and hyperglycemia. The elevated levels of cytokines, growth hormone, glucagon, and cortisol result in increased hepatic glucose production. Hepatic glycogenolysis is further enhanced by catecholamines that also inhibit glycogenesis and stimulate the release of free fatty acids (FFAs). High concentrations of FFAs will increase myocardial oxygen requirement, reduce myocardial activity and contractility, impair calcium homeostasis and increase the production of free radicals, leading to an increased risk of myocardial damage and arrhythmias [38-41]. Thus, acute hyperglycemia might contribute to a poor outcome. Previous studies reported that higher admission glucose was strongly correlated with larger infarct

size, lower LVEF, and increased mortality risk in patients with and without diabetes [42 43]. Exercise training, dietary modifications, and intervention in the hospital, such as tight glycemic control during early PCI or at least within 24 h after STEMI might reduce the mortality risk in such patients [44 45].

Lower admission HGB was associated with higher in-hospital mortality when analyzed as a continuous variable (OR=0.966, 95%CI: 0.954-0.978). The total ischemic time in patients with AMI is inversely proportional to the drop in HGB concentration [46]. HGB levels and inflammation are closely related; in patients with inflammation, inflammation block occurs, that is, an abundance of hepcidin leads to poor uptake of iron from the gastrointestinal tract, iron sequestration in macrophages, little iron recycling to the erythron for red-cell production, and microcytic anemia, which can cause a lower HGB level. [47].

Because of the important role of platelets in thrombus formation, the present study showed that prior aspirin use could reduce in-hospital mortality of STEMI patients after PCI, as supported by earlier clinical trials [48 49]. Weidmann et al. [49] provided evidence suggesting that pre-existing treatment with aspirin favorably affected the clinical presentation, infarct size, and degree of inflammation of patients with STEMI. Yonetsu et al. [50] reported that aspirin inhibits platelet aggregation and therefore reduces the probability of an occluding clot on top of a ruptured plaque and, conversely, the occurrence of STEMI.

Previous studies indicated that lesion length is associated with long-term adverse events after PCI and is an important risk factor for restenosis and stent thrombosis [51-53]. A longer lesion, with its greater plaque burden, is conceived to provide a major source of smooth muscle cells that will then proliferate to form neointima. Atherosclerotic plaques have often been found to demonstrate an increased expression of isoforms characteristic of activated

smooth muscle cells that are not present in normal vasculature [54]. Still, there are few studies on lesion length and in-hospital mortality, and further studies are still necessary. Preprocedural reperfusion might have a prognostic value [55]. A strong relationship exists between preprocedural TIMI flow grade and infarct size and predischarge LVEF [56]. SBP is a critical factor, and hypotension was associated with a decrease in survival [57].

In our multivariate analysis, the higher Killip Class is not a predictor of in-hospital mortality in STEMI patients. However, in a recent work from Del Buono et al[58], it was proved that a higher Killip Class is an independent risk factor for MACE events and in-hospital mortality in patients with anterior myocardial infarction. This the first study including only patients with STEMI in the anterior location and excluding patients with history of cardiovascular diseases in order to reduce the heterogeneity of the population enrolled. This may be one of the reasons for the inconsistency of the two studies. Nevertheless, Killip classification is a simple and convenient clinical tool that can quickly stratify the risk of ACS patients and is likely to become an independent predictor of long-term follow-up results again.

The nomogram is a simple and intuitive representation of the mathematical model [59]. In addition, to be of clinical usefulness in a routine setting, the nomogram must contain variables assessed in the routine clinical setting, which is the case with the nomogram developed here. It can simplify the statistical prediction model to the numerical probability of disease recurrence or death. The identification and stratification of patients becomes a simple tool with many advantages. The most prominent advantage is that it can predict

individualized risks based on patient and disease characteristics. Secondly, it is easy to use and can help doctors develop individualized treatment plans. However, although the current clinical use of nomograms has increased, there are limited data on patient satisfaction or quality of life after it assists in medical decision-making. In addition, although nomograms are widely used clinically, they are rarely evaluated prospectively to determine whether their use actually improves the prognosis of patients[60 61]. Therefore, it remains to be explored how this risk model can be better applied to the clinic. The results indicate that the nomogram had good discrimination and good prediction accuracy and could achieve good net benefit. Another nomogram based on other variables (left main coronary artery disease, grading of thrombus, TIMI classification, slow flow, use of IABP, use of β-blocker, use of ACEI/ARB, symptom-to-door time, symptom-to-balloon time, syntax score, LVEF, and CK-MB peak) also showed a high AUC for in-hospital mortality of patients with STEMI after PCI [62]. We think there may be three main reasons: different research methods, the hospitals and time nodes that included patients are different and different statistical methods. Nevertheless, we are planning to combine the two parts of patients to get a more accurate risk model of in-hospital mortality.

Some study limitations should be mentioned. 1. This study has limitations that are inherent to retrospective observational studies. Many hospitals and doctors involved, which can lead to some missing information, such as liver enzymes, more information regarding the PCI procedure and other inflammatory index. 2. As the ischemic time is shortened as much as

possible, patients whose symptoms and/or ECG can be diagnosed are directly treated with PCI. Therefore, other potential risk factors in our study, such as LVEF before PCI, could not be included in the analyses. And because some patients died during the PCI, resulting in the lack of postoperative treatment information. However, further prospective studies are still necessary to confirm the performance of the clinical applicability in future investigations and verify the practicality in ICU.

In conclusion, a nomogram to predict in-hospital mortality in patients with STEMI after PCI was developed and validated in Hebei, China. The nomogram showed a satisfactory performance, with a C-index of 0.948. Thus, this nomogram might be a precisely individualized predictive tool for prognosis. Still, additional studies are needed to determine whether it can be applied to other populations before its implementation in clinical practice.

Acknowledgements

We acknowledge the members of the heart team at the participating centers for their efforts in collecting clinical data and ensuring the accuracy and completeness of the data. We thank the study participants and patient advisers for accepting to be part of the study for working tirelessly to make this work a reality.

Funding

None.

Competing Interests

The authors of this work have nothing to disclose.

Ethical standards disclosure

The study was approved by the Ethics Committees of Hebei General Hospital as the lead center and the ethics committee of each participating hospital (No. 202144). The requirement for informed consent was waived by the committee. The study was conducted according to the tenets of the Declaration of Helsinki for Medical Research Involving Human Subjects and Good Clinical Practice.

Authors' contribution

Yudan Wang, Wenjing Wang, Man Gao and Shihang Zheng carried out the studies, participated in collecting data, and drafted the manuscript. Yudan Wang, Yi Dang and Xiaoyong Qi performed the statistical analysis and participated in its design. Shengqi Jia,

Jiaqi Wang and Yingxiao Li helped to draft the manuscript. All authors read and approved the final manuscript.

Data availability statement

No additional data are available.

REFERENCES

1. O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation* 2013;127(4):e362-425. doi: 10.1161/CIR.0b013e3182742cf6.

2. Trost JC, Lange RA. Treatment of acute coronary syndrome: part 2: ST-segment elevation myocardial infarction. *Crit Care Med* 2012;40(6):1939-45. doi: 10.1097/CCM.0b013e31824e18c2.

3. Vogel B, Claessen BE, Arnold SV, et al. ST-segment elevation myocardial infarction. *Nature reviews Disease primers* 2019;5(1):39. doi: 10.1038/s41572-019-0090-3.

4. Authors/Task Force M, Piepoli MF, Hoes AW, et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts): Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). *Eur J Prev Cardiol* 2016;23(11):NP1-NP96. doi: 10.1177/2047487316653709.

5. Jayaraj JC, Davatyan K, Subramanian SS, et al. Epidemiology of Myocardial Infarction. In: Pamkucu B, ed. Myocardial Infarction. London: IntechOpen 2018.

6. Ibanez B, James S, Agewall S, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for

the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *European heart journal* 2018;39(2):119-77. doi: 10.1093/eurheartj/ehx393.

7. O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Journal of the American College of Cardiology* 2013;61(4):e78-e140. doi: 10.1016/j.jacc.2012.11.019.

8. Li J, Li X, Wang Q, et al. ST-segment elevation myocardial infarction in China from 2001 to 2011 (the China PEACE-Retrospective Acute Myocardial Infarction Study): a retrospective analysis of hospital data. *Lancet* 2015;385(9966):441-51. doi: 10.1016/S0140-6736(14)60921-1.

9. Canto JG, Kiefe CI, Rogers WJ, et al. Number of coronary heart disease risk factors and mortality in patients with first myocardial infarction. *JAMA* 2011;306(19):2120-7. doi: 10.1001/jama.2011.1654.

10. Cenko E, Yoon J, Kedev S, et al. Sex Differences in Outcomes After STEMI: Effect Modification by Treatment Strategy and Age. *JAMA internal medicine* 2018;178(5):632-39. doi: 10.1001/jamainternmed.2018.0514.

11. Mehta SR, Wood DA, Storey RF, et al. Complete Revascularization with Multivessel PCI for Myocardial Infarction. *The New England journal of medicine* 2019;381(15):1411-21. doi: 10.1056/NEJMoa1907775.

12. Scholz KH, Maier SKG, Maier LS, et al. Impact of treatment delay on mortality in ST-segment elevation myocardial infarction (STEMI) patients presenting with and without haemodynamic instability: results from the German prospective, multicentre FITT-STEMI trial. *European heart journal* 2018;39(13):1065-74. doi: 10.1093/eurheartj/ehy004.

13. Levine GN, Bates ER, Bittl JA, et al. 2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines: An Update of the 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention, 2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery, 2012 ACC/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the Diagnosis and Management of Patients With Stable Ischemic Heart Disease, 2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction, 2014 AHA/ACC Guideline for the Management of Patients With Non-ST-Elevation Acute Coronary Syndromes, and 2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery. *Circulation* 2016;134(10):e123-55. doi: 10.1161/cir.0000000000000404.

14. Ottani F, Galvani M, Nicolini FA, et al. Elevated cardiac troponin levels predict the risk of adverse outcome in patients with acute coronary syndromes. *American heart journal* 2000;140(6):917-27. doi: 10.1067/mhj.2000.111107.

15. Sun T, Wang L, Zhang Y. Prognostic value of B-type natriuretic peptide in patients with acute

coronary syndromes. *Archives of medical research* 2006;37(4):502-5. doi: 10.1016/j.arcmed.2005.09.007.

16. Jaberg L, Toggweiler S, Puck M, et al. Prognostic value of N-terminal pro-B-type natriuretic peptide in patients with acute coronary syndromes undergoing left main percutaneous coronary intervention. *Circulation journal : official journal of the Japanese Circulation Society* 2011;75(11):2648-53. doi: 10.1253/circj.cj-11-0095.

17. Yu T, Jiao Y, Song J, et al. Hospital mortality in acute coronary syndrome: adjustment of GRACE score by D-dimer enables a more accurate prediction in a prospective cohort study. *BMC cardiovascular disorders* 2019;19(1):252. doi: 10.1186/s12872-019-1239-4.

18. Sianos G, Morel MA, Kappetein AP, et al. The SYNTAX Score: an angiographic tool grading the complexity of coronary artery disease. *EuroIntervention : journal of EuroPCR in collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology* 2005;1(2):219-27.

19. Mehran R, Rao SV, Bhatt DL, et al. Standardized bleeding definitions for cardiovascular clinical trials: a consensus report from the Bleeding Academic Research Consortium. *Circulation* 2011;123(23):2736-47. doi: 10.1161/circulationaha.110.009449.

20. Forman DE, Chen AY, Wiviott SD, et al. Comparison of outcomes in patients aged <75, 75 to 84, and ≥ 85 years with ST-elevation myocardial infarction (from the ACTION Registry-GWTG). *The American journal of cardiology* 2010;106(10):1382-8. doi: 10.1016/j.amjcard.2010.07.008.

21. Rathod KS, Jones DA, Gallagher S, et al. Atypical risk factor profile and excellent long-term outcomes of young patients treated with primary percutaneous coronary intervention for ST-elevation myocardial infarction. *European heart journal Acute cardiovascular care* 2016;5(1):23-32. doi: 10.1177/2048872614567453.

22. Haller PM, Jäger B, Farhan S, et al. Impact of age on short- and long-term mortality of patients with ST-elevation myocardial infarction in the VIENNA STEMI network. *Wiener klinische Wochenschrift* 2018;130(5-6):172-81. doi: 10.1007/s00508-017-1250-7.

23. Lavie CJ, De Schutter A, Milani RV. Healthy obese versus unhealthy lean: the obesity paradox. *Nature reviews Endocrinology* 2015;11(1):55-62. doi: 10.1038/nrendo.2014.165.

24. Payvar S, Kim S, Rao SV, et al. In-hospital outcomes of percutaneous coronary interventions in extremely obese and normal-weight patients: findings from the NCDR (National Cardiovascular Data Registry). *Journal of the American College of Cardiology* 2013;62(8):692-6. doi: 10.1016/j.jacc.2013.05.058.

25. Winzap P, Davies A, Klingenberg R, et al. Diabetes and baseline glucose are associated with inflammation, left ventricular function and short- and long-term outcome in acute coronary syndromes: role of the novel biomarker Cyr 61. *Cardiovascular diabetology* 2019;18(1):142. doi: 10.1186/s12933-019-0946-6.

26. Samanta R, Pouliopoulos J, Kumar S, et al. Influence of BMI on inducible ventricular tachycardia and mortality in patients with myocardial infarction and left ventricular dysfunction: The obesity paradox. *International journal of cardiology* 2018;265:148-54. doi:

10.1016/j.ijcard.2018.03.055.

27. Lavie CJ, Milani RV, Ventura HO. Obesity and cardiovascular disease: risk factor, paradox, and impact of weight loss. *Journal of the American College of Cardiology* 2009;53(21):1925-32. doi: 10.1016/j.jacc.2008.12.068.

28. Samanta R, Narayan A, Kovoor P, et al. Influence of BMI on Short and Long-Term Outcomes in Patients With STEMI and LV Dysfunction. *Heart, lung & circulation* 2020;29(3):361-67. doi: 10.1016/j.hlc.2019.01.017.

29. Fukuoka S, Kurita T, Dohi K, et al. Untangling the obesity paradox in patients with acute myocardial infarction after primary percutaneous coronary intervention (detail analysis by age). *International journal of cardiology* 2019;289:12-18. doi: 10.1016/j.ijcard.2019.01.011.

30. Ayça B, Akın F, Celik O, et al. Neutrophil to Lymphocyte Ratio is Related to Stent Thrombosis and High Mortality in Patients With Acute Myocardial Infarction. *Angiology* 2015;66(6):545-52. doi: 10.1177/0003319714542997.

31. Machado GP, Araujo GN, Carpes CK, et al. Comparison of neutrophil-to-lymphocyte ratio and mean platelet volume in the prediction of adverse events after primary percutaneous coronary intervention in patients with ST-elevation myocardial infarction. *Atherosclerosis* 2018;274:212-17. doi: 10.1016/j.atherosclerosis.2018.05.022.

32. Arbel Y, Shacham Y, Ziv-Baran T, et al. Higher neutrophil/lymphocyte ratio is related to lower ejection fraction and higher long-term all-cause mortality in ST-elevation myocardial infarction patients. *The Canadian journal of cardiology* 2014;30(10):1177-82. doi:

10.1016/j.cjca.2014.05.010.

33. Pan W, Zhao D, Zhang C, et al. Application of neutrophil/lymphocyte ratio in predicting coronary blood flow and mortality in patients with ST-elevation myocardial infarction undergoing percutaneous coronary intervention. *Journal of cardiology* 2015;66(1):9-14. doi: 10.1016/j.jjcc.2014.10.014.

34. Sen N, Afsar B, Ozcan F, et al. The neutrophil to lymphocyte ratio was associated with impaired myocardial perfusion and long term adverse outcome in patients with ST-elevated myocardial infarction undergoing primary coronary intervention. *Atherosclerosis* 2013;228(1):203-10. doi: 10.1016/j.atherosclerosis.2013.02.017.

35. Kaya MG, Akpek M, Lam YY, et al. Prognostic value of neutrophil/lymphocyte ratio in patients with ST-elevated myocardial infarction undergoing primary coronary intervention: a prospective, multicenter study. *International journal of cardiology* 2013;168(2):1154-9. doi: 10.1016/j.ijcard.2012.11.074.

36. Kirtane AJ, Bui A, Murphy SA, et al. Association of peripheral neutrophilia with adverse angiographic outcomes in ST-elevation myocardial infarction. *The American journal of cardiology* 2004;93(5):532-6. doi: 10.1016/j.amjcard.2003.11.013.

37. Sheridan FM, Cole PG, Ramage D. Leukocyte adhesion to the coronary microvasculature during ischemia and reperfusion in an in vivo canine model. *Circulation* 1996;93(10):1784-7. doi: 10.1161/01.cir.93.10.1784.

38. Dandona P, Chaudhuri A, Ghanim H, et al. Insulin as an anti-inflammatory and antiatherogenic

modulator. *Journal of the American College of Cardiology* 2009;53(5 Suppl):S14-20. doi: 10.1016/j.jacc.2008.10.038.

39. Devos P, Chioléro R, Van den Berghe G, et al. Glucose, insulin and myocardial ischaemia. *Current opinion in clinical nutrition and metabolic care* 2006;9(2):131-9. doi: 10.1097/01.mco.0000214572.97933.d1.

40. Young LH, Renfu Y, Russell R, et al. Low-flow ischemia leads to translocation of canine heart GLUT-4 and GLUT-1 glucose transporters to the sarcolemma in vivo. *Circulation* 1997;95(2):415-22. doi: 10.1161/01.cir.95.2.415.

41. Khani S, Tayek JA. Cortisol increases gluconeogenesis in humans: its role in the metabolic syndrome. *Clinical science (London, England : 1979)* 2001;101(6):739-47. doi: 10.1042/cs1010739.

42. Timmer JR, van der Horst IC, Ottervanger JP, et al. Prognostic value of admission glucose in non-diabetic patients with myocardial infarction. *American heart journal* 2004;148(3):399-404. doi: 10.1016/j.ahj.2004.04.007.

43. Planer D, Witzenbichler B, Guagliumi G, et al. Impact of hyperglycemia in patients with ST-segment elevation myocardial infarction undergoing percutaneous coronary intervention: the HORIZONS-AMI trial. *International journal of cardiology* 2013;167(6):2572-9. doi: 10.1016/j.ijcard.2012.06.054.

44. Buchanan TA, Xiang AH, Peters RK, et al. Preservation of pancreatic beta-cell function and prevention of type 2 diabetes by pharmacological treatment of insulin resistance in high-

risk hispanic women. *Diabetes* 2002;51(9):2796-803. doi: 10.2337/diabetes.51.9.2796.

45. Marfella R, Sasso FC, Siniscalchi M, et al. Peri-procedural tight glycemic control during early percutaneous coronary intervention is associated with a lower rate of in-stent restenosis in patients with acute ST-elevation myocardial infarction. *The Journal of clinical endocrinology and metabolism* 2012;97(8):2862-71. doi: 10.1210/jc.2012-1364.

46. Shacham Y, Leshem-Rubinow E, Ben-Assa E, et al. Lower admission hemoglobin levels are associated with longer symptom duration in acute ST-elevation myocardial infarction. *Clinical cardiology* 2014;37(2):73-7. doi: 10.1002/clc.22215.

47. Keel SB, Abkowitz JL. The microcytic red cell and the anemia of inflammation. *The New England journal of medicine* 2009;361(19):1904-6. doi: 10.1056/NEJMcibr0906391.

48. Brener SJ, Mehran R, Lansky AJ, et al. Pretreatment with aspirin in acute coronary syndromes: Lessons from the ACUITY and HORIZONS-AMI trials. *European heart journal Acute cardiovascular care* 2016;5(5):449-54. doi: 10.1177/2048872615624848.

49. Weidmann L, Obeid S, Mach F, et al. Pre-existing treatment with aspirin or statins influences clinical presentation, infarct size and inflammation in patients with de novo acute coronary syndromes. *International journal of cardiology* 2019;275:171-78. doi: 10.1016/j.ijcard.2018.10.050.

50. Yonetsu T, Lee T, Murai T, et al. Association Between Prior Aspirin Use and Morphological Features of Culprit Lesions at First Presentation of Acute Coronary Syndrome Assessed by Optical Coherence Tomography. *Circulation journal : official journal of the Japanese*

Circulation Society 2017;81(4):511-19. doi: 10.1253/circj.CJ-16-0957.

51. Claessen BE, Smits PC, Kereiakes DJ, et al. Impact of lesion length and vessel size on clinical outcomes after percutaneous coronary intervention with everolimus- versus paclitaxel-eluting stents pooled analysis from the SPIRIT (Clinical Evaluation of the XIENCE V Everolimus Eluting Coronary Stent System) and COMPARE (Second-generation everolimus-eluting and paclitaxel-eluting stents in real-life practice) Randomized Trials. *JACC Cardiovascular interventions* 2011;4(11):1209-15. doi: 10.1016/j.jcin.2011.07.016.

52. Kastrati A, Elezi S, Dirschinger J, et al. Influence of lesion length on restenosis after coronary stent placement. *The American journal of cardiology* 1999;83(12):1617-22. doi: 10.1016/s0002-9149(99)00165-4.

53. Choi IJ, Koh YS, Lim S, et al. Impact of the stent length on long-term clinical outcomes following newer-generation drug-eluting stent implantation. *The American journal of cardiology* 2014;113(3):457-64. doi: 10.1016/j.amjcard.2013.10.029.

54. Leclerc G, Isner JM, Kearney M, et al. Evidence implicating nonmuscle myosin in restenosis. Use of in situ hybridization to analyze human vascular lesions obtained by directional atherectomy. *Circulation* 1992;85(2):543-53. doi: 10.1161/01.cir.85.2.543.

55. Brodie BR, Stuckey TD, Hansen C, et al. Benefit of coronary reperfusion before intervention on outcomes after primary angioplasty for acute myocardial infarction. *The American journal of cardiology* 2000;85(1):13-8. doi: 10.1016/s0002-9149(99)00598-6.

56. De Luca G, Ernst N, Zijlstra F, et al. Preprocedural TIMI flow and mortality in patients with acute

myocardial infarction treated by primary angioplasty. *Journal of the American College of Cardiology* 2004;43(8):1363-7. doi: 10.1016/j.jacc.2003.11.042.

57. Lee KL, Woodlief LH, Topol EJ, et al. Predictors of 30-day mortality in the era of reperfusion for acute myocardial infarction. Results from an international trial of 41,021 patients. GUSTO-I Investigators. *Circulation* 1995;91(6):1659-68. doi: 10.1161/01.cir.91.6.1659.

58. Del Buono MG, Montone RA, Rinaldi R, et al. Clinical predictors and prognostic role of high Killip class in patients with a first episode of anterior ST-segment elevation acute myocardial infarction. *Journal of cardiovascular medicine (Hagerstown, Md)* 2021;22(7):530-38. doi: 10.2459/jcm.0000000000001168.

59. Shariat SF, Karakiewicz PI, Godoy G, et al. Use of nomograms for predictions of outcome in patients with advanced bladder cancer. *Ther Adv Urol* 2009;1(1):13-26. doi: 10.1177/1756287209103923.

60. Balachandran VP, Gonen M, Smith JJ, et al. Nomograms in oncology: more than meets the eye. *The Lancet Oncology* 2015;16(4):e173-80. doi: 10.1016/s1470-2045(14)71116-7.

61. Iasonos A, Schrag D, Raj GV, et al. How to build and interpret a nomogram for cancer prognosis. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* 2008;26(8):1364-70. doi: 10.1200/jco.2007.12.9791.

62. Gao N, Qi X, Dang Y, et al. Establishment and validation of a risk model for prediction of in-hospital mortality in patients with acute ST-elevation myocardial infarction after primary PCI. *BMC cardiovascular disorders* 2020;20(1):513. doi: 10.1186/s12872-020-01804-7.

1

Table 1 Clinical characteristics of the patients used to construct the nomogram

Variables	Training set				Testing set			
	All (n=396)	Survival (n=264)	In-hospital mortality (n=132)	*P*	All (n=459)	Survival (n=368)	In-hospital mortality (n=91)	*P*
Age (years) **(mean ±SD)**	63.3±12.7	60.3±12.9	69.3±9.8	<0.001	62.1±12.8	59.8±12.4	70.2±11.3	<0.001
Male **(n (%))**	284 (71.7)	202 (76.5)	82 (62.1)	0.004	352 (76.7)	294 (79.9)	58 (63.7)	0.001
BMI **(kg/m^2)**	25.8 (24.6, 26.1)	26.0 (25.3, 26.5)	24.9 (24.4, 25.5)	<0.001	25.4 (23.4, 27.3)	25.5±3.0	25.3 (23.4, 27.5)	0.047
Cardiac arrest **(n (%))**	10 (2.5)	6 (2.3)	4 (3.0)	0.91	8 (1.7)	6 (1.6)	2 (2.2)	0.711
Cardiogenic shock before admission **(n (%))**	34 (8.6)	6 (2.3)	28 (21.2)	<0.001	30 (6.5)	15 (4.1)	15 (16.5)	<0.001
Use of temporary pacemaker before admission **(n (%))**	3 (0.7)	0	3 (2.3)	0.065	4 (0.9)	2 (0.5)	2 (2.2)	0.128
Ventilator support before admission **(n (%))**	6 (1.5)	1 (0.4)	5 (3.8)	0.029	7 (1.5)	2 (0.5)	5 (5.5)	0.001
CPR before admission	12 (3.0)	5 (1.9)	7 (5.3)	0.12	5 (1.1)	0	5 (5.5)	<0.001

(n (%))								
SBP on admission **(median (IQR))**	128 (110, 146)	133 (114, 149)	118 (100, 140)	<0.001	125 (110, 140)	129±25	121 (107, 135)	0.009
DBP on admission **(median (IQR))**	79 (69, 89)	82 (72, 92)	73 (62, 82)	<0.001	77±16	80±15	69±16	<0.001
Heart rate on admission **(median (IQR))**	77 (65, 90)	76 (64, 89)	80 (66, 96)	0.025	79±18	78±17	82±24	0.095
Fatal arrhythmia before admission **(n (%))**	21 (5.3)	15 (5.7)	6 (4.5)	0.812	20 (4.4)	12 (3.3)	8 (8.8)	0.021
Total ischemic time **(min (median (IQR)))**	217 (124, 367)	154 (95, 250)	360 (194, 420)	<0.001	211 (130, 341)	194 (125, 307)	300 (222, 480)	<0.001
Killip class 3-4 **(n (%))**	132 (33.3)	95 (36.0)	37 (28.0)	0.142	119 (25.9)	66 (17.9)	53 (58.2)	<0.001
Past medical history								
Hypertension ***(n (%))***	211 (53.3)	137 (51.9)	74 (56.1)	0.499	73 (15.9)	38 (10.3)	35 (38.5)	<0.001
DM ***(n (%))***	96 (24.2)	49 (18.6)	47 (35.6)	<0.001	104 (22.7)	84 (22.8)	20 (22.0)	0.863
Hyperlipidemia ***(n (%))***	39 (9.8)	12 (4.5)	27 (20.5)	<0.001	41 (8.9)	23 (6.3)	18 (19.8)	<0.001

Previous PCI ***(n (%))***	18 (4.5)	8 (3.0)	10 (7.6)	0.073	23 (5.0)	17 (4.6)	6 (6.6)	0.44
Previous CABG ***(n (%))***	1 (0.2)	0	1 (0.8)	0.157	1 (0.2)	0	1 (1.1)	0.05
CAD ***(n (%))***	45 (11.4)	17 (6.4)	28 (21.2)	<0.001	40 (8.7)	20 (5.4)	20 (22.0)	<0.001
AF ***(n (%))***	11 (2.8)	1 (0.4)	10 (7.6)	<0.001	13 (2.8)	3 (0.8)	10 (11.0)	<0.001
HF ***(n (%))***	4 (1.0)	3 (1.1)	1 (0.8)	0.722	25 (5.4)	18 (4.9)	7 (7.7)	0.292
Renal insufficiency ***(n (%))***	62 (15.7)	1 (0.4)	61 (46.2)	<0.001	13 (2.8)	1 (0.3)	12 (13.2)	<0.001
History of cerebrovascular disease ***(n (%))***	64 (16.2)	40 (15.2)	24 (18.2)	0.53	72 (15.7)	60 (16.3)	12 (13.2)	0.464
Peripheral vascular disease ***(n (%))***	9 (2.3)	5 (1.9)	4 (3.0)	0.721	5 (1.1)	3 (0.8)	2 (2.2)	0.255
History of bleeding ***(n (%))***	2 (0.5)	1 (0.4)	1 (0.8)	>0.999	7 (1.5)	6 (1.6)	1 (1.1)	0.711
Family history of CAD ***(n (%))***	44 (11.1)	28 (10.6)	16 (11.1)	0.875	68 (14.8)	62 (16.8)	6 (6.6)	0.014
Angiographic characteristics								
Number of stents ***(median (IQR))***	1 (1, 1)	1 (1, 1)	1 (0, 1)	<0.001	1 (1, 1)	1 (1, 1)	1 (1, 1)	0.137
Long lesions ***(n (%))***	245 (61.9)	178 (67.4)	67 (50.8)	0.002	194 (42.3)	131 (35.6)	63 (69.2)	<0.001
Thrombus aspiration ***(n (%))***	123 (31.1)	92 (34.8)	31 (23.5)	0.029	221 (48.1)	205 (55.7)	16 (17.6)	<0.001

Residual stenosis ***(n (%))***	12 (3.0)	2 (0.8)	10 (7.6)	0.001	10 (2.2)	4 (1.1)	6 (6.6)	0.001
Use temporary pacemaker ***(n (%))***	22 (5.6)	4 (1.5)	18 (13.6)	<0.001	9 (2.0)	2 (0.5)	7 (7.7)	<0.001
IABP ***(n (%))***	19 (4.8)	4 (1.5)	15 (11.4)	<0.001	15 (3.3)	4 (1.1)	11 (12.1)	<0.001
Respirator support ***(n (%))***	20 (5.1)	1 (0.4)	19 (14.4)	<0.001	13 (2.8)	2 (0.5)	11 (12.1)	<0.001
Pericardial aspiration ***(n (%))***	3 (0.8)	0	3 (2.3)	0.065	3 (0.7)	0	3 (3.3)	<0.001
No flow ***(n (%))***	98 (24.7)	48 (18.2)	50 (37.9)	<0.001	84 (18.3)	55 (14.9)	29 (31.9)	<0.001
Coronary perforation ***(n (%))***	5 (1.3)	0	5 (3.8)	0.001	2 (0.4)	1 (0.3)	1 (1.1)	0.283
Dissection ***(n (%))***	3 (0.8)	0	3 (2.3)	0.065	5 (1.1)	0	5 (5.5)	<0.001
Pericardial tamponade ***(n (%))***	9 (2.3)	0	9 (6.8)	<0.001	2 (0.4)	0	2 (2.2)	0.004
Acute HF ***(n (%))***	55 (13.9)	22 (8.3)	33 (25.0)	<0.001	52 (11.3)	30 (7.7)	22 (24.2)	<0.001
Bleeding ***(n (%))***	2 (0.5)	0	2 (1.5)	0.21	6 (1.3)	3 (0.8)	3 (3.3)	0.062
Cardiac arrest ***(n (%))***	24 (6.1)	1 (0.4)	23 (17.4)	<0.001	14 (3.1)	6 (1.6)	8 (8.8)	<0.001
Recurrent MI ***(n (%))***	16 (4.0)	1 (0.4)	15 (11.4)	<0.001	7 (1.5)	2 (0.5)	5 (5.5)	0.001
Stent thrombosis ***(n (%))***	8 (2.0)	6 (2.3)	2 (1.5)	0.9	14 (3.1)	13 (3.5)	1 (1.1)	0.227
Type B2-C ***(n (%))***	309 (78.0)	213 (80.7)	96 (72.7)	0.094	277 (60.3)	230 (62.5)	47 (51.6)	0.058

TIMI flow grade 0-1 before PCI ***(n (%))***	311 (78.5)	197 (74.6)	114 (86.4)	0.011	339 (73.9)	274 (74.5)	65 (71.4)	0.556
Use of GP IIb/IIIa inhibitors ***(n (%))***	92 (23.2)	54 (20.5)	38 (28.8)	0.064	107 (23.3)	80 (21.7)	27 (29.7)	0.109
multivessel CAD ***(n (%))***	316 (79.8)	207 (78.4)	109 (82.6)	0.33	373 (81.3)	296 (80.4)	77 (84.6)	0.36
LAD ***(n (%))***	149 (37.6)	85 (32.2)	64 (48.5)	0.002	209 (45.5)	177 (48.1)	32 (35.2)	0.027
LCX ***(n (%))***	59 (14.9)	39 (14.8)	20 (15.2)	0.921	64 (13.9)	46 (12.5)	18 (19.8)	0.072
RCA ***(n (%))***	101 (25.5)	101 (38.3)	40 (30.3)	0.119	144 (31.4)	120 (32.6)	24 (26.4)	0.251
Biochemical markers								
Hyperkalemia ***(n (%))***	36 (9.1)	3 (1.1)	33 (25.0)	<0.001	30 (6.5)	11 (3.0)	19 (20.9)	<0.001
Hyponatremia ***(n (%))***	29 (7.3)	12 (4.5)	19 (14.4)	0.001	37 (8.1)	31 (8.4)	6 (6.6)	0.566
Anemia ***(n (%))***	26 (6.6)	12 (4.5)	14 (10.6)	0.022	40 (8.7)	21 (5.7)	19 (20.9)	<0.001
Creatinine ***(median (IQR))***	86.2 (76.9, 90.6)	86.2 (70.6, 86.2)	90.6 (77.0, 95.5)	0.111	92.5 (64.5, 93.0)	85.1±32.1	91.1±53.5	0.17
N/L ratio ***(median (IQR))***	5.47 (2.82, 10.00)	4.70 (2.68, 7.87)	8.54 (3.19, 11.46)	<0.001	6.15 (3.48, 9.52)	5.08 (3.65, 9.46)	9.1 (3.81, 12.51)	<0.001
HCT, % ***(median (IQR))***	41.0 (37.1, 44.0)	41.8 (38.0, 44.6)	38.5 (36.8, 41.3)	<0.001	40.4 (37.4, 44.5)	40.0±5.2	38.0 (32.7, 43.3)	<0.001

HGB, g/L ***(median (IQR))***	137.0 (126.0, 269.0)	142.0 (129.0, 155.0)	129.0 (119.0, 137.3)	<0.001	137.2±19.8	138.5±19.1	131.9±21.5	0.004
PLT, ×10^9/L ***(median (IQR))***	221.0 (183.5, 269.0)	224.0 (186.0, 269.0)	227.0 (194.8, 246.3)	0.554	225.0 (184.0, 260.0)	229.0 (187.0, 264.0)	215.0 (175.0, 254.0)	0.151
Random blood glucose on admission, mmol/L ***(median (IQR))***	6.84 (5.47, 9.92)	5.95 (5.02, 7.44)	9.81 (7.96, 11.04)	<0.001	6.73 (5.27, 10.10)	6.12 (5.10, 8.10)	10.96 (8.40, 11.78)	<0.001
EF after PCI ***(median (IQR))***	51.0 (43.0, 58.0)	54.0 (47.8, 59.0)	43.0 (38.0, 48.5)	<0.001	55 (46, 60)	56 (51, 61)	45 (37, 53)	<0.001
Medication list on admission ***(n (%))***								
Aspirin	379 (95.7)	262 (99.2)	117 (88.6)	<0.001	404 (88.0)	332 (90.2)	72 (79.1)	0.004
Ticagrelor/clopidogrel	393 (99.2)	262 (99.2)	131 (99.2)	>0.999	418 (91.1)	332 (90.2)	86 (94.5)	0.199
Ticagrelor	223 (56.3)	162 (61.4)	61 (46.2)		218 (47.5)	183 (49.7)	35 (38.5)	
clopidogrel	170 (42.9)	100 (37.9)	70 (53.0)		200 (43.6)	149 (40.5)	51 (56.0)	
ACEI/ARB	133 (33.6)	100 (37.9)	33 (25.0)	0.014	25 (5.4)	18 (4.9)	7 (7.7)	0.292
β-Blocker	92 (23.2)	66 (25.0)	26 (19.7)	0.239	37 (8.1)	29 (7.9)	8 (8.9)	0.753

Statin	188 (47.5)	130 (49.2)	58 (43.9)	0.319	206 (44.9)	181 (49.2)	25 (27.5)	<0.001
mean duration of hospital stay **(median (IQR))**	8.51±5.11	9 (9,11)	1 (1,4)	<0.001	8.32±4.70	9 (8,11)	2 (1,5)	<0.001

BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; DM: diabetes mellitus; PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft; CAD: coronary atherosclerotic heart disease; AF: atrial fibrillation; HF: heart failure; IABP: intra-aortic balloon pump; MI: myocardial infarction; LAD: left anterior descending branch; LCX: left circumflex artery; RCA: right coronary artery; N/L ratio: neutrophils/lymphocytes ratio; HCT: hematocrit; HGB: hemoglobin; PLT: platelets; EF: ejection fraction; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker.

Table 2 Variables selected as predictors for the nomogram according to the multivariable logistic analysis

	Univariate analysis			Multivariate analysis		
Variables	**OR**	**95% CI**	**P**	**OR**	**95% CI**	**P**
Age	1.07	1.05-1.09	<0.001	1.07	1.05-1.09	0.049
BMI	0.79	0.70-0.87	<0.001	0.55	0.31-0.87	0.019
SBP on admission	0.98	0.97-0.99	<0.001	0.92	0.86-0.97	0.009
HGB	0.97	0.95-0.98	<0.001	0.85	0.73-0.97	0.017
Random blood glucose on admission	1.38	1.27-1.51	<0.001	1.53	1.13-2.21	0.011
EF after PCI	0.91	0.88-0.93	<0.001	0.89	0.80-0.97	0.015
Use aspirin before admission	0.06	0.01-0.22	<0.001	0.01	0.009-0.04	0.001
N/L ratio	1.08	1.04-1.12	<0.001	1.34	1.12-1.69	0.004
Long lesions	0.50	0.32-0.76	0.001	2.00	1.31-3.08	<0.001
TIMI flow grade 0-1 before PCI	2.15	1.24-3.90	<0.001	2.15	1.24-3.90	0.008

OR: odds ratio; CI: confidence interval; BMI: body mass index; SBP: systolic blood pressure; HGB: hemoglobin; EF: ejection fraction; PCI: percutaneous coronary intervention; N/L ratio: neutrophils/lymphocytes ratio; TIMI: thrombolysis in myocardial infarction

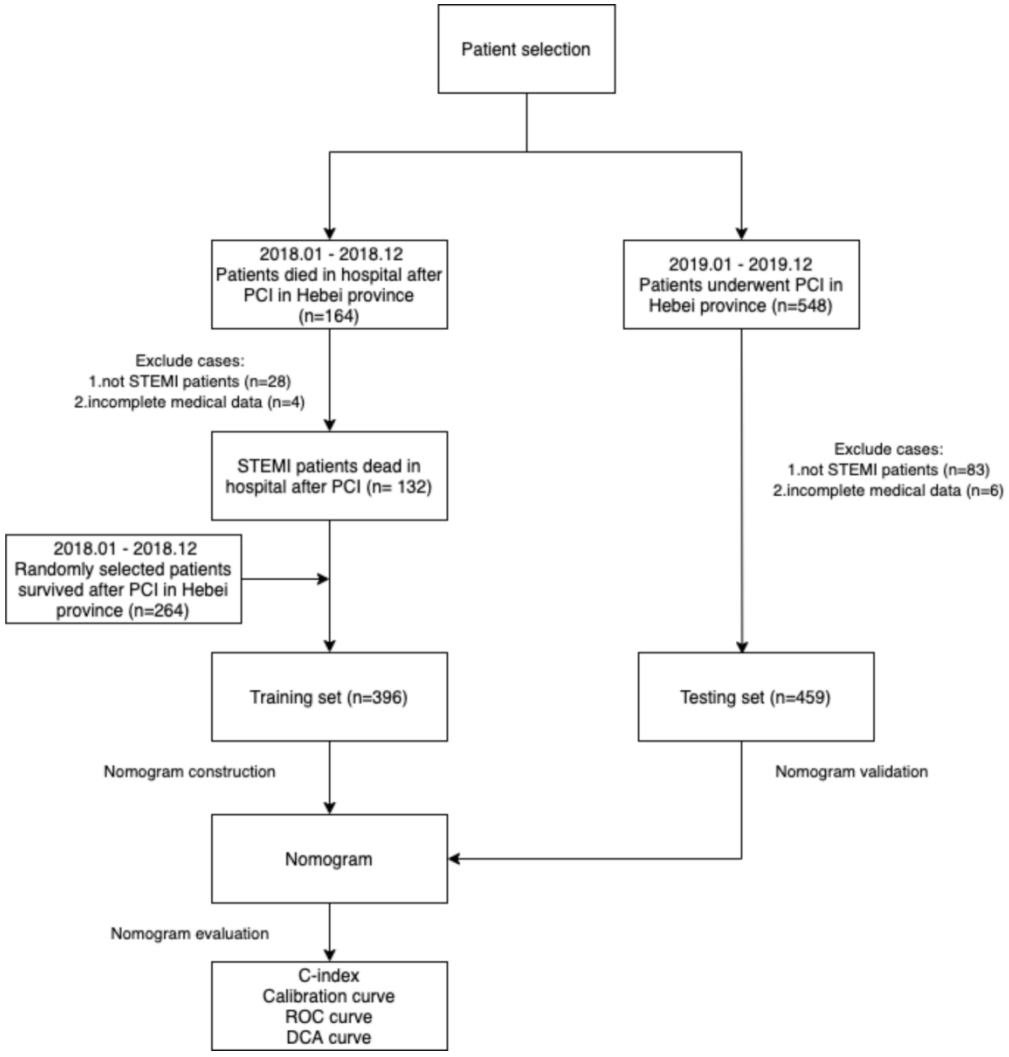

Figure 1. Flowchart illustrating the process of patient selection.

170x177mm (300 x 300 DPI)

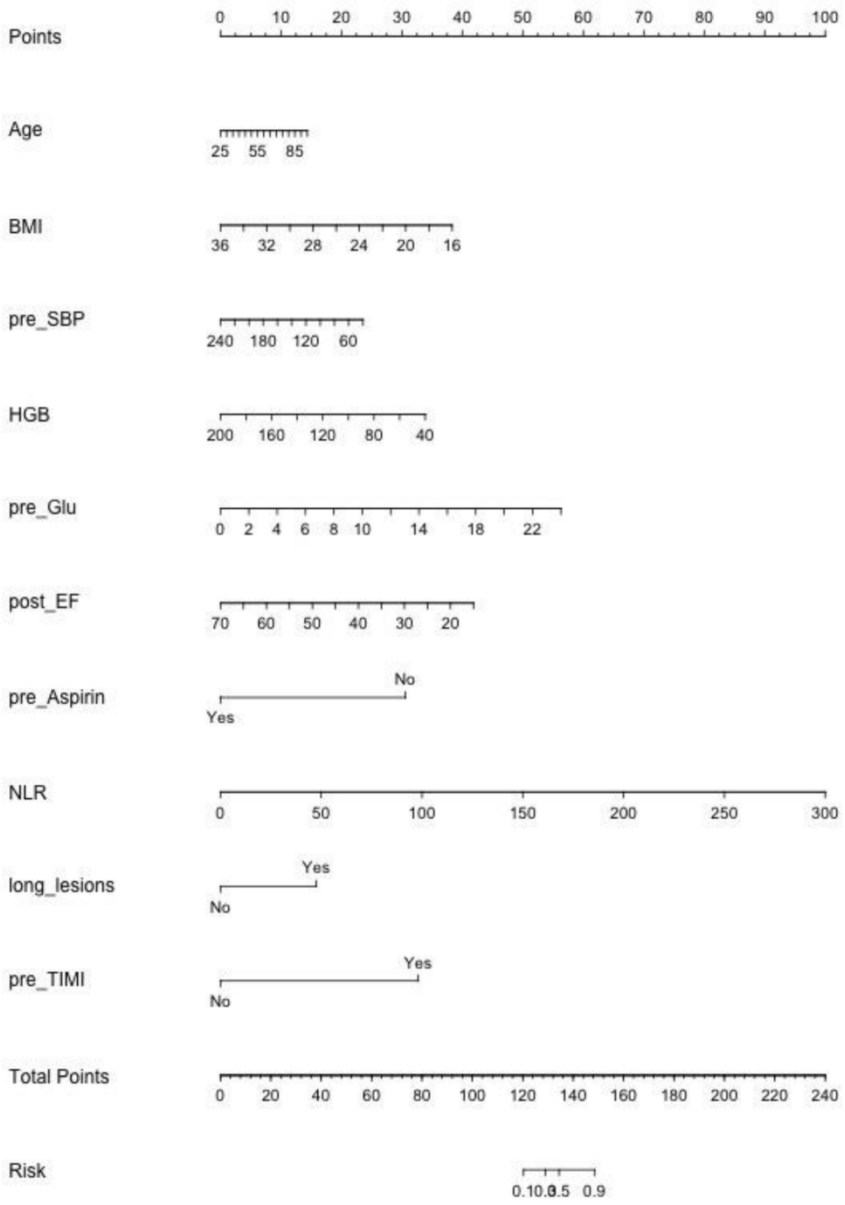

Figure 2. The nomogram for the prediction of in-hospital mortality in patients with acute ST-elevation myocardial infarction after primary PCI. BMI: body mass index; SBP: systolic blood pressure; HGB: hemoglobin; EF: ejection fraction; N/L ratio: neutrophils/lymphocytes ratio.

170x242mm (300 x 300 DPI)

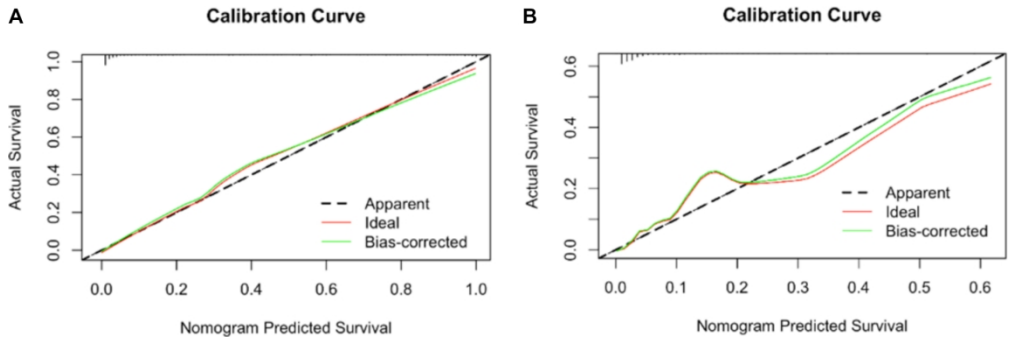

Figure 3. The calibration curves of the nomogram for the training set (A) and the testing set (B).

170x56mm (300 x 300 DPI)

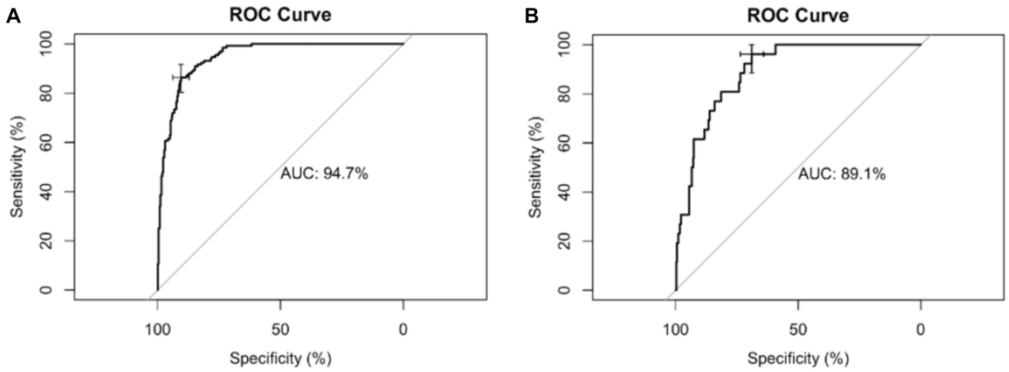

Figure 4. The received operating characteristics (ROC) curves of the nomogram for the training set (A) and the testing set (B).

170x61mm (300 x 300 DPI)

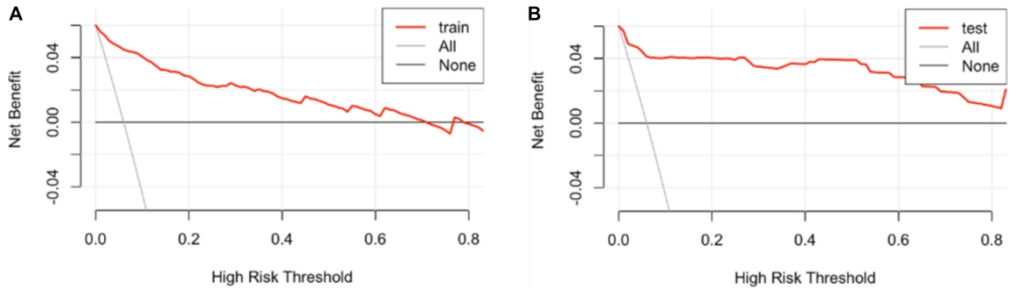

Figure 5. The decision curve analysis (DCA) for the risk model for the training set (A) and the testing set (B).

170x48mm (300 x 300 DPI)

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*
Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any pre-specified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	9
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15
Generalisability	21	Discuss the generalisability (external validity) of the study results	15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

TRIPOD Checklist: Prediction Model Development and Validation

Section/Topic	Item		Checklist Item	Page
Title and abstract				
Title	1	D;V	Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted.	1
Abstract	2	D;V	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	2
Introduction				
Background and objectives	3a	D;V	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	4
	3b	D;V	Specify the objectives, including whether the study describes the development or validation of the model or both.	5
Methods				
Source of data	4a	D;V	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	6
	4b	D;V	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	6
Participants	5a	D;V	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.	6
	5b	D;V	Describe eligibility criteria for participants.	6
	5c	D;V	Give details of treatments received, if relevant.	6
Outcome	6a	D;V	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	7
	6b	D;V	Report any actions to blind assessment of the outcome to be predicted.	NA
Predictors	7a	D;V	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured.	7
	7b	D;V	Report any actions to blind assessment of predictors for the outcome and other predictors.	NA
Sample size	8	D;V	Explain how the study size was arrived at.	NA
Missing data	9	D;V	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	NA
Statistical analysis methods	10a	D	Describe how predictors were handled in the analyses.	9
	10b	D	Specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	9
	10c	V	For validation, describe how the predictions were calculated.	9
	10d	D;V	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	9
	10e	V	Describe any model updating (e.g., recalibration) arising from the validation, if done.	9
Risk groups	11	D;V	Provide details on how risk groups were created, if done.	9
Development vs. validation	12	V	For validation, identify any differences from the development data in setting, eligibility criteria, outcome, and predictors.	9
Results				
Participants	13a	D;V	Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	10
	13b	D;V	Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome.	10
	13c	V	For validation, show a comparison with the development data of the distribution of important variables (demographics, predictors and outcome).	11
Model development	14a	D	Specify the number of participants and outcome events in each analysis.	11
	14b	D	If done, report the unadjusted association between each candidate predictor and outcome.	NA
Model specification	15a	D	Present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	12
	15b	D	Explain how to the use the prediction model.	12
Model performance	16	D;V	Report performance measures (with CIs) for the prediction model.	11
Model-updating	17	V	If done, report the results from any model updating (i.e., model specification, model performance).	NA
Discussion				
Limitations	18	D;V	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	17
Interpretation	19a	V	For validation, discuss the results with reference to performance in the development data, and any other validation data.	13
	19b	D;V	Give an overall interpretation of the results, considering objectives, limitations, results from similar studies, and other relevant evidence.	13
Implications	20	D;V	Discuss the potential clinical use of the model and implications for future research.	16
Other information				
Supplementary information	21	D;V	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	NA
Funding	22	D;V	Give the source of funding and the role of the funders for the present study.	19

*Items relevant only to the development of a prediction model are denoted by D, items relating solely to a validation of a prediction model are denoted by V, and items relating to both are denoted D;V. We recommend using the TRIPOD Checklist in conjunction with the TRIPOD Explanation and Elaboration document.

BMJ Open

Development of a nomogram for the prediction of in-hospital mortality in patients with acute ST-elevation myocardial infarction after primary percutaneous coronary intervention: a multicentre, retrospective, observational study in Hebei Province, China

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2021-056101.R2
Article Type:	Original research
Date Submitted by the Author:	18-Jan-2022
Complete List of Authors:	Wang, Yudan; Hebei Medical University, School of Graduate; Hebei General Hospital, Department of Cardiology Center Wang, Wenjing; Hebei General Hospital, Department of Cardiology Center Jia, Shengqi; Hebei Medical University, School of Graduate Gao, Man; Hebei Medical University, School of Graduate Zheng, Shihang; Hebei North University, School of Graduate Wang, Jiaqi; Hebei North University, School of Graduate Dang, Yi; Hebei General Hospital, Department of Cardiology Center Li, Yingxiao; Hebei General Hospital, Department of Cardiology Center Qi, Xiaoyong; Hebei Medical University, School of Graduate; Hebei General Hospital, Department of Cardiology Center
Primary Subject Heading:	Cardiovascular medicine
Secondary Subject Heading:	Cardiovascular medicine
Keywords:	Coronary intervention < CARDIOLOGY, Coronary heart disease < CARDIOLOGY, Myocardial infarction < CARDIOLOGY

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Development of a nomogram for the prediction of in-hospital mortality in patients with acute ST-elevation myocardial infarction after primary percutaneous coronary intervention: a multicentre, retrospective, observational study in Hebei Province, China

Running title: Nomogram for STEMI in-hospital mortality after PCI

Yudan Wang[1,2], Wenjing Wang[2], Shengqi Jia[1], Man Gao[1], Shihang Zheng[3], Jiaqi Wang[3], Yi Dang[2], Yingxiao Li[2], Xiaoyong Qi[1,2*]

[1]School of Graduate, Hebei Medical University, Shijiazhuang, Hebei Province, People's Republic of China

[2]Department of Cardiology Center, Hebei General Hospital, Shijiazhuang, Hebei Province, People's Republic of China

[3]School of Graduate, Hebei North University, Zhangjiakou, Hebei Province, People's Republic of China

[*]**Corresponding Author**

Xiaoyong Qi

School of Graduate, Hebei Medical University, Shijiazhuang, Hebei Province, People's Republic of China

Department of Cardiology Center, Hebei General Hospital, No. 348, Heping West Road, Shijiazhuang 050051, Hebei Province, People's Republic of China

E-mail address: hbghqxy@126.com

1

Word count: 2996

ABSTRACT

Objectives: To establish a clinical prognostic nomogram for predicting in-hospital mortality after primary percutaneous coronary intervention (PCI) among patients with ST-elevation myocardial infarction (STEMI).

Design: Retrospective, multicenter, observational study.

Setting: Thirty-nine hospitals in Hebei Province.

Participants: Patients with STEMI who underwent PCI from January 2018 to December 2019.

Interventions: A multivariable logistic regression model was used to identify the factors associated with in-hospital mortality, and a nomogram was established using these factors. The performance of the nomogram was evaluated by the discrimination, calibration, and clinical usefulness.

Primary and secondary outcome measures: The outcome was the factors associated with in-hospital mortality.

Results: This study included 855 patients, among whom 223 died in hospital. Age, Body Mass Index (BMI), systolic pressure on admission, hemoglobin, random blood glucose on admission, ejection fraction after PCI, use aspirin before admission, long lesions, thrombolysis in myocardial infarction (TIMI) flow grade, and neutrophils/lymphocytes ratio (N/L ratio) were independently associated with in-hospital mortality (all $P<0.05$). In the training set, the nomogram showed a C-index of 0.947, goodness-of-fit of 0.683, and area under the receiver operating characteristic curve (AUC) of 0.947 (95%CI=0.927-0.967). In the testing set, the C-index was 0.891, goodness-of-fit was 0.462, and AUC was 0.891 (95%CI=0.844-0.939). The results indicate that the nomogram had good

discrimination and good prediction accuracy and could achieve a good net benefit.

Conclusions: A nomogram to predict in-hospital mortality in patients with STEMI after PCI was developed and validated in Hebei, China and showed a satisfactory performance. Prospective studies will be necessary to confirm the performance and clinical applicability and practicality of the nomogram.

Keywords: nomogram; ST-elevated myocardial infarction; percutaneous coronary intervention; in-hospital mortality

Strengths and limitations of this study

- This is a multi-center study, included 39 tertiary centers and 855 patients, including 223 (26.1%) patients who died in the hospital.
- The data were obtained retrospectively, and some patients died during the PCI, which may have led to some missing information.
- Prospective studies will be necessary to confirm the performance and clinical applicability and practicality of the nomogram.

INTRODUCTION

ST-segment elevation myocardial infarction (STEMI), a type of coronary artery disease (CAD), is a common clinical emergency and critical illness [1]. STEMI is most often caused by plaque rupture of an atherosclerotic lesion in the affected (culprit) coronary artery followed by total occlusion of the vessel lumen with a thrombus [2 3]. Common risk factors for STEMI are tobacco abuse, dyslipidemias, hypertension, diabetes mellitus, and a family history of CAD [4]. In recent years, with well-established diagnosis and treatment guidelines, continuous standardization of the treatment of STEMI, increasing evidence of determinants of patient prognosis and development of emerging technologies, there has been a considerable reduction in STEMI mortality; still, mortality seems to have plateaued [3].

Primary percutaneous coronary intervention (PCI) has become the preferred reperfusion strategy in patients with STEMI according to the current clinical guidelines for STEMI in the United States and Europe [5 6]. Nevertheless, even if such patients receive timely PCI and/or appropriate antiplatelet drugs, the prognosis is still unsatisfying, and a substantial number of STEMI patients still die in-hospital after PCI (about 6%) [3 7 8]. Therefore, there is still room for improving the short-term outcomes of these patients on top of a timely PCI.

Various studies examined the risk factors of short and long-term mortality of STEMI patients after PCI [9-11]. Guidelines encourage the use of clinical scores such as the thrombolysis in myocardial infarction (TIMI) or The Global Registry of Acute Coronary Events (GRACE) for STEMI to assess early and long-term risk [5 6 12]. Several biomarkers have been reported to confer independent prognostic information after STEMI, including

Cardiac Troponin (cTn), Brain Natriuretic Peptide (BNP), amino-terminal pro-Brain Natriuretic Peptide (NT-proBNP), and D-dimer [13-16]. Unfortunately, these studies often exclude patients with advanced age, liver or kidney dysfunction, and other comorbidities and complications. The generalizability of those studies is limited, and it is difficult to summarize and reflect the real-world treatment situation comprehensively.

Therefore, the objective of this study was to develop a clinical nomogram for predicting in-hospital mortality of patients with STEMI after PCI. The results could provide clinical guidance and improve the outcome of STEMI patients.

PATIENTS AND METHODS

Study design and patients

This multicenter, retrospective, observational study included STEMI patients treated with PCI at 39 PCI hospitals in Hebei Province from January 2018 to December 2019. The cohort was divided into a training set and a time-independent validation set. The training set refers to the use of modeled data to verify the predictive effect of the model, while test set is to use another group of patients' data (namely external data) to verify the prediction accuracy of the model. The training set patients enrolled from January 2018 to December 2018 and the testing set patients enrolled from January 2019 to December 2019.

All patients met the diagnostic criteria of acute STEMI based on their symptoms and/or ECG, myocardial damage markers and other test results and underwent primary PCI according to the 2017 ESC guidelines for the management of STEMI [5], namely with persistent chest discomfort or other symptoms suggestive of ischemia and ST-segment elevation in at least two contiguous leads. Patients with non-ST segment myocardial infarction (NSTEMI) or unstable angina or STEMI patients who did not undergo PCI were excluded. Patients who were re-admitted to the hospital for revascularization of non-culprit vessel were also excluded. The treatment strategy after PCI of surviving patients is determined by the doctor in charge in accordance with relevant guidelines.

The study was approved by the Ethics Committees of Hebei General Hospital as the lead center and the ethics committee of each participating hospital. The requirement for informed consent was waived by the committee. The study was conducted according to the tenets of the Declaration of Helsinki for Medical Research Involving Human Subjects and Good Clinical Practice.

Patient and Public Involvement

Patients or the public were not involved in the design or reporting or dissemination plans of our research as this study is a retrospective, observational study.

Definitions

Long lesions was defined as the stenosis that has as ≥ 50% reduction and more than 20mm in luminal diameter[17].

Residual stenosis was defined as > 30% residual stenosis of the target lesion after PCI.

Bleeding was defined as a composite of major bleeding according to Bleeding Academic Research Consortium Definition for Bleeding (BARC) type 3 or 5, but was not related to coronary-artery bypass grafting (CABG)[18].

Data collection

Demographics (age, sex, and BMI), medical history (hypertension, diabetes mellitus, atrial fibrillation (AF), hyperlipidemia and family history of coronary artery disease (CAD), stroke, renal failure, and peripheral artery disease), angiographic characteristics and information of cardiac procedures (disease condition, TIMI flow grade, number of stents, use of intra-aortic balloon pump (IABP), use of temporary pacemaker, use of ventilator, and whether there was no-reflow, coronary perforation, and cardiac arrest), medications on admission (antiplatelet agents, β-blockers, nitrate, angiotensin-converting enzyme inhibitors (ACEI), angiotensin receptor blockers (ARB), and statin), biochemical markers (N/L ratio), hematocrit (HCT), hemoglobin (HGB), platelets (PLT), and random

blood glucose on admission), and left ventricular ejection fraction (LVEF) after PCI were extracted from the medical charts. All treatments were according to the current guidelines.

Nomogram construction

Demographics, medical history, vital signs before and after PCI, and auxiliary examinations were evaluated using univariable logistic regression. Variables with $P<0.05$ in the univariable logistic analyses were included for multivariable logistic analysis and nomogram construction. Receiver operator characteristic (ROC) curve analysis was used to quantify the prediction performance of the nomogram. A calibration curve was used to evaluate the calibration of the nomogram, and its goodness of fit was assessed using the Hosmer-Lemeshow test. Finally, the clinical usefulness of the nomogram was accessed using a decision curve analysis (DCA).

Statistical analysis

Statistical analyses were performed using *R version 4.0.3* (R Foundation for Statistical Computing) with *RStudio* (version 1.3.959; RStudio, Auckland, New Zealand). R packages used in this study were *rms*, *reader*, *tableone*, *pROC*, *ResourceSelection*, and *rmda*. The predictive accuracy of the nomogram was measured using the C-statistic (Bootstrap method, 1000 times). Calibration was evaluated using the Hosmer-Lemeshow statistic. Categorical variables were presented as frequencies with percentages, normally distributed continuous variables as means ± SD, and other data as medians with interquartile ranges (IQRs). Categorical variables were compared using the chi-square

test or Fisher's test if the expected cell count was <5. Student's t-test was used to compare normally distributed continuous variables. Otherwise, the Mann-Whitney U-test was used. The significance level was set at 0.05, and two-sided tests were used.

RESULTS

Characteristics of the patients

The whole study population consisted of 855 patients diagnosed with STEMI and who underwent PCI, including 396 in the training set (132 (33.3%) dead patients and, 264 (66.7%) survivors) and 459 (91 (19.8%) dead patients, 368 (80.2%) survivors) in the test set (Figure 1). The clinical characteristics, including demographic, medical history, angiographic characteristics, and information of cardiac procedures, medications, and biochemical markers, are summarized in *supplementary file*. The Clinical characteristics selected as predictors for the nomogram are summarized in Table 1. The patients who died in the hospital were older (69.8±10.2 vs. 60.2±12.6 years, P<0.01), more likely to be women (32.7% vs. 21.5%, P<0.01), and more had complications like hypertension, AF, and hyperlipidemia. The hospital stay was 8.51±5.11 days in the training set and 8.32±4.70 days in the test set.

Nomogram construction

According to the multivariable logistic analysis, 10 variables meet the threshold of P<0.05. Age (OR=1.069, 95% CI=1.048-1.092, P=0.049), BMI (OR=0.55, 95% CI=0.31=0.87, P=0.019), SBP on admission (OR=0.92, 95% CI=0.86-0.97, P=0.009), HGB (OR=0.85, 95% CI=0.73-0.97, P=0.017), random blood glucose on admission (OR=1.53, 95% CI=1.13-2.21, P=0.011), EF after PCI (OR=0.89, 95% CI=0.80-0.97, P=0.015), aspirin (OR=0.001, 95% CI=0.009-0.04, P=0.001), N/L ratio (OR=1.34, 95% CI=1.12-1.69, P=0.004), long lesions (OR=2.00, 95% CI=1.310-3.084, P<0.001), and TIMI flow grade (OR=2.15, 95% CI=1.242-3.900, P=0.008) were independently

associated with in-hospital mortality after PCI of STEMI (Table 2). The nomogram is shown in Figure 2. The formula for calculating the total point of the nomogram is showed below:

Score=15.5628+0.0320×age-0.2991×BMI-0.0184×SBP-0.0331×HGB+0.3663×random blood glucose on admission-0.1188×LVEF after PCI-4.7705×aspirin+0.0521×N/L ratio-2.4688×long leisions+5.1018×TIMI flow grade.

Evaluation of the nomogram

In the training set, the C-index was 0.947, indicating that the prediction model was valuable in clinical practice (Figure 3a). The value of goodness-of-fit was 0.683, indicating a good prediction accuracy. The ROC curve is shown in Figure 4a (AUC=0.947, 95% CI: 0.927-0.967). Figure 5a shows the DCA curve for the training set, indicating that the nomogram had a high overall net benefit in predicting in-hospital mortality after PCI treatment.

In the testing set, the C-index was 0.891. Figure 3b shows the calibration curve, and the value of goodness-of-fit was 0.462. The ROC curve is shown in Figure 4b (AUC=0.891, 95% CI: 0.844-0.939). The DCA curve is shown in Figure 5b. The results of the testing set indicate that the nomogram had good discrimination and good prediction accuracy which could achieve a good net benefit.

DISCUSSION

In this study, a relatively accurate clinical nomogram was constructed, which demonstrated adequate discrimination and calibration power to provide an individualized estimation for the in-hospital mortality in STEMI patients after PCI. For the construction of the nomogram, 10 significant predictors were screened by multivariable logistic analysis.

In our study, age was an independent risk factor of STEMI patients, in accordance with other analyses of STEMI patients and underlining the high-risk profile of elderly patients, as they usually present with more risk factors and comorbidities than younger patients[19] [20], such as the higher prevalence of renal insufficiency, lower LVEF. High mortality in the older patients might also result from end-organ dysfunction, competing risks might also offset the benefits from reperfusion, such that successful outcomes are more dependent on overall health issues. Therefore, for older patients, some authors have also questioned the benefit of reperfusion therapy[21].

For previous view, obesity increases insulin resistance, worsens plasma lipid profiles, and increases arterial blood pressure, which has adverse effects on patients with CAD through the indirect effects of other risk factors (such as hypertension, impaired glucose tolerance, and hyperinsulinemia) [22]. Therefore, obese patients demonstrate greater adverse left ventricle (LV) remodeling and more impaired LV deformation after STEMI compared with those similar infarct characteristics but normal BMI [23 24]. Interestingly, some studies have shown the so-called “obesity paradox”, whereby obesity is related to better clinical outcomes [22 25-27], consistent with the present study. Fukuoka *et al.* [28] reported that this phenomenon is only observed in elderly patients, not in younger patients, so the influence

of BMI on risk factors for death might vary with age. Nevertheless, obesity is currently recognized as a risk factor for the long-term prognosis of patients with CAD, and it is worth recommending maintaining BMI at a normal level [28].

Acute stress has been shown to regulate the immune response of lymphocytes and reduce the number of peripheral blood lymphocytes. The smaller the value, the higher the body's stress level. Therefore, the N/L ratio, an index for systemic inflammatory status, usually increases after STEMI [29-31]. Pan *et al.* [32] demonstrated the independent association between increased N/L ratio and short-term mortality in STEMI patients after PCI. The predictive value of the N/L ratio may be based on the following reasons. Stimulated neutrophils release superoxide radicals, proteolytic enzymes, and arachidonic acid metabolites that increase the infarct size and lead to cardiac electrical instability by damaging endothelial cells, activating coagulation cascade, aggregation of leukocytic cells, and plugging the micro-arteries [33]. These actions will participate in the extension of the areas of myocardial infarction, impaired epicardial and microvascular perfusion, no-reflow/slow flow during PCI, decreased LVEF, and post-infarction death [34-36].

The acute phase of STEMI leads to insulin resistance, glucose intolerance, and hyperglycemia. The elevated levels of cytokines, growth hormone, glucagon, and cortisol result in increased hepatic glucose production. Hepatic glycogenolysis is further enhanced by catecholamines that also inhibit glycogenesis and stimulate the release of free fatty acids (FFAs). High concentrations of FFAs will increase myocardial oxygen requirement, reduce myocardial activity and contractility, impair calcium homeostasis and increase the production of free radicals, leading to an increased risk of myocardial damage and arrhythmias [37-40]. Thus, acute hyperglycemia might contribute to a poor

outcome. Previous studies reported that higher admission glucose was strongly correlated with larger infarct size, lower LVEF, and increased mortality risk in patients with and without diabetes [41 42]. Exercise training, dietary modifications, and intervention in the hospital, such as tight glycemic control during early PCI or at least within 24 h after STEMI might reduce the mortality risk in such patients [43 44].

Lower admission HGB was associated with higher in-hospital mortality when analyzed as a continuous variable (OR=0.966, 95%CI: 0.954-0.978). In the study from Shacham Y *et al.* [45], they revealed the longer total ischemic time, namely an ongoing inflammatory process, the lower admission HGB levels. HGB levels and inflammation are closely related. In patients with STEMI, inflammation block occurs, that is, an abundance of hepcidin leads to poor uptake of iron from the gastrointestinal tract, iron sequestration in macrophages, little iron recycling to the erythron for red-cell production, and microcytic anemia, which can cause a lower HGB level [46].

Because of the important role of platelets in thrombus formation, the present study showed that prior aspirin use could reduce in-hospital mortality of STEMI patients after PCI, as supported by earlier clinical trials [47 48]. Weidmann *et al.* [48] provided evidence suggesting that pre-existing treatment with aspirin favorably affected the clinical presentation, infarct size, and degree of inflammation of patients with STEMI. Yonetsu *et al.* [49] reported that aspirin inhibits platelet aggregation and therefore reduces the probability of an occluding clot on top of a ruptured plaque and, conversely, the occurrence of STEMI.

Previous studies indicated that lesion length is associated with long-term adverse events after PCI and is an important risk factor for restenosis and stent thrombosis [50-52]. A longer

lesion, with its greater plaque burden, is conceived to provide a major source of smooth muscle cells that will then proliferate to form neointima. Atherosclerotic plaques have often been found to demonstrate an increased expression of isoforms characteristic of activated smooth muscle cells that are not present in normal vasculature [53]. Still, there are few studies on lesion length and in-hospital mortality, and further studies are still necessary. Preprocedural reperfusion might have a prognostic value [54]. A strong relationship exists between preprocedural TIMI flow grade and infarct size and predischarge LVEF [55]. SBP is a critical factor, and hypotension was associated with a decrease in survival [56].

In our multivariate analysis, the higher Killip Class is not a predictor of in-hospital mortality in STEMI patients. However, in a recent work from Del Buono *et al.*[57], it was proved that a higher Killip Class is an independent risk factor for MACE events and in-hospital mortality in patients with anterior myocardial infarction. This is the first study including only patients with STEMI in the anterior location and excluding patients with history of cardiovascular diseases in order to reduce the heterogeneity of the population enrolled. This may be one of the reasons for the inconsistency of the two studies. Nevertheless, Killip classification is a simple and convenient clinical tool that can quickly stratify the risk of ACS patients and is likely to become an independent predictor of long-term follow-up results again.

The nomogram is a simple and intuitive representation of the mathematical model [58]. In addition, to be of clinical usefulness in a routine setting, the nomogram must contain variables assessed in the routine clinical setting, which is the case with the nomogram

developed here. It can simplify the statistical prediction model to the numerical probability of disease recurrence or death. The identification and stratification of patients becomes a simple tool with many advantages. The most prominent advantage is that it can predict individualized risks based on patient and disease characteristics. Secondly, it is easy to use and can help doctors develop individualized treatment plans. However, although the current clinical use of nomograms has increased, there are limited data on patient satisfaction or quality of life after it assists in medical decision-making. In addition, although nomograms are widely used clinically, they are rarely evaluated prospectively to determine whether their use actually improves the prognosis of patients[59] [60]. Therefore, it remains to be explored how this risk model can be better applied to the clinic. The results indicate that the nomogram had good discrimination, well prediction accuracy and could achieve satisfactory net benefit. Another nomogram based on other variables (left main coronary artery disease, grading of thrombus, TIMI classification, slow flow, use of IABP, use of β-blocker, use of ACEI/ARB, symptom-to-door time, symptom-to-balloon time, syntax score, LVEF, and CK-MB peak) also showed a high AUC for in-hospital mortality of patients with STEMI after PCI [61]. Three main reasons fame justify the different predictors we found in our study: different research methods, the hospitals and time nodes that included patients are different and different statistical methods. Nevertheless, we are planning to combine the two parts of patients to get a more accurate risk model of in-hospital mortality.

Some study limitations should be mentioned: 1. This study has limitations that are inherent to retrospective observational studies. Many hospitals and doctors involved, which can lead to some missing information, such as liver enzymes, more information regarding the PCI procedure and other inflammatory index; 2. As the ischemic time is shortened as much as possible, patients whose symptoms and/or ECG can be diagnosed are directly treated with PCI. Therefore, other potential risk factors in our study, such as LVEF before PCI, could not be included in the analyses. And some patients died during the PCI, resulting in the lack of postoperative treatment information. Further prospective studies are still necessary to confirm the performance of the clinical applicability in future investigations and verify the practicality in ICU.

In conclusion, a nomogram to predict in-hospital mortality in patients with STEMI after PCI was developed and validated in Hebei, China. The nomogram showed a satisfactory performance, with a C-index of 0.948. Thus, this nomogram might be a precisely individualized predictive tool for prognosis. However, additional studies are needed to confirm the performance and clinical applicability and practicality of the nomogram.

Acknowledgements

We acknowledge the members of the heart team at the participating centers for their efforts in collecting clinical data and ensuring the accuracy and completeness of the data. We thank the study participants and patient advisers for accepting to be part of the study for working tirelessly to make this work a reality.

Funding

None.

Competing interests

The authors of this work have nothing to disclose.

Ethical standards disclosure

The study was approved by the Ethics Committees of Hebei General Hospital as the lead center and the ethics committee of each participating hospital (No. 202144). The requirement for informed consent was waived by the committee. The study was conducted according to the tenets of the Declaration of Helsinki for Medical Research Involving Human Subjects and Good Clinical Practice.

Authors' contribution

Yudan Wang, Wenjing Wang, Man Gao and Shihang Zheng carried out the studies, participated in collecting data, and drafted the manuscript. Yudan Wang, Yi Dang and Xiaoyong Qi performed the statistical analysis and participated in its design. Shengqi Jia,

Jiaqi Wang and Yingxiao Li helped to draft the manuscript. All authors read and approved the final manuscript.

Data availability statement

No additional data are available.

REFERENCES

1. O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation* 2013;127(4):e362-425. doi: 10.1161/CIR.0b013e3182742cf6.
2. Trost JC, Lange RA. Treatment of acute coronary syndrome: part 2: ST-segment elevation myocardial infarction. *Crit Care Med* 2012;40(6):1939-45. doi: 10.1097/CCM.0b013e31824e18c2.
3. Vogel B, Claessen BE, Arnold SV, et al. ST-segment elevation myocardial infarction. *Nature reviews Disease primers* 2019;5(1):39. doi: 10.1038/s41572-019-0090-3.
4. Authors/Task Force M, Piepoli MF, Hoes AW, et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts): Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). *Eur J Prev Cardiol* 2016;23(11):NP1-NP96. doi: 10.1177/2047487316653709.
5. Ibanez B, James S, Agewall S, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *European heart journal* 2018;39(2):119-77. doi: 10.1093/eurheartj/ehx393.
6. O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Journal of the American College of Cardiology* 2013;61(4):e78-e140. doi: 10.1016/j.jacc.2012.11.019.
7. Li J, Li X, Wang Q, et al. ST-segment elevation myocardial infarction in China from 2001 to 2011 (the China PEACE-Retrospective Acute Myocardial Infarction Study): a retrospective analysis of hospital data. *Lancet* 2015;385(9966):441-51. doi: 10.1016/S0140-6736(14)60921-1.
8. Canto JG, Kiefe CI, Rogers WJ, et al. Number of coronary heart disease risk factors and mortality in patients with first myocardial infarction. *JAMA* 2011;306(19):2120-7. doi: 10.1001/jama.2011.1654.
9. Cenko E, Yoon J, Kedev S, et al. Sex Differences in Outcomes After STEMI: Effect Modification by Treatment Strategy and Age. *JAMA internal medicine* 2018;178(5):632-39. doi: 10.1001/jamainternmed.2018.0514.
10. Mehta SR, Wood DA, Storey RF, et al. Complete Revascularization with Multivessel PCI for Myocardial Infarction. *The New England journal of medicine* 2019;381(15):1411-21. doi: 10.1056/NEJMoa1907775.

11. Scholz KH, Maier SKG, Maier LS, et al. Impact of treatment delay on mortality in ST-segment elevation myocardial infarction (STEMI) patients presenting with and without haemodynamic instability: results from the German prospective, multicentre FITT-STEMI trial. *European heart journal* 2018;39(13):1065-74. doi: 10.1093/eurheartj/ehy004.
12. Levine GN, Bates ER, Bittl JA, et al. 2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines: An Update of the 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention, 2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery, 2012 ACC/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the Diagnosis and Management of Patients With Stable Ischemic Heart Disease, 2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction, 2014 AHA/ACC Guideline for the Management of Patients With Non-ST-Elevation Acute Coronary Syndromes, and 2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery. *Circulation* 2016;134(10):e123-55. doi: 10.1161/cir.0000000000000404.
13. Ottani F, Galvani M, Nicolini FA, et al. Elevated cardiac troponin levels predict the risk of adverse outcome in patients with acute coronary syndromes. *American heart journal* 2000;140(6):917-27. doi: 10.1067/mhj.2000.111107.
14. Sun T, Wang L, Zhang Y. Prognostic value of B-type natriuretic peptide in patients with acute coronary syndromes. *Archives of medical research* 2006;37(4):502-5. doi: 10.1016/j.arcmed.2005.09.007.
15. Jaberg L, Toggweiler S, Puck M, et al. Prognostic value of N-terminal pro-B-type natriuretic peptide in patients with acute coronary syndromes undergoing left main percutaneous coronary intervention. *Circulation journal : official journal of the Japanese Circulation Society* 2011;75(11):2648-53. doi: 10.1253/circj.cj-11-0095.
16. Yu T, Jiao Y, Song J, et al. Hospital mortality in acute coronary syndrome: adjustment of GRACE score by D-dimer enables a more accurate prediction in a prospective cohort study. *BMC cardiovascular disorders* 2019;19(1):252. doi: 10.1186/s12872-019-1239-4.
17. Sianos G, Morel MA, Kappetein AP, et al. The SYNTAX Score: an angiographic tool grading the complexity of coronary artery disease. *EuroIntervention : journal of EuroPCR in collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology* 2005;1(2):219-27.
18. Mehran R, Rao SV, Bhatt DL, et al. Standardized bleeding definitions for cardiovascular clinical trials: a consensus report from the Bleeding Academic Research Consortium. *Circulation* 2011;123(23):2736-47. doi: 10.1161/circulationaha.110.009449.
19. Forman DE, Chen AY, Wiviott SD, et al. Comparison of outcomes in patients aged <75,

75 to 84, and ⩾ 85 years with ST-elevation myocardial infarction (from the ACTION Registry-GWTG). *The American journal of cardiology* 2010;106(10):1382-8. doi: 10.1016/j.amjcard.2010.07.008.

20. Rathod KS, Jones DA, Gallagher S, et al. Atypical risk factor profile and excellent long-term outcomes of young patients treated with primary percutaneous coronary intervention for ST-elevation myocardial infarction. *European heart journal Acute cardiovascular care* 2016;5(1):23-32. doi: 10.1177/2048872614567453.
21. Haller PM, Jäger B, Farhan S, et al. Impact of age on short- and long-term mortality of patients with ST-elevation myocardial infarction in the VIENNA STEMI network. *Wiener klinische Wochenschrift* 2018;130(5-6):172-81. doi: 10.1007/s00508-017-1250-7.
22. Lavie CJ, De Schutter A, Milani RV. Healthy obese versus unhealthy lean: the obesity paradox. *Nature reviews Endocrinology* 2015;11(1):55-62. doi: 10.1038/nrendo.2014.165.
23. Payvar S, Kim S, Rao SV, et al. In-hospital outcomes of percutaneous coronary interventions in extremely obese and normal-weight patients: findings from the NCDR (National Cardiovascular Data Registry). *Journal of the American College of Cardiology* 2013;62(8):692-6. doi: 10.1016/j.jacc.2013.05.058.
24. Winzap P, Davies A, Klingenberg R, et al. Diabetes and baseline glucose are associated with inflammation, left ventricular function and short- and long-term outcome in acute coronary syndromes: role of the novel biomarker Cyr 61. *Cardiovascular diabetology* 2019;18(1):142. doi: 10.1186/s12933-019-0946-6.
25. Samanta R, Pouliopoulos J, Kumar S, et al. Influence of BMI on inducible ventricular tachycardia and mortality in patients with myocardial infarction and left ventricular dysfunction: The obesity paradox. *International journal of cardiology* 2018;265:148-54. doi: 10.1016/j.ijcard.2018.03.055.
26. Lavie CJ, Milani RV, Ventura HO. Obesity and cardiovascular disease: risk factor, paradox, and impact of weight loss. *Journal of the American College of Cardiology* 2009;53(21):1925-32. doi: 10.1016/j.jacc.2008.12.068.
27. Samanta R, Narayan A, Kovoor P, et al. Influence of BMI on Short and Long-Term Outcomes in Patients With STEMI and LV Dysfunction. *Heart, lung & circulation* 2020;29(3):361-67. doi: 10.1016/j.hlc.2019.01.017.
28. Fukuoka S, Kurita T, Dohi K, et al. Untangling the obesity paradox in patients with acute myocardial infarction after primary percutaneous coronary intervention (detail analysis by age). *International journal of cardiology* 2019;289:12-18. doi: 10.1016/j.ijcard.2019.01.011.
29. Ayça B, Akın F, Celik O, et al. Neutrophil to Lymphocyte Ratio is Related to Stent Thrombosis and High Mortality in Patients With Acute Myocardial Infarction. *Angiology* 2015;66(6):545-52. doi: 10.1177/0003319714542997.
30. Machado GP, Araujo GN, Carpes CK, et al. Comparison of neutrophil-to-lymphocyte

ratio and mean platelet volume in the prediction of adverse events after primary percutaneous coronary intervention in patients with ST-elevation myocardial infarction. *Atherosclerosis* 2018;274:212-17. doi: 10.1016/j.atherosclerosis.2018.05.022.

31. Arbel Y, Shacham Y, Ziv-Baran T, et al. Higher neutrophil/lymphocyte ratio is related to lower ejection fraction and higher long-term all-cause mortality in ST-elevation myocardial infarction patients. *The Canadian journal of cardiology* 2014;30(10):1177-82. doi: 10.1016/j.cjca.2014.05.010.
32. Pan W, Zhao D, Zhang C, et al. Application of neutrophil/lymphocyte ratio in predicting coronary blood flow and mortality in patients with ST-elevation myocardial infarction undergoing percutaneous coronary intervention. *Journal of cardiology* 2015;66(1):9-14. doi: 10.1016/j.jjcc.2014.10.014.
33. Sen N, Afsar B, Ozcan F, et al. The neutrophil to lymphocyte ratio was associated with impaired myocardial perfusion and long term adverse outcome in patients with ST-elevated myocardial infarction undergoing primary coronary intervention. *Atherosclerosis* 2013;228(1):203-10. doi: 10.1016/j.atherosclerosis.2013.02.017.
34. Kaya MG, Akpek M, Lam YY, et al. Prognostic value of neutrophil/lymphocyte ratio in patients with ST-elevated myocardial infarction undergoing primary coronary intervention: a prospective, multicenter study. *International journal of cardiology* 2013;168(2):1154-9. doi: 10.1016/j.ijcard.2012.11.074.
35. Kirtane AJ, Bui A, Murphy SA, et al. Association of peripheral neutrophilia with adverse angiographic outcomes in ST-elevation myocardial infarction. *The American journal of cardiology* 2004;93(5):532-6. doi: 10.1016/j.amjcard.2003.11.013.
36. Sheridan FM, Cole PG, Ramage D. Leukocyte adhesion to the coronary microvasculature during ischemia and reperfusion in an in vivo canine model. *Circulation* 1996;93(10):1784-7. doi: 10.1161/01.cir.93.10.1784.
37. Dandona P, Chaudhuri A, Ghanim H, et al. Insulin as an anti-inflammatory and antiatherogenic modulator. *Journal of the American College of Cardiology* 2009;53(5 Suppl):S14-20. doi: 10.1016/j.jacc.2008.10.038.
38. Devos P, Chioléro R, Van den Berghe G, et al. Glucose, insulin and myocardial ischaemia. *Current opinion in clinical nutrition and metabolic care* 2006;9(2):131-9. doi: 10.1097/01.mco.0000214572.97933.d1.
39. Young LH, Renfu Y, Russell R, et al. Low-flow ischemia leads to translocation of canine heart GLUT-4 and GLUT-1 glucose transporters to the sarcolemma in vivo. *Circulation* 1997;95(2):415-22. doi: 10.1161/01.cir.95.2.415.
40. Khani S, Tayek JA. Cortisol increases gluconeogenesis in humans: its role in the metabolic syndrome. *Clinical science (London, England : 1979)* 2001;101(6):739-47. doi: 10.1042/cs1010739.
41. Timmer JR, van der Horst IC, Ottervanger JP, et al. Prognostic value of admission glucose in non-diabetic patients with myocardial infarction. *American heart journal* 2004;148(3):399-404. doi: 10.1016/j.ahj.2004.04.007.

42. Planer D, Witzenbichler B, Guagliumi G, et al. Impact of hyperglycemia in patients with ST-segment elevation myocardial infarction undergoing percutaneous coronary intervention: the HORIZONS-AMI trial. *International journal of cardiology* 2013;167(6):2572-9. doi: 10.1016/j.ijcard.2012.06.054.

43. Buchanan TA, Xiang AH, Peters RK, et al. Preservation of pancreatic beta-cell function and prevention of type 2 diabetes by pharmacological treatment of insulin resistance in high-risk hispanic women. *Diabetes* 2002;51(9):2796-803. doi: 10.2337/diabetes.51.9.2796.

44. Marfella R, Sasso FC, Siniscalchi M, et al. Peri-procedural tight glycemic control during early percutaneous coronary intervention is associated with a lower rate of in-stent restenosis in patients with acute ST-elevation myocardial infarction. *The Journal of clinical endocrinology and metabolism* 2012;97(8):2862-71. doi: 10.1210/jc.2012-1364.

45. Shacham Y, Leshem-Rubinow E, Ben-Assa E, et al. Lower admission hemoglobin levels are associated with longer symptom duration in acute ST-elevation myocardial infarction. *Clinical cardiology* 2014;37(2):73-7. doi: 10.1002/clc.22215.

46. Keel SB, Abkowitz JL. The microcytic red cell and the anemia of inflammation. *The New England journal of medicine* 2009;361(19):1904-6. doi: 10.1056/NEJMcibr0906391.

47. Brener SJ, Mehran R, Lansky AJ, et al. Pretreatment with aspirin in acute coronary syndromes: Lessons from the ACUITY and HORIZONS-AMI trials. *European heart journal Acute cardiovascular care* 2016;5(5):449-54. doi: 10.1177/2048872615624848.

48. Weidmann L, Obeid S, Mach F, et al. Pre-existing treatment with aspirin or statins influences clinical presentation, infarct size and inflammation in patients with de novo acute coronary syndromes. *International journal of cardiology* 2019;275:171-78. doi: 10.1016/j.ijcard.2018.10.050.

49. Yonetsu T, Lee T, Murai T, et al. Association Between Prior Aspirin Use and Morphological Features of Culprit Lesions at First Presentation of Acute Coronary Syndrome Assessed by Optical Coherence Tomography. *Circulation journal : official journal of the Japanese Circulation Society* 2017;81(4):511-19. doi: 10.1253/circj.CJ-16-0957.

50. Claessen BE, Smits PC, Kereiakes DJ, et al. Impact of lesion length and vessel size on clinical outcomes after percutaneous coronary intervention with everolimus- versus paclitaxel-eluting stents pooled analysis from the SPIRIT (Clinical Evaluation of the XIENCE V Everolimus Eluting Coronary Stent System) and COMPARE (Second-generation everolimus-eluting and paclitaxel-eluting stents in real-life practice) Randomized Trials. *JACC Cardiovascular interventions* 2011;4(11):1209-15. doi: 10.1016/j.jcin.2011.07.016.

51. Kastrati A, Elezi S, Dirschinger J, et al. Influence of lesion length on restenosis after coronary stent placement. *The American journal of cardiology* 1999;83(12):1617-22. doi: 10.1016/s0002-9149(99)00165-4.

52. Choi IJ, Koh YS, Lim S, et al. Impact of the stent length on long-term clinical outcomes following newer-generation drug-eluting stent implantation. *The American journal of cardiology* 2014;113(3):457-64. doi: 10.1016/j.amjcard.2013.10.029.
53. Leclerc G, Isner JM, Kearney M, et al. Evidence implicating nonmuscle myosin in restenosis. Use of in situ hybridization to analyze human vascular lesions obtained by directional atherectomy. *Circulation* 1992;85(2):543-53. doi: 10.1161/01.cir.85.2.543.
54. Brodie BR, Stuckey TD, Hansen C, et al. Benefit of coronary reperfusion before intervention on outcomes after primary angioplasty for acute myocardial infarction. *The American journal of cardiology* 2000;85(1):13-8. doi: 10.1016/s0002-9149(99)00598-6.
55. De Luca G, Ernst N, Zijlstra F, et al. Preprocedural TIMI flow and mortality in patients with acute myocardial infarction treated by primary angioplasty. *Journal of the American College of Cardiology* 2004;43(8):1363-7. doi: 10.1016/j.jacc.2003.11.042.
56. Lee KL, Woodlief LH, Topol EJ, et al. Predictors of 30-day mortality in the era of reperfusion for acute myocardial infarction. Results from an international trial of 41,021 patients. GUSTO-I Investigators. *Circulation* 1995;91(6):1659-68. doi: 10.1161/01.cir.91.6.1659.
57. Del Buono MG, Montone RA, Rinaldi R, et al. Clinical predictors and prognostic role of high Killip class in patients with a first episode of anterior ST-segment elevation acute myocardial infarction. *Journal of cardiovascular medicine (Hagerstown, Md)* 2021;22(7):530-38. doi: 10.2459/jcm.0000000000001168.
58. Shariat SF, Karakiewicz PI, Godoy G, et al. Use of nomograms for predictions of outcome in patients with advanced bladder cancer. *Ther Adv Urol* 2009;1(1):13-26. doi: 10.1177/1756287209103923.
59. Balachandran VP, Gonen M, Smith JJ, et al. Nomograms in oncology: more than meets the eye. *The Lancet Oncology* 2015;16(4):e173-80. doi: 10.1016/s1470-2045(14)71116-7.
60. Iasonos A, Schrag D, Raj GV, et al. How to build and interpret a nomogram for cancer prognosis. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* 2008;26(8):1364-70. doi: 10.1200/jco.2007.12.9791.
61. Gao N, Qi X, Dang Y, et al. Establishment and validation of a risk model for prediction of in-hospital mortality in patients with acute ST-elevation myocardial infarction after primary PCI. *BMC cardiovascular disorders* 2020;20(1):513. doi: 10.1186/s12872-020-01804-7.

Table 1 Clinical characteristics of the patients selected as predictors for the nomogram

Variables	Training set				Testing set			
	All (n=396)	**Survival (n=264)**	**In-hospital mortality (n=132)**	***P***	**All (n=459)**	**Survival (n=368)**	**In-hospital mortality (n=91)**	***P***
Age (years) **(mean ±SD)**	63.3±12.7	60.3±12.9	69.3±9.8	<0.001	62.1±12.8	59.8±12.4	70.2±11.3	<0.001
BMI **(kg/m²)**	25.8 (24.6, 26.1)	26.0 (25.3, 26.5)	24.9 (24.4, 25.5)	<0.001	25.4 (23.4, 27.3)	25.5±3.0	25.3 (23.4, 27.5)	0.047
SBP on admission **(median (IQR))**	128 (110, 146)	133 (114, 149)	118 (100, 140)	<0.001	125 (110, 140)	129±25	121 (107, 135)	0.009
Long lesions ***(n (%))***	245 (61.9)	178 (67.4)	67 (50.8)	0.002	194 (42.3)	131 (35.6)	63 (69.2)	<0.001
TIMI flow grade 0-1 before PCI ***(n (%))***	311 (78.5)	197 (74.6)	114 (86.4)	0.011	339 (73.9)	274 (74.5)	65 (71.4)	0.556
N/L ratio ***(median (IQR))***	5.47 (2.82, 10.00)	4.70 (2.68, 7.87)	8.54 (3.19, 11.46)	<0.001	6.15 (3.48, 9.52)	5.08 (3.65, 9.46)	9.1 (3.81, 12.51)	<0.001
HGB, g/L ***(median (IQR))***	137.0 (126.0, 269.0)	142.0 (129.0, 155.0)	129.0 (119.0, 137.3)	<0.001	137.2±19.8	138.5±19.1	131.9±21.5	0.004
Random blood glucose on admission, mmol/L ***(median (IQR))***	6.84 (5.47, 9.92)	5.95 (5.02, 7.44)	9.81 (7.96, 11.04)	<0.001	6.73 (5.27, 10.10)	6.12 (5.10, 8.10)	10.96 (8.40, 11.78)	<0.001
EF after PCI ***(median (IQR))***	51.0 (43.0, 58.0)	54.0 (47.8, 59.0)	43.0 (38.0, 48.5)	<0.001	55 (46, 60)	56 (51, 61)	45 (37, 53)	<0.001
Use Aspirin on admission**(n(%))**	379 (95.7)	262 (99.2)	117 (88.6)	<0.001	404 (88.0)	332 (90.2)	72 (79.1)	0.004

BMI: body mass index; SBP: systolic blood pressure; N/L ratio: neutrophils/lymphocytes ratio; HGB: hemoglobin; EF: ejection fraction

Table 2 Variables selected as predictors for the nomogram according to the multivariable logistic analysis

Variables	Univariate analysis			Multivariate analysis		
	OR	95% CI	P	OR	95% CI	P
Age	1.07	1.05-1.09	<0.001	1.07	1.05-1.09	0.049
BMI	0.79	0.70-0.87	<0.001	0.55	0.31-0.87	0.019
SBP on admission	0.98	0.97-0.99	<0.001	0.92	0.86-0.97	0.009
HGB	0.97	0.95-0.98	<0.001	0.85	0.73-0.97	0.017
Random blood glucose on admission	1.38	1.27-1.51	<0.001	1.53	1.13-2.21	0.011
EF after PCI	0.91	0.88-0.93	<0.001	0.89	0.80-0.97	0.015
Use aspirin before admission	0.06	0.01-0.22	<0.001	0.01	0.009-0.04	0.001
N/L ratio	1.08	1.04-1.12	<0.001	1.34	1.12-1.69	0.004
Long lesions	0.50	0.32-0.76	0.001	2.00	1.31-3.08	<0.001
TIMI flow grade 0-1 before PCI	2.15	1.24-3.90	<0.001	2.15	1.24-3.90	0.008

OR: odds ratio; CI: confidence interval; BMI: body mass index; SBP: systolic blood pressure; HGB: hemoglobin; EF: ejection fraction; PCI: percutaneous coronary intervention; N/L ratio: neutrophils/lymphocytes ratio; TIMI: thrombolysis in myocardial infarction

Figure legends

Figure 1. Flowchart illustrating the process of patient selection.

Figure 2. The nomogram for the prediction of in-hospital mortality in patients with acute ST-elevation myocardial infarction after primary PCI. BMI: body mass index; SBP: systolic blood pressure; HGB: hemoglobin; EF: ejection fraction; N/L ratio: neutrophils/lymphocytes ratio.

Figure 3. The calibration curves of the nomogram for the training set (A) and the testing set (B).

Figure 4. The received operating characteristics (ROC) curves of the nomogram for the training set (A) and the testing set (B).

Figure 5. The decision curve analysis (DCA) for the risk model for the training set (A) and the testing set (B).

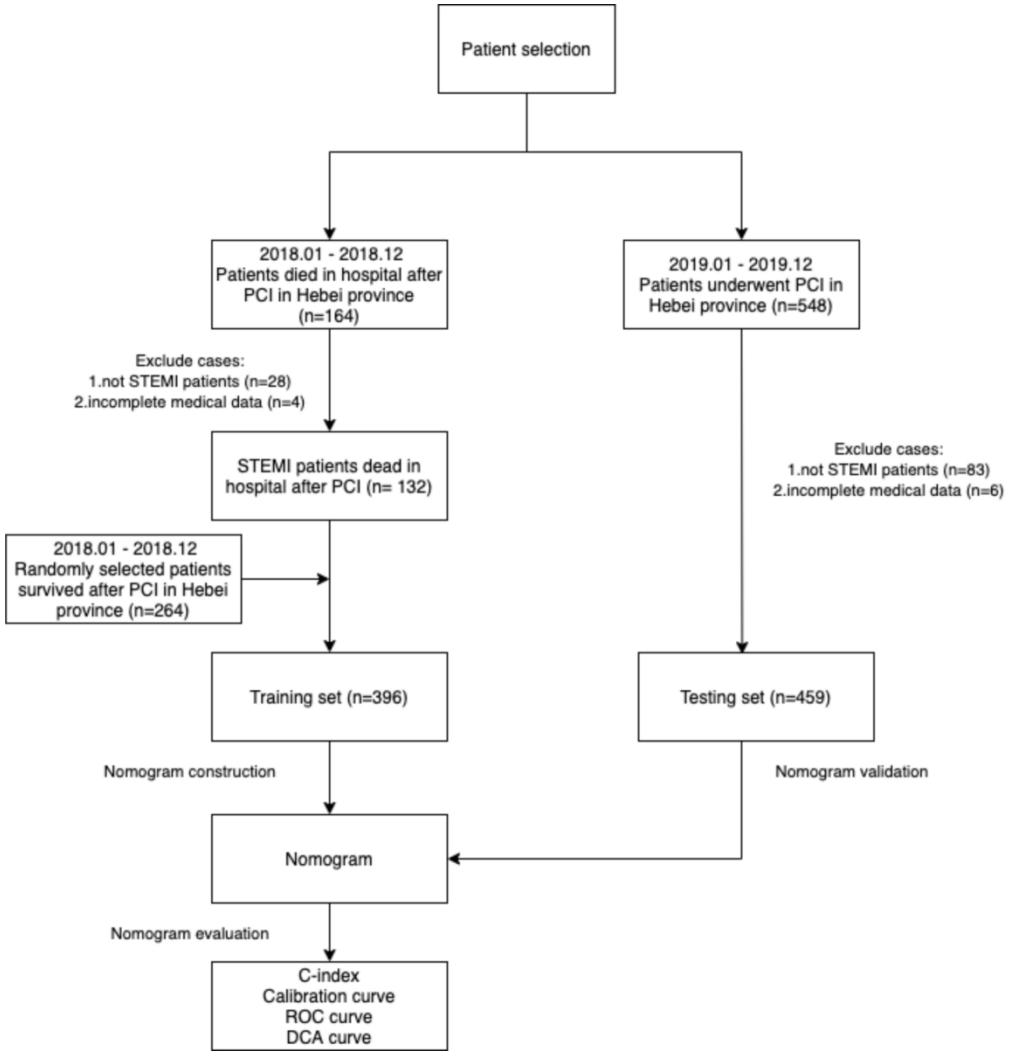

Figure 1. Flowchart illustrating the process of patient selection.

170x177mm (300 x 300 DPI)

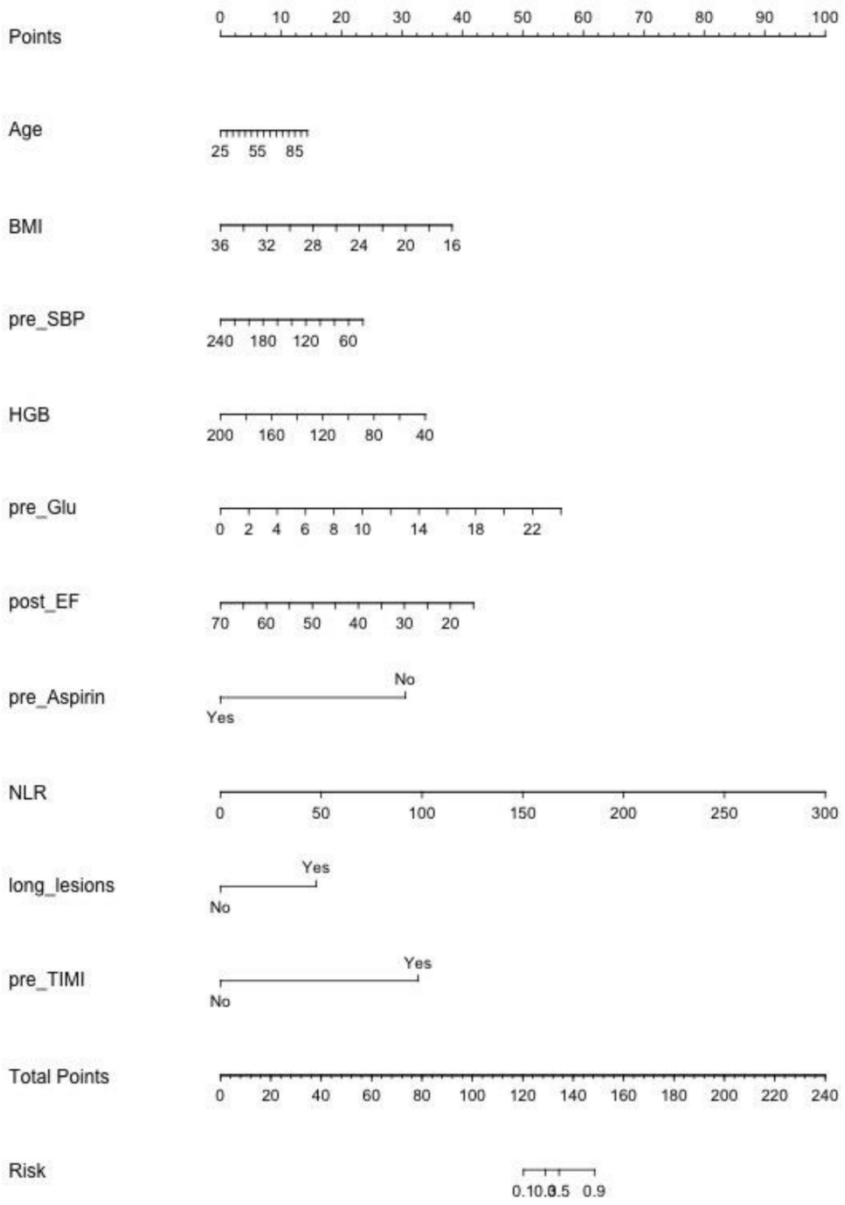

Figure 2. The nomogram for the prediction of in-hospital mortality in patients with acute ST-elevation myocardial infarction after primary PCI. BMI: body mass index; SBP: systolic blood pressure; HGB: hemoglobin; EF: ejection fraction; N/L ratio: neutrophils/lymphocytes ratio.

170x242mm (300 x 300 DPI)

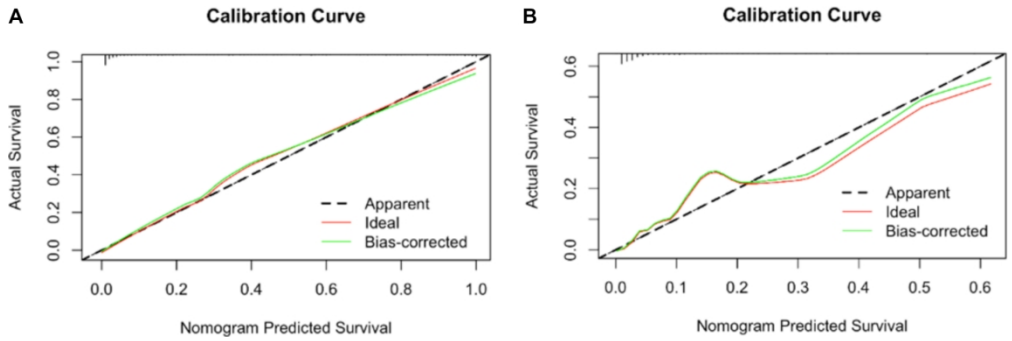

Figure 3. The calibration curves of the nomogram for the training set (A) and the testing set (B).

170x56mm (300 x 300 DPI)

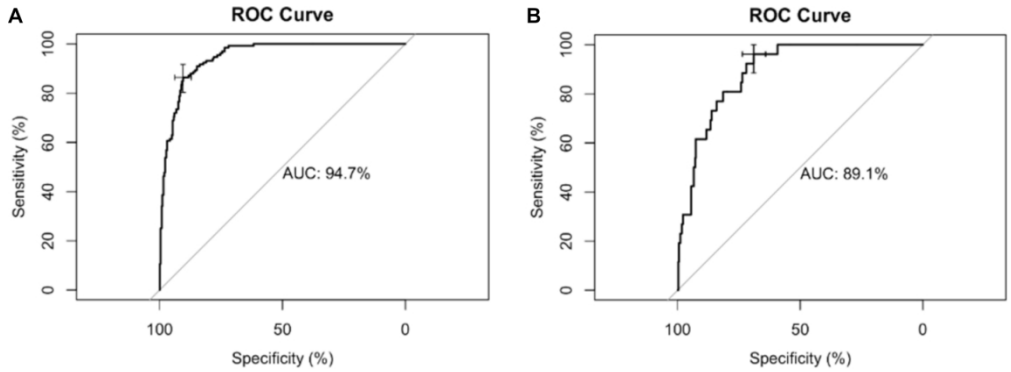

Figure 4. The received operating characteristics (ROC) curves of the nomogram for the training set (A) and the testing set (B).

170x61mm (300 x 300 DPI)

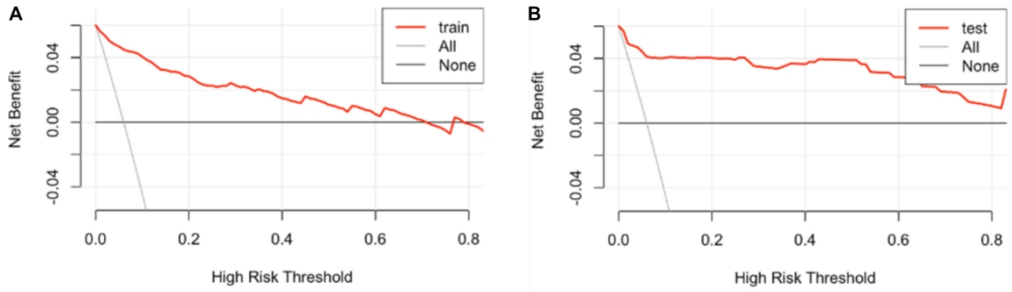

Figure 5. The decision curve analysis (DCA) for the risk model for the training set (A) and the testing set (B).

170x48mm (300 x 300 DPI)

Supplement Table 1. Clinical characteristics of the patients used to construct the nomogram

Variables	Training set				Testing set			
	All (n=396)	Survival (n=264)	In-hospital mortality (n=132)	*P*	All (n=459)	Survival (n=368)	In-hospital mortality (n=91)	*P*
Age (years) **(mean ±SD)**	63.3±12.7	60.3±12.9	69.3±9.8	<0.001	62.1±12.8	59.8±12.4	70.2±11.3	<0.001
Male **(n (%))**	284 (71.7)	202 (76.5)	82 (62.1)	0.004	352 (76.7)	294 (79.9)	58 (63.7)	0.001
BMI **(kg/m^2)**	25.8 (24.6, 26.1)	26.0 (25.3, 26.5)	24.9 (24.4, 25.5)	<0.001	25.4 (23.4, 27.3)	25.5±3.0	25.3 (23.4, 27.5)	0.047
Cardiac arrest **(n (%))**	10 (2.5)	6 (2.3)	4 (3.0)	0.91	8 (1.7)	6 (1.6)	2 (2.2)	0.711
Cardiogenic shock before admission **(n (%))**	34 (8.6)	6 (2.3)	28 (21.2)	<0.001	30 (6.5)	15 (4.1)	15 (16.5)	<0.001
Use of temporary pacemaker before admission **(n (%))**	3 (0.7)	0	3 (2.3)	0.065	4 (0.9)	2 (0.5)	2 (2.2)	0.128
Ventilator support before admission **(n (%))**	6 (1.5)	1 (0.4)	5 (3.8)	0.029	7 (1.5)	2 (0.5)	5 (5.5)	0.001
CPR before admission	12 (3.0)	5 (1.9)	7 (5.3)	0.12	5 (1.1)	0	5 (5.5)	<0.001

(n (%))								
SBP on admission **(median (IQR))**	128 (110, 146)	133 (114, 149)	118 (100, 140)	<0.001	125 (110, 140)	129±25	121 (107, 135)	0.009
DBP on admission **(median (IQR))**	79 (69, 89)	82 (72, 92)	73 (62, 82)	<0.001	77±16	80±15	69±16	<0.001
Heart rate on admission **(median (IQR))**	77 (65, 90)	76 (64, 89)	80 (66, 96)	0.025	79±18	78±17	82±24	0.095
Fatal arrhythmia before admission **(n (%))**	21 (5.3)	15 (5.7)	6 (4.5)	0.812	20 (4.4)	12 (3.3)	8 (8.8)	0.021
Total ischemic time **(min (median (IQR)))**	217 (124, 367)	154 (95, 250)	360 (194, 420)	<0.001	211 (130, 341)	194 (125, 307)	300 (222, 480)	<0.001
Killip class 3-4 **(n (%))**	132 (33.3)	95 (36.0)	37 (28.0)	0.142	119 (25.9)	66 (17.9)	53 (58.2)	<0.001
Past medical history								
Hypertension ***(n (%))***	211 (53.3)	137 (51.9)	74 (56.1)	0.499	73 (15.9)	38 (10.3)	35 (38.5)	<0.001
DM ***(n (%))***	96 (24.2)	49 (18.6)	47 (35.6)	<0.001	104 (22.7)	84 (22.8)	20 (22.0)	0.863

Hyperlipidemia ***(n (%))***	39 (9.8)	12 (4.5)	27 (20.5)	<0.001	41 (8.9)	23 (6.3)	18 (19.8)	<0.001
Previous PCI ***(n (%))***	18 (4.5)	8 (3.0)	10 (7.6)	0.073	23 (5.0)	17 (4.6)	6 (6.6)	0.44
Previous CABG ***(n (%))***	1 (0.2)	0	1 (0.8)	0.157	1 (0.2)	0	1 (1.1)	0.05
CAD ***(n (%))***	45 (11.4)	17 (6.4)	28 (21.2)	<0.001	40 (8.7)	20 (5.4)	20 (22.0)	<0.001
AF ***(n (%))***	11 (2.8)	1 (0.4)	10 (7.6)	<0.001	13 (2.8)	3 (0.8)	10 (11.0)	<0.001
HF ***(n (%))***	4 (1.0)	3 (1.1)	1 (0.8)	0.722	25 (5.4)	18 (4.9)	7 (7.7)	0.292
Renal insufficiency ***(n (%))***	62 (15.7)	1 (0.4)	61 (46.2)	<0.001	13 (2.8)	1 (0.3)	12 (13.2)	<0.001
History of cerebrovascular disease ***(n (%))***	64 (16.2)	40 (15.2)	24 (18.2)	0.53	72 (15.7)	60 (16.3)	12 (13.2)	0.464
Peripheral vascular disease ***(n (%))***	9 (2.3)	5 (1.9)	4 (3.0)	0.721	5 (1.1)	3 (0.8)	2 (2.2)	0.255
History of bleeding ***(n (%))***	2 (0.5)	1 (0.4)	1 (0.8)	>0.999	7 (1.5)	6 (1.6)	1 (1.1)	0.711
Family history of CAD ***(n (%))***	44 (11.1)	28 (10.6)	16 (11.1)	0.875	68 (14.8)	62 (16.8)	6 (6.6)	0.014
Angiographic characteristics								
Number of stents ***(median (IQR))***	1 (1, 1)	1 (1, 1)	1 (0, 1)	<0.001	1 (1, 1)	1 (1, 1)	1 (1, 1)	0.137

Long lesions ***(n (%))***	245 (61.9)	178 (67.4)	67 (50.8)	0.002	194 (42.3)	131 (35.6)	63 (69.2)	<0.001
Thrombus aspiration ***(n (%))***	123 (31.1)	92 (34.8)	31 (23.5)	0.029	221 (48.1)	205 (55.7)	16 (17.6)	<0.001
Residual stenosis ***(n (%))***	12 (3.0)	2 (0.8)	10 (7.6)	0.001	10 (2.2)	4 (1.1)	6 (6.6)	0.001
Use temporary pacemaker ***(n (%))***	22 (5.6)	4 (1.5)	18 (13.6)	<0.001	9 (2.0)	2 (0.5)	7 (7.7)	<0.001
IABP ***(n (%))***	19 (4.8)	4 (1.5)	15 (11.4)	<0.001	15 (3.3)	4 (1.1)	11 (12.1)	<0.001
Respirator support ***(n (%))***	20 (5.1)	1 (0.4)	19 (14.4)	<0.001	13 (2.8)	2 (0.5)	11 (12.1)	<0.001
Pericardial aspiration ***(n (%))***	3 (0.8)	0	3 (2.3)	0.065	3 (0.7)	0	3 (3.3)	<0.001
No flow ***(n (%))***	98 (24.7)	48 (18.2)	50 (37.9)	<0.001	84 (18.3)	55 (14.9)	29 (31.9)	<0.001
Coronary perforation ***(n (%))***	5 (1.3)	0	5 (3.8)	0.001	2 (0.4)	1 (0.3)	1 (1.1)	0.283
Dissection ***(n (%))***	3 (0.8)	0	3 (2.3)	0.065	5 (1.1)	0	5 (5.5)	<0.001
Pericardial tamponade ***(n (%))***	9 (2.3)	0	9 (6.8)	<0.001	2 (0.4)	0	2 (2.2)	0.004
Acute HF ***(n (%))***	55 (13.9)	22 (8.3)	33 (25.0)	<0.001	52 (11.3)	30 (7.7)	22 (24.2)	<0.001
Bleeding ***(n (%))***	2 (0.5)	0	2 (1.5)	0.21	6 (1.3)	3 (0.8)	3 (3.3)	0.062
Cardiac arrest ***(n (%))***	24 (6.1)	1 (0.4)	23 (17.4)	<0.001	14 (3.1)	6 (1.6)	8 (8.8)	<0.001
Recurrent MI ***(n (%))***	16 (4.0)	1 (0.4)	15 (11.4)	<0.001	7 (1.5)	2 (0.5)	5 (5.5)	0.001

Stent thrombosis ***(n (%))***	8 (2.0)	6 (2.3)	2 (1.5)	0.9	14 (3.1)	13 (3.5)	1 (1.1)	0.227
Type B2-C ***(n (%))***	309 (78.0)	213 (80.7)	96 (72.7)	0.094	277 (60.3)	230 (62.5)	47 (51.6)	0.058
TIMI flow grade 0-1 before PCI ***(n (%))***	311 (78.5)	197 (74.6)	114 (86.4)	0.011	339 (73.9)	274 (74.5)	65 (71.4)	0.556
Use of GP IIb/IIIa inhibitors ***(n (%))***	92 (23.2)	54 (20.5)	38 (28.8)	0.064	107 (23.3)	80 (21.7)	27 (29.7)	0.109
multivessel CAD ***(n (%))***	316 (79.8)	207 (78.4)	109 (82.6)	0.33	373 (81.3)	296 (80.4)	77 (84.6)	0.36
LAD ***(n (%))***	149 (37.6)	85 (32.2)	64 (48.5)	0.002	209 (45.5)	177 (48.1)	32 (35.2)	0.027
LCX ***(n (%))***	59 (14.9)	39 (14.8)	20 (15.2)	0.921	64 (13.9)	46 (12.5)	18 (19.8)	0.072
RCA ***(n (%))***	101 (25.5)	101 (38.3)	40 (30.3)	0.119	144 (31.4)	120 (32.6)	24 (26.4)	0.251
Biochemical markers								
Hyperkalemia ***(n (%))***	36 (9.1)	3 (1.1)	33 (25.0)	<0.001	30 (6.5)	11 (3.0)	19 (20.9)	<0.001
Hyponatremia ***(n (%))***	29 (7.3)	12 (4.5)	19 (14.4)	0.001	37 (8.1)	31 (8.4)	6 (6.6)	0.566
Anemia ***(n (%))***	26 (6.6)	12 (4.5)	14 (10.6)	0.022	40 (8.7)	21 (5.7)	19 (20.9)	<0.001
Creatinine ***(median (IQR))***	86.2 (76.9, 90.6)	86.2 (70.6, 86.2)	90.6 (77.0, 95.5)	0.111	92.5 (64.5, 93.0)	85.1±32.1	91.1±53.5	0.17

N/L ratio ***(median (IQR))***	5.47 (2.82, 10.00)	4.70 (2.68, 7.87)	8.54 (3.19, 11.46)	<0.001	6.15 (3.48, 9.52)	5.08 (3.65, 9.46)	9.1 (3.81, 12.51)	<0.001
HCT, % ***(median (IQR))***	41.0 (37.1, 44.0)	41.8 (38.0, 44.6)	38.5 (36.8, 41.3)	<0.001	40.4 (37.4, 44.5)	40.0±5.2	38.0 (32.7, 43.3)	<0.001
HGB, g/L ***(median (IQR))***	137.0 (126.0, 269.0)	142.0 (129.0, 155.0)	129.0 (119.0, 137.3)	<0.001	137.2±19.8	138.5±19.1	131.9±21.5	0.004
PLT, ×10⁹/L ***(median (IQR))***	221.0 (183.5, 269.0)	224.0 (186.0, 269.0)	227.0 (194.8, 246.3)	0.554	225.0 (184.0, 260.0)	229.0 (187.0, 264.0)	215.0 (175.0, 254.0)	0.151
Random blood glucose on admission, mmol/L ***(median (IQR))***	6.84 (5.47, 9.92)	5.95 (5.02, 7.44)	9.81 (7.96, 11.04)	<0.001	6.73 (5.27, 10.10)	6.12 (5.10, 8.10)	10.96 (8.40, 11.78)	<0.001
EF after PCI ***(median (IQR))***	51.0 (43.0, 58.0)	54.0 (47.8, 59.0)	43.0 (38.0, 48.5)	<0.001	55 (46, 60)	56 (51, 61)	45 (37, 53)	<0.001
Medication list on admission ***(n (%))***								
Aspirin	379 (95.7)	262 (99.2)	117 (88.6)	<0.001	404 (88.0)	332 (90.2)	72 (79.1)	0.004
Ticagrelor/clopidogrel	393 (99.2)	262 (99.2)	131 (99.2)	>0.999	418 (91.1)	332 (90.2)	86 (94.5)	0.199

Ticagrelor	223 (56.3)	162 (61.4)	61 (46.2)		218 (47.5)	183 (49.7)	35 (38.5)	
clopidogrel	170 (42.9)	100 (37.9)	70 (53.0)		200 (43.6)	149 (40.5)	51 (56.0)	
ACEI/ARB	133 (33.6)	100 (37.9)	33 (25.0)	0.014	25 (5.4)	18 (4.9)	7 (7.7)	0.292
β-Blocker	92 (23.2)	66 (25.0)	26 (19.7)	0.239	37 (8.1)	29 (7.9)	8 (8.9)	0.753
Statin	188 (47.5)	130 (49.2)	58 (43.9)	0.319	206 (44.9)	181 (49.2)	25 (27.5)	<0.001
mean duration of hospital stay **(median (IQR))**	8.51±5.11	9 (9,11)	1 (1,4)	<0.001	8.32±4.70	9 (8,11)	2 (1,5)	<0.001

BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; DM: diabetes mellitus; PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft; CAD: coronary atherosclerotic heart disease; AF: atrial fibrillation; HF: heart failure; IABP: intra-aortic balloon pump; MI: myocardial infarction; LAD: left anterior descending branch; LCX: left circumflex artery; RCA: right coronary artery; N/L ratio: neutrophils/lymphocytes ratio; HCT: hematocrit; HGB: hemoglobin; PLT: platelets; EF: ejection fraction; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker.

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any pre-specified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	9
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15
Generalisability	21	Discuss the generalisability (external validity) of the study results	15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

TRIPOD

TRIPOD Checklist: Prediction Model Development and Validation

Section/Topic	Item		Checklist Item	Page
Title and abstract				
Title	1	D;V	Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted.	1
Abstract	2	D;V	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	2
Introduction				
Background and objectives	3a	D;V	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	4
	3b	D;V	Specify the objectives, including whether the study describes the development or validation of the model or both.	5
Methods				
Source of data	4a	D;V	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	6
	4b	D;V	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	6
Participants	5a	D;V	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.	6
	5b	D;V	Describe eligibility criteria for participants.	6
	5c	D;V	Give details of treatments received, if relevant.	6
Outcome	6a	D;V	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	7
	6b	D;V	Report any actions to blind assessment of the outcome to be predicted.	NA
Predictors	7a	D;V	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured.	7
	7b	D;V	Report any actions to blind assessment of predictors for the outcome and other predictors.	NA
Sample size	8	D;V	Explain how the study size was arrived at.	NA
Missing data	9	D;V	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	NA
Statistical analysis methods	10a	D	Describe how predictors were handled in the analyses.	9
	10b	D	Specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	9
	10c	V	For validation, describe how the predictions were calculated.	9
	10d	D;V	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	9
	10e	V	Describe any model updating (e.g., recalibration) arising from the validation, if done.	9
Risk groups	11	D;V	Provide details on how risk groups were created, if done.	9
Development vs. validation	12	V	For validation, identify any differences from the development data in setting, eligibility criteria, outcome, and predictors.	9
Results				
Participants	13a	D;V	Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	10
	13b	D;V	Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome.	10
	13c	V	For validation, show a comparison with the development data of the distribution of important variables (demographics, predictors and outcome).	11
Model development	14a	D	Specify the number of participants and outcome events in each analysis.	11
	14b	D	If done, report the unadjusted association between each candidate predictor and outcome.	NA
Model specification	15a	D	Present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	12
	15b	D	Explain how to the use the prediction model.	12
Model performance	16	D;V	Report performance measures (with CIs) for the prediction model.	11
Model-updating	17	V	If done, report the results from any model updating (i.e., model specification, model performance).	NA
Discussion				
Limitations	18	D;V	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	17
Interpretation	19a	V	For validation, discuss the results with reference to performance in the development data, and any other validation data.	13
	19b	D;V	Give an overall interpretation of the results, considering objectives, limitations, results from similar studies, and other relevant evidence.	13
Implications	20	D;V	Discuss the potential clinical use of the model and implications for future research.	16
Other information				
Supplementary information	21	D;V	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	NA
Funding	22	D;V	Give the source of funding and the role of the funders for the present study.	19

*Items relevant only to the development of a prediction model are denoted by D, items relating solely to a validation of a prediction model are denoted by V, and items relating to both are denoted D;V. We recommend using the TRIPOD Checklist in conjunction with the TRIPOD Explanation and Elaboration document.