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

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3 **A nomogram for the prediction of in-hospital mortality in patients with acute ST-**
4 **elevation myocardial infarction after primary percutaneous coronary intervention**
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10 **Running title:** Nomogram for STEMI in-hospital mortality after PCI
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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

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3 discrimination and good prediction accuracy and could achieve a good net benefit.
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5 **Conclusions:** A nomogram that provides an individual prediction of in-hospital mortality
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7 for patients with STEMI after PCI in a Chinese population was established and validated.
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12 **Keywords:** nomogram; ST-elevated myocardial infarction; percutaneous coronary
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14 intervention; in-hospital mortality
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17 18 19 **ARTICLE SUMMARY** 20

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

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3 biomarkers have been reported to confer independent prognostic information after STEMI,
4 including Cardiac Troponin (cTn), Brain Natriuretic Peptide (BNP), amino-terminal pro-
5 Brain Natriuretic Peptide (NT-proBNP), and D-dimer [14-17]. Unfortunately, these studies
6 often exclude patients with advanced age, liver or kidney dysfunction, and other
7 comorbidities and complications. Therefore, the generalizability of those studies is limited,
8 and it is difficult to summarize and reflect the real-world treatment situation
9 comprehensively.
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19 Therefore, the objective of this study was to develop a clinical nomogram for predicting
20 in-hospital mortality of patients with STEMI after PCI. The results could provide clinical
21 guidance and improve the outcome of STEMI patients.
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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 assessed 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 \pm 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 $15.5628 + 0.0320 \times \text{age} - 0.2991 \times \text{BMI} - 0.0184 \times \text{SBP} - 0.0331 \times \text{HGB} + 0.3663 \times \text{random blood}$

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3 glucose on admission-0.1188×LVEF after PCI-4.7705×aspirin+0.0521×N/L ratio-
4
5 2.4688×long lesions+5.1018×TIMI flow grade.
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10 **Evaluation of the nomogram**

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12 In the training set, the C-index was 0.947, indicating that the prediction model was valuable
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14 in clinical practice (Figure 3a). The value of goodness-of-fit was 0.683, indicating a good
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16 prediction accuracy. The ROC curve is shown in Figure 4a (AUC=0.947, 95% CI: 0.927-
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18 0.967). Figure 5a shows the DCA curve for the training set, indicating that the nomogram
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20 had a high overall net benefit in predicting in-hospital mortality after PCI treatment.
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24 In the testing set, the C-index was 0.891. Figure 3b shows the calibration curve, and the
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26 value of goodness-of-fit was 0.462. The ROC curve is shown in Figure 4b (AUC=0.891,
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28 95% CI: 0.844-0.939). The DCA curve is shown in Figure 5b. The results of the testing set
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30 indicate that the nomogram had good discrimination and good prediction accuracy and
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32 could achieve a good net benefit.
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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 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

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3 glucose tolerance, and hyperinsulinemia) [25]. Therefore, obese patients demonstrate
4 greater adverse left ventricle (LV) remodeling and more impaired LV deformation after
5 STEMI compared with those similar infarct characteristics but normal BMI [21, 26].
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7 Interestingly, on the other hand, some studies have shown the so-called “obesity paradox”,
8 whereby obesity is related to better clinical outcomes [23, 25, 27, 28], consistent with the
9 present study. Fukuoka et al. [29] reported that this phenomenon is only observed in elderly
10 patients, not in younger patients, so the influence of BMI on risk factors for death might
11 vary with age. Nevertheless, obesity is currently recognized as a risk factor for the long-
12 term prognosis of patients with CAD, and it is worth recommending maintaining BMI at a
13 normal level [29].
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17 As a key factor in the inflammatory response, neutrophils play an irreplaceable role in
18 STEMI. Lymphocytes reflect the body’s stress level. Acute stress has been shown to
19 regulate the immune response of lymphocytes and reduce the number of peripheral blood
20 lymphocytes. The smaller the value, the higher the body’s stress level. Therefore, the N/L
21 ratio is an index for systemic inflammatory status and usually increases after STEMI [30-
22 32]. Pan et al. [33] demonstrated the independent association between increased N/L ratio
23 and short-term mortality in STEMI patients after PCI. The predictive value of the N/L ratio
24 may be based on the following reasons. Stimulated neutrophils release superoxide radicals,
25 proteolytic enzymes, and arachidonic acid metabolites that increase the infarct size and
26 lead to cardiac electrical instability by damaging endothelial cells, activating coagulation
27 cascade, aggregation of leukocytic cells, and plugging the micro-arteries [34]. These
28 actions will participate in the extension of the areas of myocardial infarction, impaired
29 epicardial and microvascular perfusion, no-reflow/slow flow during PCI, decreased
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3 ejection fraction (LVEF), and post-infarction death [35-37].
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5 The acute phase of STEMI leads to insulin resistance, glucose intolerance, and
6 hyperglycemia. The elevated levels of cytokines, growth hormone, glucagon, and cortisol
7 result in increased hepatic glucose production. Hepatic glycogenolysis is further enhanced
8 by catecholamines that also inhibit glycogenesis and stimulate the release of free fatty acids
9 (FFAs). High concentrations of FFAs will increase myocardial oxygen requirement, reduce
10 myocardial activity and contractility, impair calcium homeostasis and increase the
11 production of free radicals, leading to an increased risk of myocardial damage and
12 arrhythmias [38-41]. Thus, acute hyperglycemia is associated with adverse metabolic
13 effects that might contribute to a poor outcome. Previous studies reported that higher
14 admission glucose was strongly correlated with larger infarct size, lower LVEF, and
15 increased mortality risk in patients with and without diabetes [22, 42]. Exercise training,
16 dietary modifications, and medical intervention might reduce the mortality risk in such
17 patients. Intervention in the hospital, such as tight glycemic control during early PCI or at
18 least within 24 h after STEMI, is also beneficial [43, 44].
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37 Lower admission HGB was associated with higher in-hospital mortality when analyzed as
38 a continuous variable (OR=0.966, 95%CI: 0.954-0.978). The time from onset of precordial
39 pain to coronary angiography in patients with AMI is inversely proportional to the drop in
40 HGB concentration [45]. HGB levels and inflammation are closely related; in patients with
41 inflammation, an abundance of hepcidin leads to poor uptake of iron from the
42 gastrointestinal tract, iron sequestration in macrophages, little iron recycling to the erythron
43 for red-cell production, and microcytic anemia, and this process is termed inflammatory
44 block [46].
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3 Because of the important role of platelets in thrombus formation, the present study showed
4 that prior aspirin use could reduce in-hospital mortality of STEMI patients after PCI, as
5 supported by earlier clinical trials [47, 48]. Weidmann et al. [48] provided evidence
6 suggesting that pre-existing treatment with aspirin favorably affected the clinical
7 presentation, infarct size, and degree of inflammation of patients with STEMI. Yonetsu et
8 al. [49] reported that aspirin inhibits platelet aggregation and therefore reduces the
9 probability of an occluding clot on top of a ruptured plaque and, conversely, the occurrence
10 of STEMI. Despite these proven benefits, some studies revealed the existence of an “aspirin
11 paradox”, namely that prior aspirin use may predispose to worse outcomes than those not
12 previously taking aspirin, such as recurrent MI and ischemic events [50, 51].

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

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

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3 the nomogram must contain variables assessed in the routine clinical setting, which is the
4 case with the nomogram developed here. The results indicate that the nomogram had good
5 discrimination and good prediction accuracy and could achieve good net benefit. Another
6 nomogram based on other variables (left main coronary artery disease, grading of thrombus,
7 TIMI classification, slow flow, use of IABP, use of β -blocker, use of ACEI/ARB,
8 symptom-to-door time, symptom-to-balloon time, syntax score, LVEF, and CK-MB peak)
9 also showed a high AUC for in-hospital mortality of patients with STEMI after PCI [60].
10 Nevertheless, since the two nomograms were obtained in different study populations, the
11 two nomograms should be compared within the same study.
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24 Some study limitations should be mentioned. This study has limitations that are inherent to
25 retrospective observational studies. The data were obtained retrospectively, which can lead
26 to less reliable information. As the ischemic time is shortened as much as possible, patients
27 whose symptoms and/or ECG can be diagnosed are directly treated with PCI. Therefore,
28 other potential risk factors in our study, such as LVEF before PCI, could not be included
29 in the analyses. Further studies are still necessary to confirm the performance of the clinical
30 nomogram in future investigations.
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40 In conclusion, a nomogram to predict in-hospital mortality in patients with STEMI after
41 PCI was developed and validated in Hebei, China. The nomogram showed a satisfactory
42 performance, with a C-index of 0.948. Thus, this nomogram might be a precisely
43 individualized predictive tool for prognosis. Still, additional studies are needed to
44 determine whether it can be applied to other populations before its implementation in
45 clinical practice.
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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

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3 and Yingxiao Li helped to draft the manuscript. All authors read and approved the final
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5 manuscript.
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10 **Data sharing statement**

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12 All data generated or analyzed during this study are included in this published article.
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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, ×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)	58 (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).

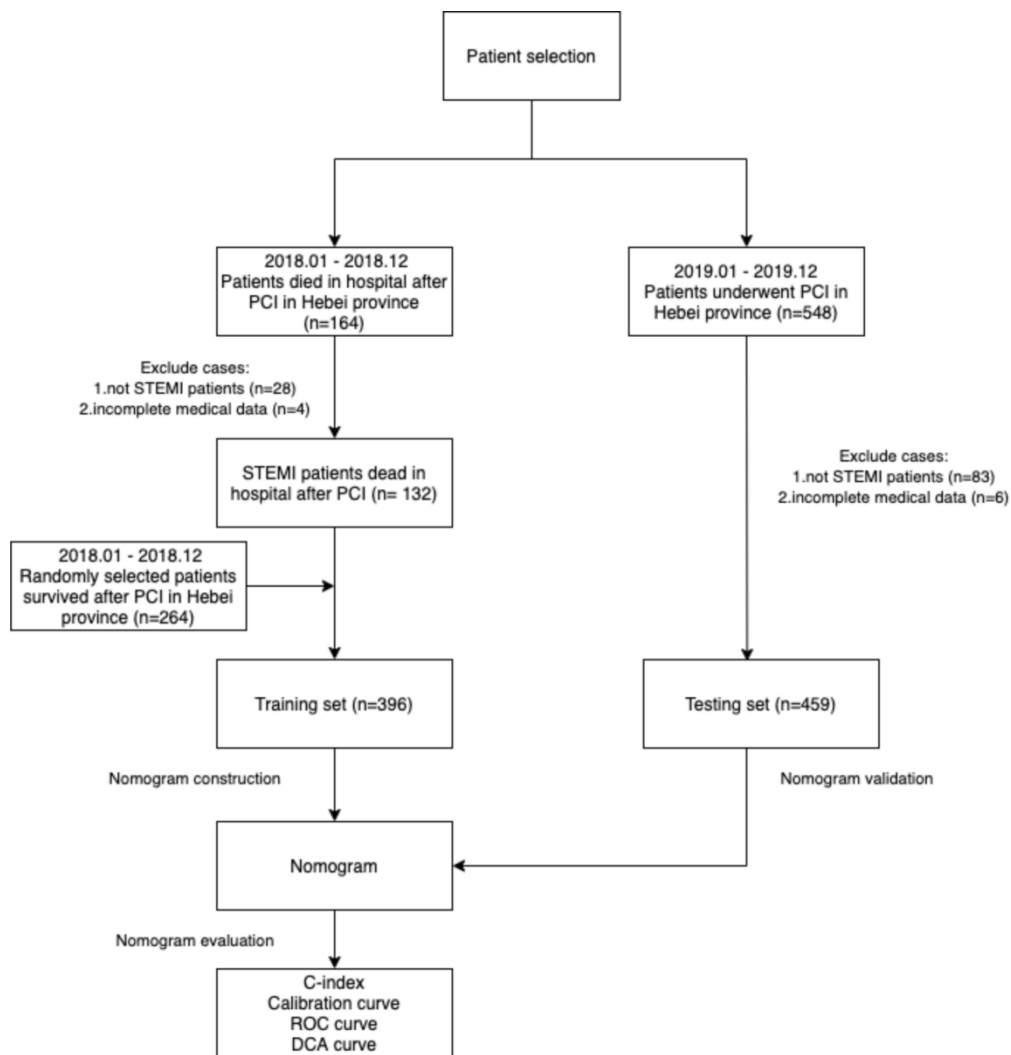


Figure 1. Flowchart illustrating the process of patient selection.

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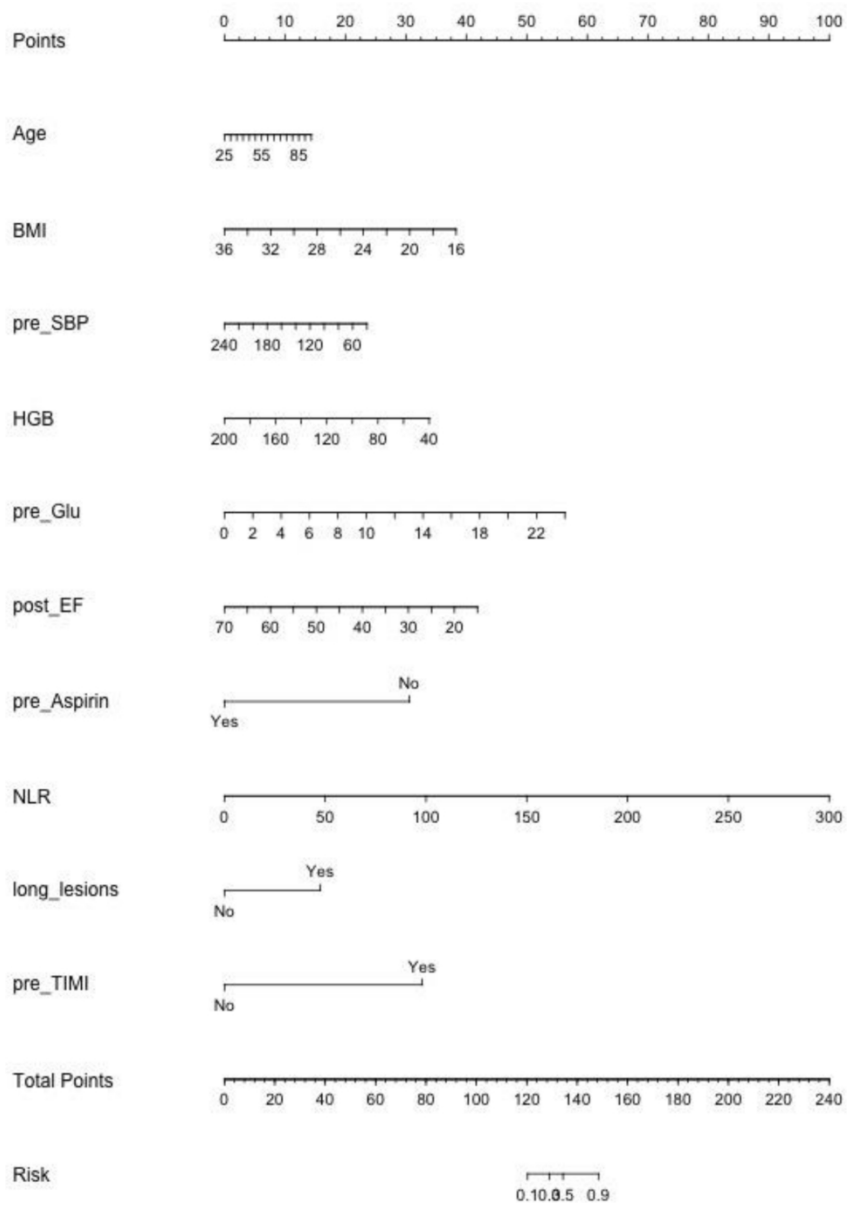


Figure 2. The nomogram for the prediction of in-hospital mortality in patients with acute ST-elevation myocardial infarction after primary PCI. BMI: body mass index; SBP: systolic blood pressure; HGB: hemoglobin; EF: ejection fraction; N/L ratio: neutrophils/lymphocytes ratio.

170x242mm (300 x 300 DPI)

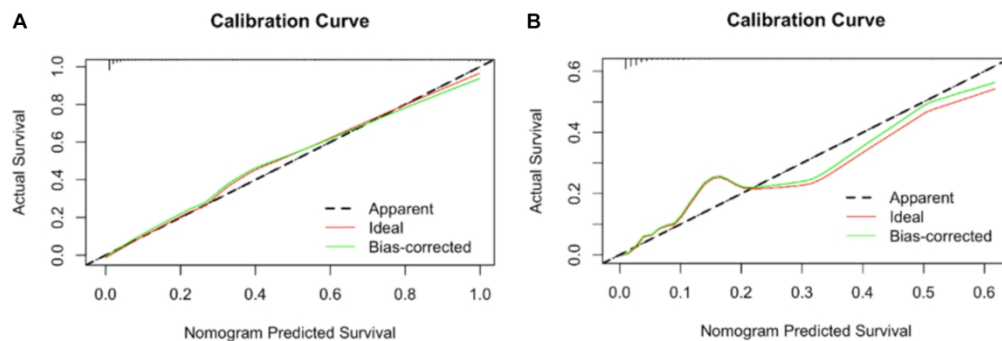


Figure 3. The calibration curves of the nomogram for the training set (A) and the testing set (B).

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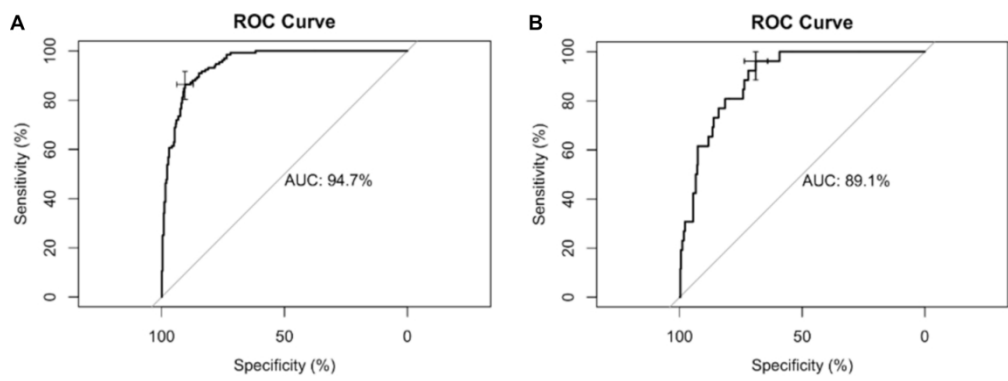


Figure 4. The received operating characteristics (ROC) curves of the nomogram for the training set (A) and the testing set (B).

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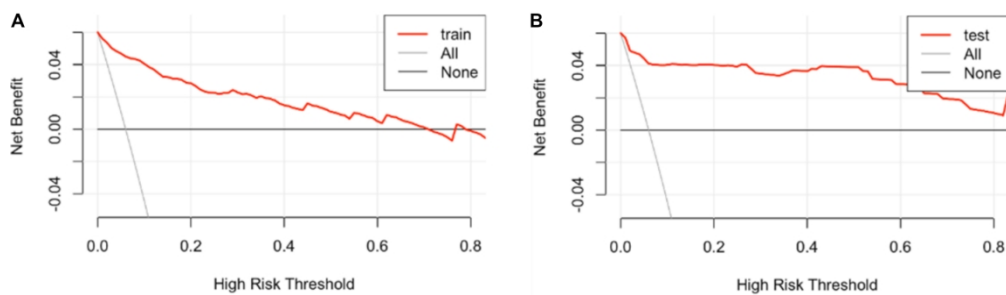


Figure 5. The decision curve analysis (DCA) for the risk model for the training set (A) and the testing set (B).

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) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —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 <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	6
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —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) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	

		<i>Cross-sectional study</i> —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 (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	9
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	9
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time <i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure <i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	9
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 (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	9
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

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Primary Subject Heading:	Cardiovascular medicine
Secondary Subject Heading:	Cardiovascular medicine
Keywords:	Coronary intervention < CARDIOLOGY, Coronary heart disease < CARDIOLOGY, Myocardial infarction < CARDIOLOGY

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3 1 **A nomogram for the prediction of in-hospital mortality in patients with acute ST-**
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5 **elevation myocardial infarction after primary percutaneous coronary intervention: a**
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7 **multicentre, retrospective, observation study in Hebei Province, China**
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12 5 **Running title:** Nomogram for STEMI in-hospital mortality after PCI
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17 7 **Yudan Wang^{1,2}, Wenjing Wang², Shengqi Jia¹, Man Gao¹, Shihang Zheng³, Jiaqi**
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19 8 **Wang³, Yi Dang², Yingxiao Li², Xiaoyong Qi^{1,2*}**
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54 23 **Word count:** 3020
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3 1 **ABSTRACT**
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5 2 **Objectives:** To establish a clinical prognostic nomogram for predicting in-hospital
6 mortality after primary percutaneous coronary intervention (PCI) among patients with ST-
7 elevation myocardial infarction (STEMI).
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12 5 **Design:** Retrospective, multicenter, observational study.
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14 6 **Setting:** Thirty-nine hospitals in Hebei Province.
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16 7 **Participants:** Patients with STEMI who underwent PCI from January 2018 to December
17 2019.
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21 9 **Interventions:** A multivariable logistic regression model was used to identify the factors
22 associated with in-hospital mortality. Then, they were incorporated into a nomogram. The
23 performance of the nomogram was evaluated by the discrimination, calibration, and
24 clinical usefulness.
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31 11 **Primary and secondary outcome measures:** The outcome was the factors associated with
32 in-hospital mortality.
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36 13 **Results:** This study included 855 patients, among whom 223 died in hospital. Age, Body
37 Mass Index (BMI), systolic pressure on admission, hemoglobin, random blood glucose on
38 admission, ejection fraction after PCI, use aspirin before admission, long lesions,
39 thrombolysis in myocardial infarction (TIMI) flow grade, and neutrophils/lymphocytes
40 ratio (N/L ratio) were independently associated with in-hospital mortality (all $P < 0.05$). In
41 the training set, the nomogram showed a C-index of 0.947, goodness-of-fit of 0.683, and
42 area under the receiver operating characteristic curve (AUC) of 0.947 (95%CI=0.927-
43 0.967). In the testing set, the C-index was 0.891, goodness-of-fit was 0.462, and AUC was
44 0.891 (95%CI=0.844-0.939). The results indicate that the nomogram had good
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1 discrimination and good prediction accuracy and could achieve a good net benefit.

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

4
5 **Keywords:** nomogram; ST-elevated myocardial infarction; percutaneous coronary
6 intervention; in-hospital mortality

7
8 **Strengths and limitations of this study**

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

1 INTRODUCTION

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

14 Primary percutaneous coronary intervention (PCI) has become the preferred reperfusion
15 strategy in patients with STEMI according to the current clinical guidelines for STEMI in
16 the United States and Europe ^{6,7}. Nevertheless, even if such patients receive timely PCI
17 and/or appropriate antiplatelet drugs, the prognosis is still poor, and a substantial number
18 of patients still die in-hospital after PCI. About 6% of STEMI patients die in the hospital ³
19 ^{8,9}. Therefore, there is still room for improving the short-term outcomes after PCI.

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

1 have been reported to confer independent prognostic information after STEMI, including
2 Cardiac Troponin (cTn), Brain Natriuretic Peptide (BNP), amino-terminal pro-Brain
3 Natriuretic Peptide (NT-proBNP), and D-dimer¹⁴⁻¹⁷. Unfortunately, these studies often
4 exclude patients with advanced age, liver or kidney dysfunction, and other comorbidities
5 and complications. Therefore, the generalizability of those studies is limited, and it is
6 difficult to summarize and reflect the real-world treatment situation comprehensively.
7 Therefore, the objective of this study was to develop a clinical nomogram for predicting
8 in-hospital mortality of patients with STEMI after PCI. The results could provide clinical
9 guidance and improve the outcome of STEMI patients.

1 PATIENTS AND METHODS

2 Study design and patients

3 This multicenter, retrospective, observational study included STEMI patients treated with
4 PCI at 39 PCI hospitals in Hebei Province from January 2018 to December 2019. The
5 cohort was divided into a training set and a time-independent validation set. The training
6 set refers to the use of modeled data to verify the predictive effect of the model, while test
7 set is to use another set of patients' data (namely external data) to verify the prediction
8 accuracy of the model. The training set patients enrolled from January 2018 to December
9 2018 and the testing set patients enrolled from January 2019 to December 2019.

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

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

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4**2 Patient and Public Involvement**

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

6 Definitions

7 Long lesions was defined as the stenosis that has as $\geq 50\%$ reduction and more than 20mm
8 in luminal diameter¹⁸.

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

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

14 Data collection

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

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

3 4 **Nomogram construction**

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

13 14 **Statistical analysis**

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

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3 1 continuous variables. Otherwise, the Mann-Whitney U-test was used. The significance
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5 2 level was set at 0.05, and two-sided tests were used.
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1 RESULTS

2 Characteristics of the patients

3 The whole study population consisted of 855 patients diagnosed with STEMI and who
4 underwent PCI, including 396 in the training set (132 (33.3%) dead patients and 264
5 (66.7%) survivors) and 459 (91 (19.8%) dead patients, and 368 (80.2%) survivors) in the
6 test set (Figure 1). The clinical characteristics, including demographic, medical history,
7 angiographic characteristics, and information of cardiac procedures, medications, and
8 biochemical markers, are summarized in Table 1. The patients who died in the hospital
9 were older (69.8 ± 10.2 vs. 60.2 ± 12.6 years, $P < 0.01$), more likely to be women (32.7% vs.
10 21.5%, $P < 0.01$), and more had complications like hypertension, AF, and hyperlipidemia.
11 The hospital stay was 8.51 ± 5.11 days in the training set and 8.32 ± 4.70 days in the test set.

13 Nomogram construction

14 According to the multivariable logistic analysis, the 10 variables were found to meet the
15 threshold of $P < 0.05$. Age (OR=1.069, 95% CI=1.048-1.092, $P=0.049$), BMI (OR=0.55, 95%
16 CI=0.31-0.87, $P=0.019$), SBP on admission (OR=0.92, 95% CI=0.86-0.97, $P=0.009$),
17 HGB (OR=0.85, 95% CI=0.73-0.97, $P=0.017$), random blood glucose on admission
18 (OR=1.53, 95% CI=1.13-2.21, $P=0.011$), EF after PCI (OR=0.89, 95% CI=0.80-0.97,
19 $P=0.015$), aspirin (OR=0.001, 95% CI=0.009-0.04, $P=0.001$), N/L ratio (OR=1.34, 95%
20 CI=1.12-1.69, $P=0.004$), long lesions (OR=2.00, 95% CI=1.310-3.084, $P < 0.001$), and
21 TIMI flow grade (OR=2.15, 95% CI=1.242-3.900, $P=0.008$) were independently
22 associated with in-hospital mortality after PCI of STEMI (Table 2). The nomogram is
23 shown in Figure 2. The formula for calculating the total point of the nomogram is

1 15.5628+0.0320×age-0.2991×BMI-0.0184×SBP-0.0331×HGB+0.3663×random blood
2 glucose on admission-0.1188×LVEF after PCI-4.7705×aspirin+0.0521×N/L ratio-
3 2.4688×long lesions+5.1018×TIMI flow grade.

5 **Evaluation of the nomogram**

6 In the training set, the C-index was 0.947, indicating that the prediction model was valuable
7 in clinical practice (Figure 3a). The value of goodness-of-fit was 0.683, indicating a good
8 prediction accuracy. The ROC curve is shown in Figure 4a (AUC=0.947, 95% CI: 0.927-
9 0.967). Figure 5a shows the DCA curve for the training set, indicating that the nomogram
10 had a high overall net benefit in predicting in-hospital mortality after PCI treatment.

11 In the testing set, the C-index was 0.891. Figure 3b shows the calibration curve, and the
12 value of goodness-of-fit was 0.462. The ROC curve is shown in Figure 4b (AUC=0.891,
13 95% CI: 0.844-0.939). The DCA curve is shown in Figure 5b. The results of the testing set
14 indicate that the nomogram had good discrimination and good prediction accuracy and
15 could achieve a good net benefit.

1 DISCUSSION

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

6 In our study, age was an independent risk factor of STEMI patients, in accordance with
7 other analyses of STEMI patients and underlining the high-risk profile of elderly patients,
8 as they usually present with more risk factors and comorbidities than younger patients^{20 21},
9 such as the higher prevalence of renal insufficiency, lower LVEF. High mortality in the
10 older patients might also result from end-organ dysfunction, competing risks might also
11 offset the benefits from reperfusion, such that successful outcomes are more dependent on
12 overall health issues. Therefore, for older patients, some authors have also questioned the
13 benefit of reperfusion therapy²².

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

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3 1 recognized as a risk factor for the long-term prognosis of patients with CAD, and it is worth
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5 2 recommending maintaining BMI at a normal level ²⁹.

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7 3 Acute stress has been shown to regulate the immune response of lymphocytes and reduce
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9 4 the number of peripheral blood lymphocytes. The smaller the value, the higher the body's
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11 5 stress level. Therefore, the N/L ratio, as an index for systemic inflammatory status and
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13 6 usually increases after STEMI ³⁰⁻³². Pan et al. ³³ demonstrated the independent association
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15 7 between increased N/L ratio and short-term mortality in STEMI patients after PCI. The
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17 8 predictive value of the N/L ratio may be based on the following reasons. Stimulated
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19 9 neutrophils release superoxide radicals, proteolytic enzymes, and arachidonic acid
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21 10 metabolites that increase the infarct size and lead to cardiac electrical instability by
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23 11 damaging endothelial cells, activating coagulation cascade, aggregation of leukocytic cells,
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25 12 and plugging the micro-arteries ³⁴. These actions will participate in the extension of the
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27 13 areas of myocardial infarction, impaired epicardial and microvascular perfusion, no-
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29 14 reflow/slow flow during PCI, decreased LVEF, and post-infarction death ³⁵⁻³⁷.

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31 15 The acute phase of STEMI leads to insulin resistance, glucose intolerance, and
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33 16 hyperglycemia. The elevated levels of cytokines, growth hormone, glucagon, and cortisol
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35 17 result in increased hepatic glucose production. Hepatic glycogenolysis is further enhanced
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37 18 by catecholamines that also inhibit glycogenesis and stimulate the release of free fatty acids
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39 19 (FFAs). High concentrations of FFAs will increase myocardial oxygen requirement, reduce
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41 20 myocardial activity and contractility, impair calcium homeostasis and increase the
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43 21 production of free radicals, leading to an increased risk of myocardial damage and
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45 22 arrhythmias ³⁸⁻⁴¹. Thus, acute hyperglycemia might contribute to a poor outcome. Previous
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47 23 studies reported that higher admission glucose was strongly correlated with larger infarct
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1 size, lower LVEF, and increased mortality risk in patients with and without diabetes ^{42 43}.

2 Exercise training, dietary modifications, and intervention in the hospital, such as tight

3 glycemic control during early PCI or at least within 24 h after STEMI might reduce the

4 mortality risk in such patients ^{44 45}.

5 Lower admission HGB was associated with higher in-hospital mortality when analyzed as

6 a continuous variable (OR=0.966, 95%CI: 0.954-0.978). The total ischemic time in patients

7 with AMI is inversely proportional to the drop in HGB concentration ⁴⁶. HGB levels and

8 inflammation are closely related; in patients with inflammation, inflammation block occurs,

9 that is, an abundance of hepcidin leads to poor uptake of iron from the gastrointestinal tract,

10 iron sequestration in macrophages, little iron recycling to the erythron for red-cell

11 production, and microcytic anemia, which can cause a lower HGB level. ⁴⁷.

12 Because of the important role of platelets in thrombus formation, the present study showed

13 that prior aspirin use could reduce in-hospital mortality of STEMI patients after PCI, as

14 supported by earlier clinical trials ^{48 49}. Weidmann et al. ⁴⁹ provided evidence suggesting

15 that pre-existing treatment with aspirin favorably affected the clinical presentation, infarct

16 size, and degree of inflammation of patients with STEMI. Yonetsu et al. ⁵⁰ reported that

17 aspirin inhibits platelet aggregation and therefore reduces the probability of an occluding

18 clot on top of a ruptured plaque and, conversely, the occurrence of STEMI.

19 Previous studies indicated that lesion length is associated with long-term adverse events

20 after PCI and is an important risk factor for restenosis and stent thrombosis ⁵¹⁻⁵³. A longer

21 lesion, with its greater plaque burden, is conceived to provide a major source of smooth

22 muscle cells that will then proliferate to form neointima. Atherosclerotic plaques have often

23 been found to demonstrate an increased expression of isoforms characteristic of activated

1 smooth muscle cells that are not present in normal vasculature⁵⁴. Still, there are few studies
2 on lesion length and in-hospital mortality, and further studies are still necessary.
3 Preprocedural reperfusion might have a prognostic value⁵⁵. A strong relationship exists
4 between preprocedural TIMI flow grade and infarct size and predischage LVEF⁵⁶. SBP
5 is a critical factor, and hypotension was associated with a decrease in survival⁵⁷.

6 In our multivariate analysis, the higher Killip Class is not a predictor of in-hospital
7 mortality in STEMI patients. However, in a recent work from Del Buono et al⁵⁸, it was
8 proved that a higher Killip Class is an independent risk factor for MACE events and in-
9 hospital mortality in patients with anterior myocardial infarction. This the first study
10 including only patients with STEMI in the anterior location and excluding patients with
11 history of cardiovascular diseases in order to reduce the heterogeneity of the population
12 enrolled. This may be one of the reasons for the inconsistency of the two studies.
13 Nevertheless, Killip classification is a simple and convenient clinical tool that can quickly
14 stratify the risk of ACS patients and is likely to become an independent predictor of long-
15 term follow-up results again.

16 The nomogram is a simple and intuitive representation of the mathematical model⁵⁹.
17 In addition, to be of clinical usefulness in a routine setting, the nomogram must contain
18 variables assessed in the routine clinical setting, which is the case with the nomogram
19 developed here. It can simplify the statistical prediction model to the numerical probability
20 of disease recurrence or death. The identification and stratification of patients becomes a
21 simple tool with many advantages. The most prominent advantage is that it can predict

1 individualized risks based on patient and disease characteristics. Secondly, it is easy to use
2 and can help doctors develop individualized treatment plans. However, although the
3 current clinical use of nomograms has increased, there are limited data on patient
4 satisfaction or quality of life after it assists in medical decision-making. In addition,
5 although nomograms are widely used clinically, they are rarely evaluated prospectively to
6 determine whether their use actually improves the prognosis of patients^{60 61}. Therefore, it
7 remains to be explored how this risk model can be better applied to the clinic. The results
8 indicate that the nomogram had good discrimination and good prediction accuracy and
9 could achieve good net benefit. Another nomogram based on other variables (left main
10 coronary artery disease, grading of thrombus, TIMI classification, slow flow, use of IABP,
11 use of β -blocker, use of ACEI/ARB, symptom-to-door time, symptom-to-balloon time,
12 syntax score, LVEF, and CK-MB peak) also showed a high AUC for in-hospital mortality
13 of patients with STEMI after PCI⁶². We think there may be three main reasons: different
14 research methods, the hospitals and time nodes that included patients are different and
15 different statistical methods. Nevertheless, we are planning to combine the two parts of
16 patients to get a more accurate risk model of in-hospital mortality.

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

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

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

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8 **Competing Interests**

9 The authors of this work have nothing to disclose.

10 **Ethical standards disclosure**

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

16 **Authors' contribution**

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

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3 1 Jiaqi Wang and Yingxiao Li helped to draft the manuscript. All authors read and approved
4
5 2 the final manuscript.

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10 4 **Data availability statement**

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5 **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)	<i>P</i>	All (n=459)	Survival (n=368)	In-hospital mortality (n=91)	<i>P</i>
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

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5	(n (%))								
6									
7	SBP on admission								
8		128 (110, 146)	133 (114, 149)	118 (100, 140)	<0.001	125 (110, 140)	129±25	121 (107, 135)	0.009
9	(median (IQR))								
10									
11	DBP on admission								
12		79 (69, 89)	82 (72, 92)	73 (62, 82)	<0.001	77±16	80±15	69±16	<0.001
13	(median (IQR))								
14									
15	Heart rate on admission								
16		77 (65, 90)	76 (64, 89)	80 (66, 96)	0.025	79±18	78±17	82±24	0.095
17	(median (IQR))								
18									
19	Fatal arrhythmia before								
20	admission (n (%))	21 (5.3)	15 (5.7)	6 (4.5)	0.812	20 (4.4)	12 (3.3)	8 (8.8)	0.021
21									
22									
23	Total ischemic time								
24		217 (124, 367)	154 (95, 250)	360 (194, 420)	<0.001	211 (130, 341)	194 (125, 307)	300 (222, 480)	<0.001
25	(min (median (IQR)))								
26									
27	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
28									
29									
30	Past medical history								
31									
32									
33	<i>Hypertension (n (%))</i>	211 (53.3)	137 (51.9)	74 (56.1)	0.499	73 (15.9)	38 (10.3)	35 (38.5)	<0.001
34									
35	<i>DM (n (%))</i>	96 (24.2)	49 (18.6)	47 (35.6)	<0.001	104 (22.7)	84 (22.8)	20 (22.0)	0.863
36									
37	<i>Hyperlipidemia (n (%))</i>	39 (9.8)	12 (4.5)	27 (20.5)	<0.001	41 (8.9)	23 (6.3)	18 (19.8)	<0.001
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5	<i>Previous PCI (n (%))</i>	18 (4.5)	8 (3.0)	10 (7.6)	0.073	23 (5.0)	17 (4.6)	6 (6.6)	0.44
6									
7	<i>Previous CABG (n (%))</i>	1 (0.2)	0	1 (0.8)	0.157	1 (0.2)	0	1 (1.1)	0.05
8									
9									
10	<i>CAD (n (%))</i>	45 (11.4)	17 (6.4)	28 (21.2)	<0.001	40 (8.7)	20 (5.4)	20 (22.0)	<0.001
11									
12	<i>AF (n (%))</i>	11 (2.8)	1 (0.4)	10 (7.6)	<0.001	13 (2.8)	3 (0.8)	10 (11.0)	<0.001
13									
14	<i>HF (n (%))</i>	4 (1.0)	3 (1.1)	1 (0.8)	0.722	25 (5.4)	18 (4.9)	7 (7.7)	0.292
15									
16	<i>Renal insufficiency (n (%))</i>	62 (15.7)	1 (0.4)	61 (46.2)	<0.001	13 (2.8)	1 (0.3)	12 (13.2)	<0.001
17									
18	<i>History of cerebrovascular disease</i>								
19	<i>(n (%))</i>	64 (16.2)	40 (15.2)	24 (18.2)	0.53	72 (15.7)	60 (16.3)	12 (13.2)	0.464
20									
21									
22	<i>Peripheral vascular disease (n</i>								
23	<i>(%))</i>	9 (2.3)	5 (1.9)	4 (3.0)	0.721	5 (1.1)	3 (0.8)	2 (2.2)	0.255
24									
25									
26	<i>History of bleeding (n (%))</i>	2 (0.5)	1 (0.4)	1 (0.8)	>0.999	7 (1.5)	6 (1.6)	1 (1.1)	0.711
27									
28	<i>Family history of CAD (n (%))</i>	44 (11.1)	28 (10.6)	16 (11.1)	0.875	68 (14.8)	62 (16.8)	6 (6.6)	0.014
29									
30									
31	Angiographic characteristics								
32									
33	<i>Number of stents (median (IQR))</i>	1 (1, 1)	1 (1, 1)	1 (0, 1)	<0.001	1 (1, 1)	1 (1, 1)	1 (1, 1)	0.137
34									
35	<i>Long lesions (n (%))</i>	245 (61.9)	178 (67.4)	67 (50.8)	0.002	194 (42.3)	131 (35.6)	63 (69.2)	<0.001
36									
37	<i>Thrombus aspiration (n (%))</i>	123 (31.1)	92 (34.8)	31 (23.5)	0.029	221 (48.1)	205 (55.7)	16 (17.6)	<0.001
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5	<i>Residual stenosis (n (%))</i>	12 (3.0)	2 (0.8)	10 (7.6)	0.001	10 (2.2)	4 (1.1)	6 (6.6)	0.001
6									
7	<i>Use temporary pacemaker (n (%))</i>	22 (5.6)	4 (1.5)	18 (13.6)	<0.001	9 (2.0)	2 (0.5)	7 (7.7)	<0.001
8									
9	<i>IABP (n (%))</i>	19 (4.8)	4 (1.5)	15 (11.4)	<0.001	15 (3.3)	4 (1.1)	11 (12.1)	<0.001
10									
11	<i>Respirator support (n (%))</i>	20 (5.1)	1 (0.4)	19 (14.4)	<0.001	13 (2.8)	2 (0.5)	11 (12.1)	<0.001
12									
13	<i>Pericardial aspiration (n (%))</i>	3 (0.8)	0	3 (2.3)	0.065	3 (0.7)	0	3 (3.3)	<0.001
14									
15	<i>No flow (n (%))</i>	98 (24.7)	48 (18.2)	50 (37.9)	<0.001	84 (18.3)	55 (14.9)	29 (31.9)	<0.001
16									
17	<i>Coronary perforation (n (%))</i>	5 (1.3)	0	5 (3.8)	0.001	2 (0.4)	1 (0.3)	1 (1.1)	0.283
18									
19	<i>Dissection (n (%))</i>	3 (0.8)	0	3 (2.3)	0.065	5 (1.1)	0	5 (5.5)	<0.001
20									
21	<i>Pericardial tamponade (n (%))</i>	9 (2.3)	0	9 (6.8)	<0.001	2 (0.4)	0	2 (2.2)	0.004
22									
23	<i>Acute HF (n (%))</i>	55 (13.9)	22 (8.3)	33 (25.0)	<0.001	52 (11.3)	30 (7.7)	22 (24.2)	<0.001
24									
25	<i>Bleeding (n (%))</i>	2 (0.5)	0	2 (1.5)	0.21	6 (1.3)	3 (0.8)	3 (3.3)	0.062
26									
27	<i>Cardiac arrest (n (%))</i>	24 (6.1)	1 (0.4)	23 (17.4)	<0.001	14 (3.1)	6 (1.6)	8 (8.8)	<0.001
28									
29	<i>Recurrent MI (n (%))</i>	16 (4.0)	1 (0.4)	15 (11.4)	<0.001	7 (1.5)	2 (0.5)	5 (5.5)	0.001
30									
31	<i>Stent thrombosis (n (%))</i>	8 (2.0)	6 (2.3)	2 (1.5)	0.9	14 (3.1)	13 (3.5)	1 (1.1)	0.227
32									
33	<i>Type B2-C (n (%))</i>	309 (78.0)	213 (80.7)	96 (72.7)	0.094	277 (60.3)	230 (62.5)	47 (51.6)	0.058
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5	<i>TIMI flow grade 0-1 before PCI</i>								
6		311 (78.5)	197 (74.6)	114 (86.4)	0.011	339 (73.9)	274 (74.5)	65 (71.4)	0.556
7	(n (%))								
8									
9	<i>Use of GP IIb/IIIa inhibitors (n</i>								
10	<i>(%))</i>	92 (23.2)	54 (20.5)	38 (28.8)	0.064	107 (23.3)	80 (21.7)	27 (29.7)	0.109
11									
12									
13	<i>multivessel CAD (n (%))</i>	316 (79.8)	207 (78.4)	109 (82.6)	0.33	373 (81.3)	296 (80.4)	77 (84.6)	0.36
14									
15	<i>LAD (n (%))</i>	149 (37.6)	85 (32.2)	64 (48.5)	0.002	209 (45.5)	177 (48.1)	32 (35.2)	0.027
16									
17	<i>LCX (n (%))</i>	59 (14.9)	39 (14.8)	20 (15.2)	0.921	64 (13.9)	46 (12.5)	18 (19.8)	0.072
18									
19	<i>RCA (n (%))</i>	101 (25.5)	101 (38.3)	40 (30.3)	0.119	144 (31.4)	120 (32.6)	24 (26.4)	0.251
20									
21	Biochemical markers								
22									
23									
24	<i>Hyperkalemia (n (%))</i>	36 (9.1)	3 (1.1)	33 (25.0)	<0.001	30 (6.5)	11 (3.0)	19 (20.9)	<0.001
25									
26	<i>Hyponatremia (n (%))</i>	29 (7.3)	12 (4.5)	19 (14.4)	0.001	37 (8.1)	31 (8.4)	6 (6.6)	0.566
27									
28									
29	<i>Anemia (n (%))</i>	26 (6.6)	12 (4.5)	14 (10.6)	0.022	40 (8.7)	21 (5.7)	19 (20.9)	<0.001
30									
31	<i>Creatinine (median (IQR))</i>	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
32									
33	<i>N/L ratio (median (IQR))</i>	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
34									
35									
36	<i>HCT, % (median (IQR))</i>	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
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	<i>HGB, g/L (median (IQR))</i>	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
	<i>PLT, ×10⁹/L (median (IQR))</i>	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
	<i>Random blood glucose on admission, mmol/L (median (IQR))</i>	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
	<i>EF after PCI (median (IQR))</i>	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									
	<i>(n (%))</i>								
	<i>Aspirin</i>	379 (95.7)	262 (99.2)	117 (88.6)	<0.001	404 (88.0)	332 (90.2)	72 (79.1)	0.004
	<i>Ticagrelor/clopidogrel</i>	393 (99.2)	262 (99.2)	131 (99.2)	>0.999	418 (91.1)	332 (90.2)	86 (94.5)	0.199
	<i>Ticagrelor</i>	223 (56.3)	162 (61.4)	61 (46.2)		218 (47.5)	183 (49.7)	35 (38.5)	
	<i>clopidogrel</i>	170 (42.9)	100 (37.9)	70 (53.0)		200 (43.6)	149 (40.5)	51 (56.0)	
	<i>ACEI/ARB</i>	133 (33.6)	100 (37.9)	33 (25.0)	0.014	25 (5.4)	18 (4.9)	7 (7.7)	0.292
	<i>β-Blocker</i>	92 (23.2)	66 (25.0)	26 (19.7)	0.239	37 (8.1)	29 (7.9)	8 (8.9)	0.753

	<i>Statin</i>	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

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- 1 BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; DM: diabetes mellitus; PCI: percutaneous
 - 2 coronary intervention; CABG: coronary artery bypass graft; CAD: coronary atherosclerotic heart disease; AF: atrial fibrillation; HF:
 - 3 heart failure; IABP: intra-aortic balloon pump; MI: myocardial infarction; LAD: left anterior descending branch; LCX: left circumflex
 - 4 artery; RCA: right coronary artery; N/L ratio: neutrophils/lymphocytes ratio; HCT: hematocrit; HGB: hemoglobin; PLT: platelets; EF:
 - 5 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	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

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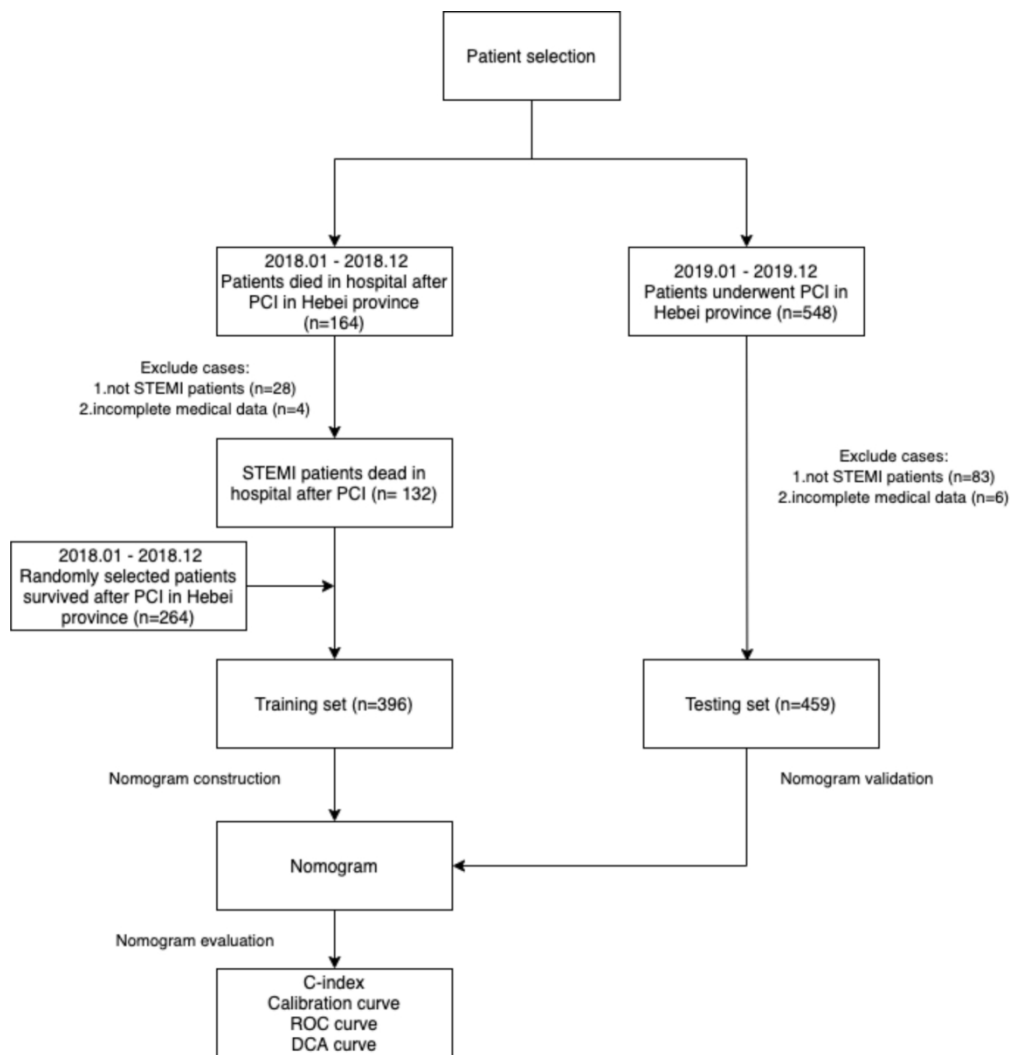


Figure 1. Flowchart illustrating the process of patient selection.

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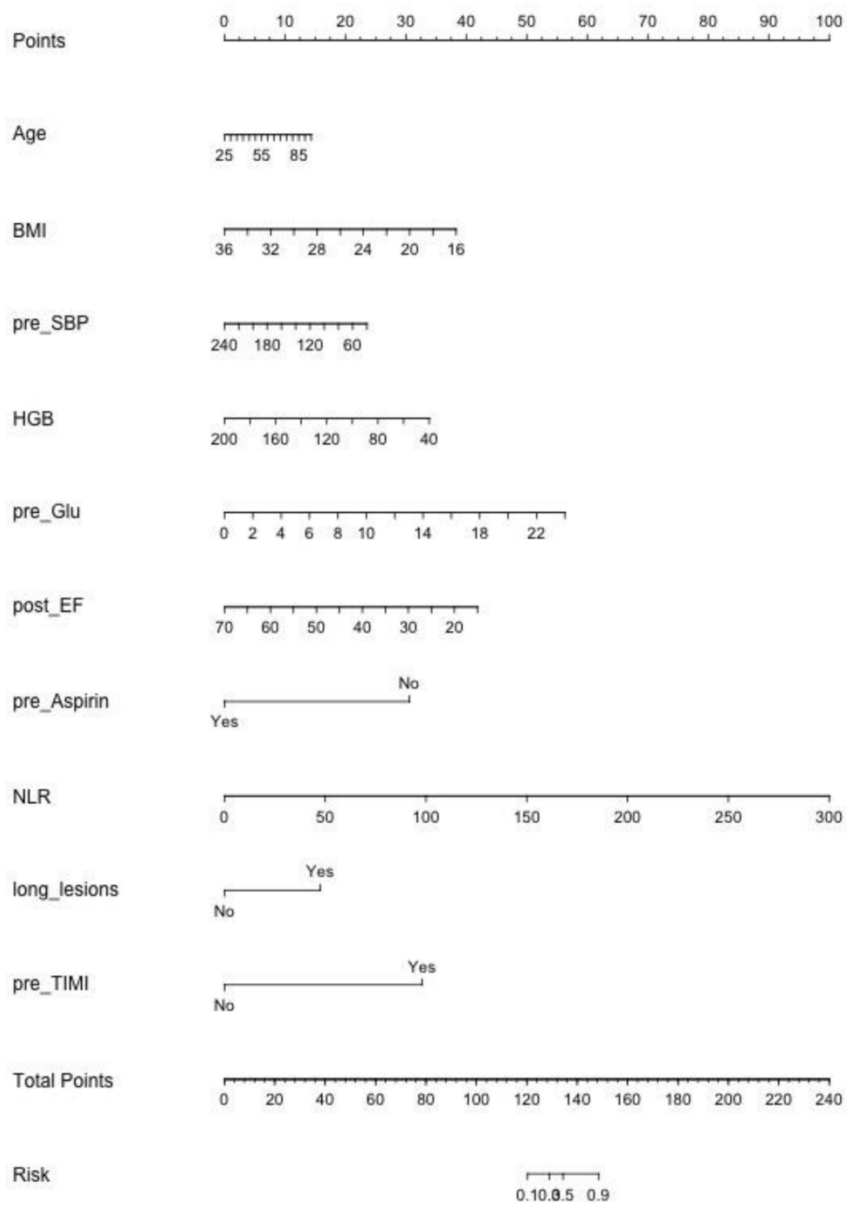


Figure 2. The nomogram for the prediction of in-hospital mortality in patients with acute ST-elevation myocardial infarction after primary PCI. BMI: body mass index; SBP: systolic blood pressure; HGB: hemoglobin; EF: ejection fraction; N/L ratio: neutrophils/lymphocytes ratio.

170x242mm (300 x 300 DPI)

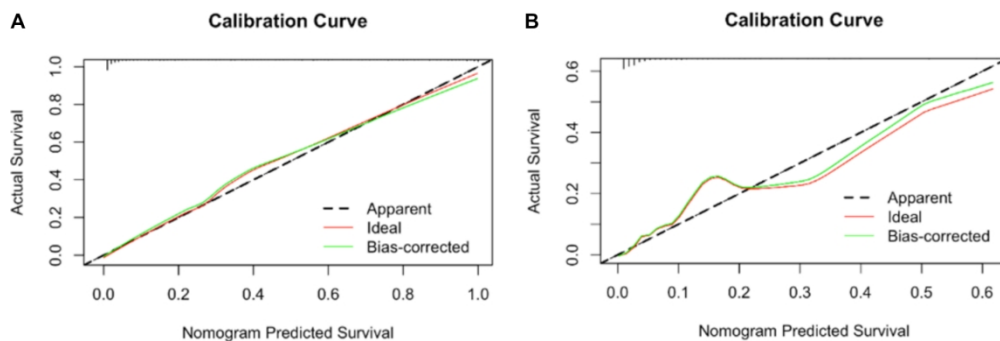


Figure 3. The calibration curves of the nomogram for the training set (A) and the testing set (B).

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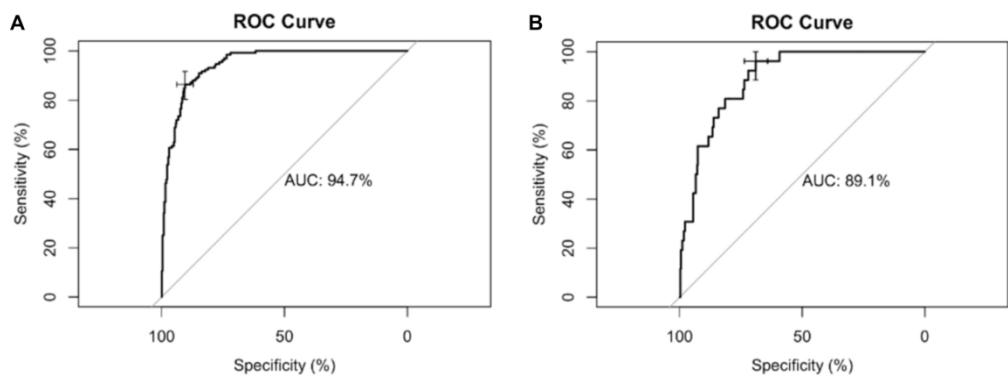


Figure 4. The received operating characteristics (ROC) curves of the nomogram for the training set (A) and the testing set (B).

170x61mm (300 x 300 DPI)

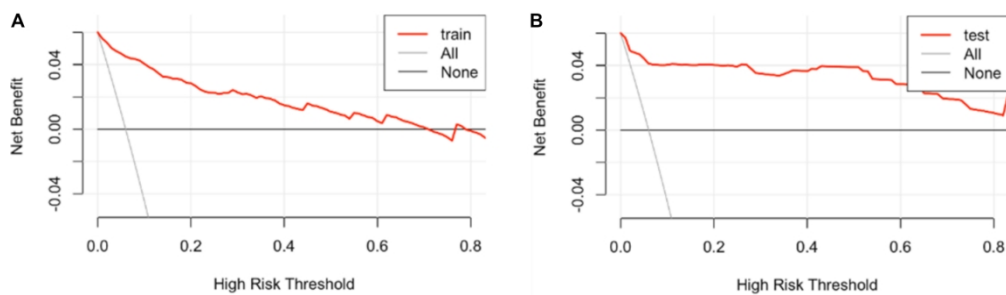


Figure 5. The decision curve analysis (DCA) for the risk model for the training set (A) and the testing set (B).

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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) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —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 <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	6
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —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) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	

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		<i>Cross-sectional study</i> —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 (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	9
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	9
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time <i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure <i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	9
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 (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	9
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 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

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Manuscript ID	bmjopen-2021-056101.R2
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Date Submitted by the Author:	18-Jan-2022
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Primary Subject Heading:	Cardiovascular medicine
Secondary Subject Heading:	Cardiovascular medicine
Keywords:	Coronary intervention < CARDIOLOGY, Coronary heart disease < CARDIOLOGY, Myocardial infarction < CARDIOLOGY

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

5
6 **Running title:** Nomogram for STEMI in-hospital mortality after PCI

7
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1 **Word count: 2996**

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3 1 **ABSTRACT**
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5 2 **Objectives:** To establish a clinical prognostic nomogram for predicting in-hospital
6 3 mortality after primary percutaneous coronary intervention (PCI) among patients with
7 4 ST-elevation myocardial infarction (STEMI).
8 5

9 6 **Design:** Retrospective, multicenter, observational study.
10 7

11 8 **Setting:** Thirty-nine hospitals in Hebei Province.
12 9

13 10 **Participants:** Patients with STEMI who underwent PCI from January 2018 to December
14 11 2019.
15 12

16 13 **Interventions:** A multivariable logistic regression model was used to identify the factors
17 14 associated with in-hospital mortality, and a nomogram was established using these
18 15 factors. The performance of the nomogram was evaluated by the discrimination,
19 16 calibration, and clinical usefulness.
20 17

21 18 **Primary and secondary outcome measures:** The outcome was the factors associated
22 19 with in-hospital mortality.
23 20

24 21 **Results:** This study included 855 patients, among whom 223 died in hospital. Age, Body
25 22 Mass Index (BMI), systolic pressure on admission, hemoglobin, random blood glucose
26 23 on admission, ejection fraction after PCI, use aspirin before admission, long lesions,
27 24 thrombolysis in myocardial infarction (TIMI) flow grade, and neutrophils/lymphocytes
28 25 ratio (N/L ratio) were independently associated with in-hospital mortality (all $P < 0.05$). In
29 26 the training set, the nomogram showed a C-index of 0.947, goodness-of-fit of 0.683, and
30 27 area under the receiver operating characteristic curve (AUC) of 0.947 (95%CI=0.927-
31 28 0.967). In the testing set, the C-index was 0.891, goodness-of-fit was 0.462, and AUC
32 29 was 0.891 (95%CI=0.844-0.939). The results indicate that the nomogram had good
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1 discrimination and good prediction accuracy and could achieve a good net benefit.

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

6
7 **Keywords:** nomogram; ST-elevated myocardial infarction; percutaneous coronary
8 intervention; in-hospital mortality

9
10 **Strengths and limitations of this study**

- 11 - This is a multi-center study, included 39 tertiary centers and 855 patients, including
12 223 (26.1%) patients who died in the hospital.
- 13 - The data were obtained retrospectively, and some patients died during the PCI, which
14 may have led to some missing information.
- 15 - Prospective studies will be necessary to confirm the performance and clinical
16 applicability and practicality of the nomogram.

1 INTRODUCTION

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

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

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

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3 1 Cardiac Troponin (cTn), Brain Natriuretic Peptide (BNP), amino-terminal pro-Brain
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5 2 Natriuretic Peptide (NT-proBNP), and D-dimer¹³⁻¹⁶. Unfortunately, these studies often
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7 3 exclude patients with advanced age, liver or kidney dysfunction, and other comorbidities
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9 4 and complications. The generalizability of those studies is limited, and it is difficult to
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11 5 summarize and reflect the real-world treatment situation comprehensively.
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13 6 Therefore, the objective of this study was to develop a clinical nomogram for predicting
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15 7 in-hospital mortality of patients with STEMI after PCI. The results could provide clinical
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17 8 guidance and improve the outcome of STEMI patients.
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1 PATIENTS AND METHODS

2 Study design and patients

3 This multicenter, retrospective, observational study included STEMI patients treated with
4 PCI at 39 PCI hospitals in Hebei Province from January 2018 to December 2019. The
5 cohort was divided into a training set and a time-independent validation set. The training
6 set refers to the use of modeled data to verify the predictive effect of the model, while test
7 set is to use another group of patients' data (namely external data) to verify the prediction
8 accuracy of the model. The training set patients enrolled from January 2018 to December
9 2018 and the testing set patients enrolled from January 2019 to December 2019.

10 All patients met the diagnostic criteria of acute STEMI based on their symptoms and/or
11 ECG, myocardial damage markers and other test results and underwent primary PCI
12 according to the 2017 ESC guidelines for the management of STEMI ⁵, namely with
13 persistent chest discomfort or other symptoms suggestive of ischemia and ST-segment
14 elevation in at least two contiguous leads. Patients with non-ST segment myocardial
15 infarction (NSTEMI) or unstable angina or STEMI patients who did not undergo PCI
16 were excluded. Patients who were re-admitted to the hospital for revascularization of
17 non-culprit vessel were also excluded. The treatment strategy after PCI of surviving
18 patients is determined by the doctor in charge in accordance with relevant guidelines.
19 The study was approved by the Ethics Committees of Hebei General Hospital as the lead
20 center and the ethics committee of each participating hospital. The requirement for
21 informed consent was waived by the committee. The study was conducted according to
22 the tenets of the Declaration of Helsinki for Medical Research Involving Human Subjects
23 and Good Clinical Practice.

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6 **Patient and Public Involvement**

7 Patients or the public were not involved in the design or reporting or dissemination plans
8 of our research as this study is a retrospective, observational study.
9

10 **Definitions**

11 Long lesions was defined as the stenosis that has as $\geq 50\%$ reduction and more than
12 20mm in luminal diameter¹⁷.

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

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

17 **Data collection**

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

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

5 **Nomogram construction**

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

15 **Statistical analysis**

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

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3 1 test or Fisher's test if the expected cell count was <5 . Student's t-test was used to
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5 2 compare normally distributed continuous variables. Otherwise, the Mann-Whitney U-test
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7 3 was used. The significance level was set at 0.05, and two-sided tests were used.
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1 RESULTS

2 Characteristics of the patients

3 The whole study population consisted of 855 patients diagnosed with STEMI and who
4 underwent PCI, including 396 in the training set (132 (33.3%) dead patients and, 264
5 (66.7%) survivors) and 459 (91 (19.8%) dead patients, 368 (80.2%) survivors) in the test
6 set (Figure 1). The clinical characteristics, including demographic, medical history,
7 angiographic characteristics, and information of cardiac procedures, medications, and
8 biochemical markers, are summarized in *supplementary file*. The Clinical characteristics
9 selected as predictors for the nomogram are summarized in Table 1. The patients who
10 died in the hospital were older (69.8 ± 10.2 vs. 60.2 ± 12.6 years, $P<0.01$), more likely to be
11 women (32.7% vs. 21.5%, $P<0.01$), and more had complications like hypertension, AF,
12 and hyperlipidemia. The hospital stay was 8.51 ± 5.11 days in the training set and
13 8.32 ± 4.70 days in the test set.

15 Nomogram construction

16 According to the multivariable logistic analysis, 10 variables meet the threshold of
17 $P<0.05$. Age (OR=1.069, 95% CI=1.048-1.092, $P=0.049$), BMI (OR=0.55, 95%
18 CI=0.31-0.87, $P=0.019$), SBP on admission (OR=0.92, 95% CI=0.86-0.97, $P=0.009$),
19 HGB (OR=0.85, 95% CI=0.73-0.97, $P=0.017$), random blood glucose on admission
20 (OR=1.53, 95% CI=1.13-2.21, $P=0.011$), EF after PCI (OR=0.89, 95% CI=0.80-0.97,
21 $P=0.015$), aspirin (OR=0.001, 95% CI=0.009-0.04, $P=0.001$), N/L ratio (OR=1.34, 95%
22 CI=1.12-1.69, $P=0.004$), long lesions (OR=2.00, 95% CI=1.310-3.084, $P<0.001$), and
23 TIMI flow grade (OR=2.15, 95% CI=1.242-3.900, $P=0.008$) were independently

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

4 $Score=15.5628+0.0320\times age-0.2991\times BMI-0.0184\times SBP-0.0331\times HGB+0.3663\times random$
5 $blood\ glucose\ on\ admission-0.1188\times LVEF\ after\ PCI-4.7705\times aspirin+0.0521\times N/L\ ratio-$
6 $2.4688\times long\ lesions+5.1018\times TIMI\ flow\ grade.$

8 **Evaluation of the nomogram**

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

15 In the testing set, the C-index was 0.891. Figure 3b shows the calibration curve, and the
16 value of goodness-of-fit was 0.462. The ROC curve is shown in Figure 4b (AUC=0.891,
17 95% CI: 0.844-0.939). The DCA curve is shown in Figure 5b. The results of the testing
18 set indicate that the nomogram had good discrimination and good prediction accuracy
19 which could achieve a good net benefit.

1 DISCUSSION

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

7 In our study, age was an independent risk factor of STEMI patients, in accordance with
8 other analyses of STEMI patients and underlining the high-risk profile of elderly patients,
9 as they usually present with more risk factors and comorbidities than younger patients¹⁹
10 ²⁰, such as the higher prevalence of renal insufficiency, lower LVEF. High mortality in
11 the older patients might also result from end-organ dysfunction, competing risks might
12 also offset the benefits from reperfusion, such that successful outcomes are more
13 dependent on overall health issues. Therefore, for older patients, some authors have also
14 questioned the benefit of reperfusion therapy²¹.

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

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

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

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

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

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

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

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

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

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

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

1 developed here. It can simplify the statistical prediction model to the numerical
2 probability of disease recurrence or death. The identification and stratification of patients
3 becomes a simple tool with many advantages. The most prominent advantage is that it
4 can predict individualized risks based on patient and disease characteristics. Secondly, it
5 is easy to use and can help doctors develop individualized treatment plans. However,
6 although the current clinical use of nomograms has increased, there are limited data on
7 patient satisfaction or quality of life after it assists in medical decision-making. In
8 addition, although nomograms are widely used clinically, they are rarely evaluated
9 prospectively to determine whether their use actually improves the prognosis of patients⁵⁹
10 ⁶⁰. Therefore, it remains to be explored how this risk model can be better applied to the
11 clinic. The results indicate that the nomogram had good discrimination, well prediction
12 accuracy and could achieve satisfactory net benefit. Another nomogram based on other
13 variables (left main coronary artery disease, grading of thrombus, TIMI classification,
14 slow flow, use of IABP, use of β -blocker, use of ACEI/ARB, symptom-to-door time,
15 symptom-to-balloon time, syntax score, LVEF, and CK-MB peak) also showed a high
16 AUC for in-hospital mortality of patients with STEMI after PCI ⁶¹. Three main reasons
17 fame justify the different predictors we found in our study: different research methods,
18 the hospitals and time nodes that included patients are different and different statistical
19 methods. Nevertheless, we are planning to combine the two parts of patients to get a more
20 accurate risk model of in-hospital mortality.

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4 1 Some study limitations should be mentioned: 1. This study has limitations that are
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6 2 inherent to retrospective observational studies. Many hospitals and doctors involved,
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9 3 which can lead to some missing information, such as liver enzymes, more information
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11 4 regarding the PCI procedure and other inflammatory index; 2. As the ischemic time is
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14 5 shortened as much as possible, patients whose symptoms and/or ECG can be diagnosed
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16 6 are directly treated with PCI. Therefore, other potential risk factors in our study, such as
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19 7 LVEF before PCI, could not be included in the analyses. And some patients died during
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21 8 the PCI, resulting in the lack of postoperative treatment information. Further prospective
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23 9 studies are still necessary to confirm the performance of the clinical applicability in future
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25 10 investigations and verify the practicality in ICU.

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30 11 In conclusion, a nomogram to predict in-hospital mortality in patients with STEMI after
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32 12 PCI was developed and validated in Hebei, China. The nomogram showed a satisfactory
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34 13 performance, with a C-index of 0.948. Thus, this nomogram might be a precisely
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36 14 individualized predictive tool for prognosis. However, additional studies are needed to
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38 15 confirm the performance and clinical applicability and practicality of the nomogram.
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10 **Competing interests**

11 The authors of this work have nothing to disclose.

13 **Ethical standards disclosure**

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

20 **Authors' contribution**

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

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

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4 **Data availability statement**

5 No additional data are available.

For peer review only

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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/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
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).

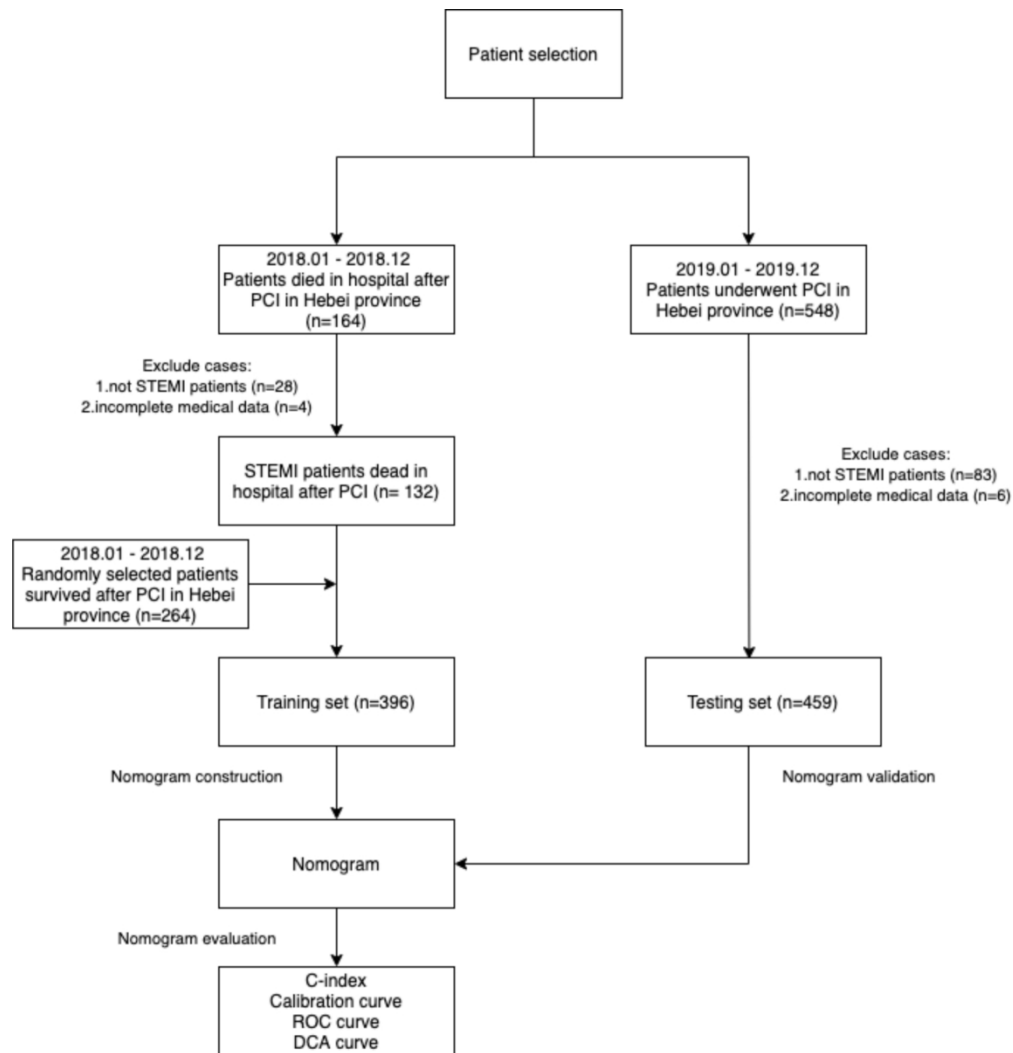


Figure 1. Flowchart illustrating the process of patient selection.

170x177mm (300 x 300 DPI)

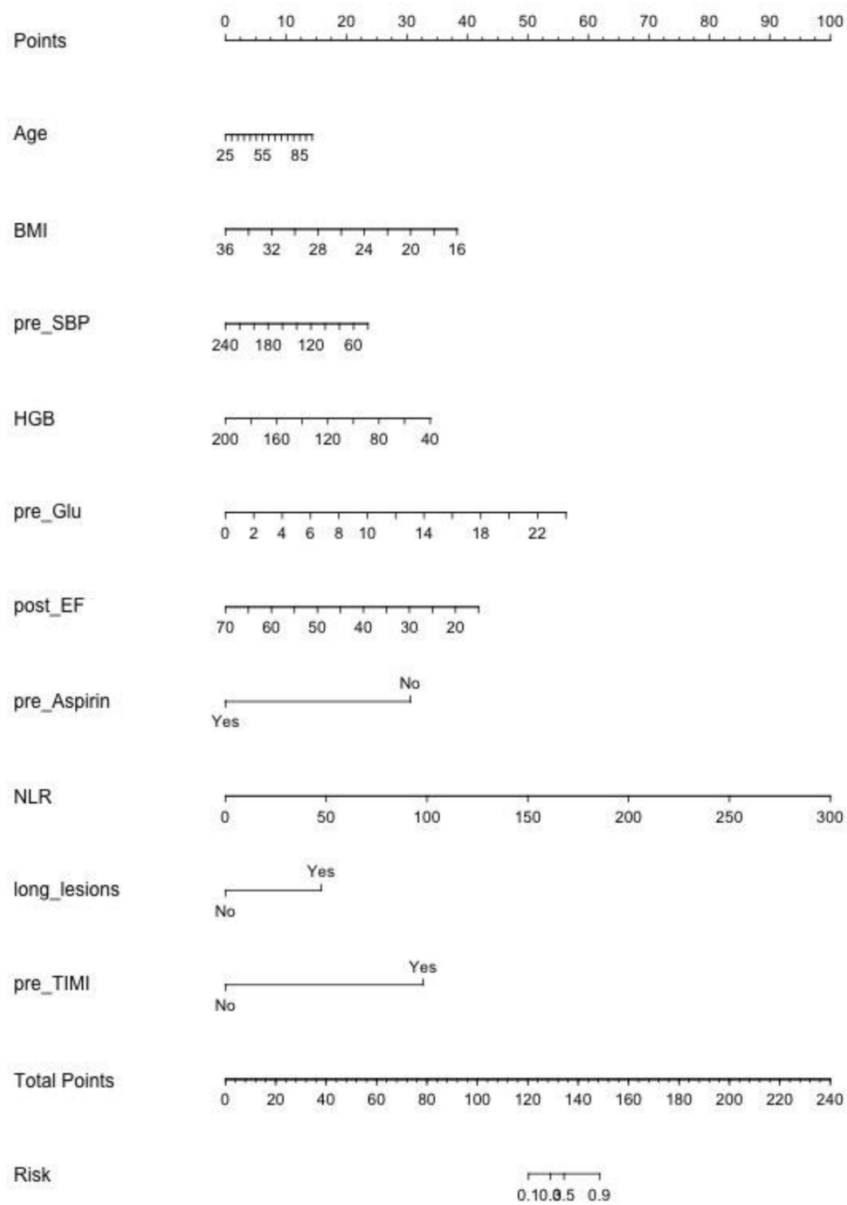


Figure 2. The nomogram for the prediction of in-hospital mortality in patients with acute ST-elevation myocardial infarction after primary PCI. BMI: body mass index; SBP: systolic blood pressure; HGB: hemoglobin; EF: ejection fraction; N/L ratio: neutrophils/lymphocytes ratio.

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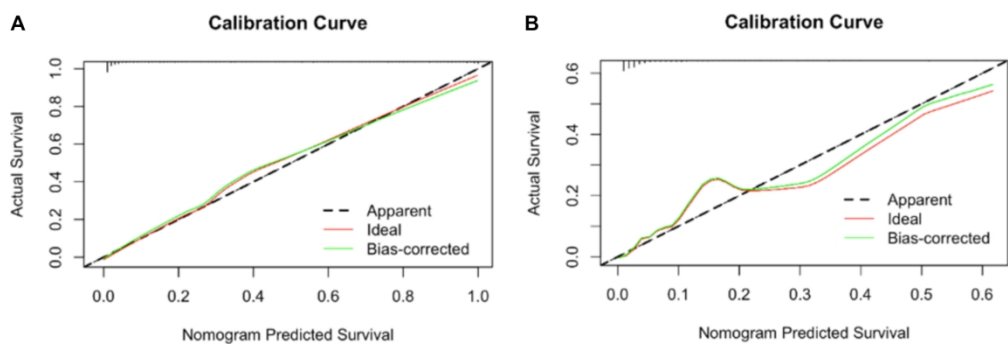


Figure 3. The calibration curves of the nomogram for the training set (A) and the testing set (B).

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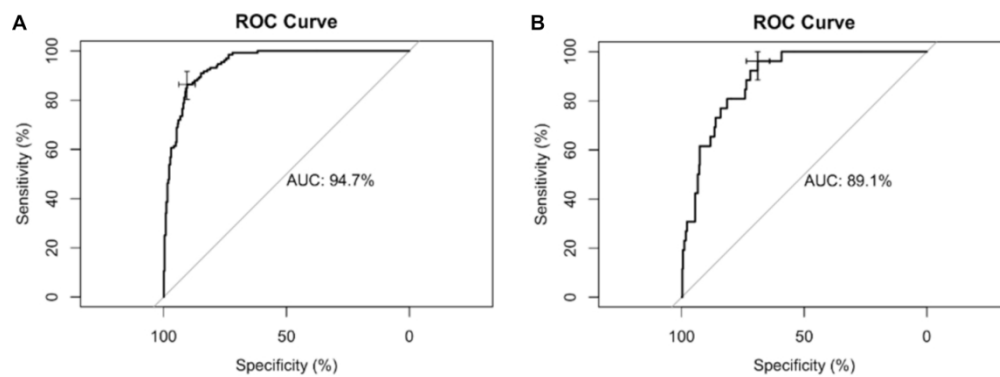


Figure 4. The received operating characteristics (ROC) curves of the nomogram for the training set (A) and the testing set (B).

170x61mm (300 x 300 DPI)

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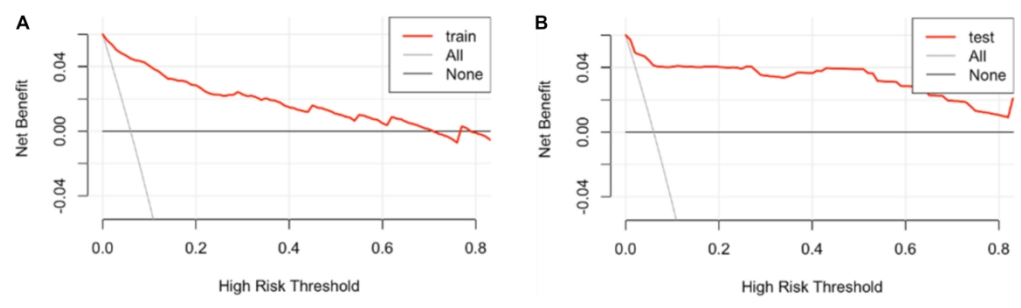


Figure 5. The decision curve analysis (DCA) for the risk model for the training set (A) and the testing set (B).

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)	<i>P</i>	All (n=459)	Survival (n=368)	In-hospital mortality (n=91)	<i>P</i>
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

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5		(n (%))							
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8	SBP on admission								
9		128 (110, 146)	133 (114, 149)	118 (100, 140)	<0.001	125 (110, 140)	129±25	121 (107, 135)	0.009
10	(median (IQR))								
11									
12	DBP on admission								
13		79 (69, 89)	82 (72, 92)	73 (62, 82)	<0.001	77±16	80±15	69±16	<0.001
14	(median (IQR))								
15									
16	Heart rate on admission								
17		77 (65, 90)	76 (64, 89)	80 (66, 96)	0.025	79±18	78±17	82±24	0.095
18	(median (IQR))								
19									
20	Fatal arrhythmia before admission								
21	(n (%))	21 (5.3)	15 (5.7)	6 (4.5)	0.812	20 (4.4)	12 (3.3)	8 (8.8)	0.021
22									
23									
24	Total ischemic time								
25		217 (124, 367)	154 (95, 250)	360 (194, 420)	<0.001	211 (130, 341)	194 (125, 307)	300 (222, 480)	<0.001
26	(min (median (IQR)))								
27									
28	Killip class 3-4								
29	(n (%))	132 (33.3)	95 (36.0)	37 (28.0)	0.142	119 (25.9)	66 (17.9)	53 (58.2)	<0.001
30									
31	Past medical history								
32									
33	<i>Hypertension</i>								
34	(n (%))	211 (53.3)	137 (51.9)	74 (56.1)	0.499	73 (15.9)	38 (10.3)	35 (38.5)	<0.001
35									
36	<i>DM</i>								
37	(n (%))	96 (24.2)	49 (18.6)	47 (35.6)	<0.001	104 (22.7)	84 (22.8)	20 (22.0)	0.863
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5	<i>Hyperlipidemia (n (%))</i>	39 (9.8)	12 (4.5)	27 (20.5)	<0.001	41 (8.9)	23 (6.3)	18 (19.8)	<0.001
6									
7	<i>Previous PCI (n (%))</i>	18 (4.5)	8 (3.0)	10 (7.6)	0.073	23 (5.0)	17 (4.6)	6 (6.6)	0.44
8									
9	<i>Previous CABG (n (%))</i>	1 (0.2)	0	1 (0.8)	0.157	1 (0.2)	0	1 (1.1)	0.05
10									
11									
12	<i>CAD (n (%))</i>	45 (11.4)	17 (6.4)	28 (21.2)	<0.001	40 (8.7)	20 (5.4)	20 (22.0)	<0.001
13									
14	<i>AF (n (%))</i>	11 (2.8)	1 (0.4)	10 (7.6)	<0.001	13 (2.8)	3 (0.8)	10 (11.0)	<0.001
15									
16	<i>HF (n (%))</i>	4 (1.0)	3 (1.1)	1 (0.8)	0.722	25 (5.4)	18 (4.9)	7 (7.7)	0.292
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19	<i>Renal insufficiency (n (%))</i>	62 (15.7)	1 (0.4)	61 (46.2)	<0.001	13 (2.8)	1 (0.3)	12 (13.2)	<0.001
20									
21	<i>History of cerebrovascular disease (n (%))</i>	64 (16.2)	40 (15.2)	24 (18.2)	0.53	72 (15.7)	60 (16.3)	12 (13.2)	0.464
22									
23									
24	<i>Peripheral vascular disease (n (%))</i>	9 (2.3)	5 (1.9)	4 (3.0)	0.721	5 (1.1)	3 (0.8)	2 (2.2)	0.255
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27									
28	<i>History of bleeding (n (%))</i>	2 (0.5)	1 (0.4)	1 (0.8)	>0.999	7 (1.5)	6 (1.6)	1 (1.1)	0.711
29									
30	<i>Family history of CAD (n (%))</i>	44 (11.1)	28 (10.6)	16 (11.1)	0.875	68 (14.8)	62 (16.8)	6 (6.6)	0.014
31									
32									
33	Angiographic characteristics								
34									
35	<i>Number of stents (median (IQR))</i>	1 (1, 1)	1 (1, 1)	1 (0, 1)	<0.001	1 (1, 1)	1 (1, 1)	1 (1, 1)	0.137
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5	<i>Long lesions (n (%))</i>	245 (61.9)	178 (67.4)	67 (50.8)	0.002	194 (42.3)	131 (35.6)	63 (69.2)	<0.001
6									
7	<i>Thrombus aspiration (n (%))</i>	123 (31.1)	92 (34.8)	31 (23.5)	0.029	221 (48.1)	205 (55.7)	16 (17.6)	<0.001
8									
9	<i>Residual stenosis (n (%))</i>	12 (3.0)	2 (0.8)	10 (7.6)	0.001	10 (2.2)	4 (1.1)	6 (6.6)	0.001
10									
11	<i>Use temporary pacemaker (n (%))</i>	22 (5.6)	4 (1.5)	18 (13.6)	<0.001	9 (2.0)	2 (0.5)	7 (7.7)	<0.001
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13									
14	<i>IABP (n (%))</i>	19 (4.8)	4 (1.5)	15 (11.4)	<0.001	15 (3.3)	4 (1.1)	11 (12.1)	<0.001
15									
16	<i>Respirator support (n (%))</i>	20 (5.1)	1 (0.4)	19 (14.4)	<0.001	13 (2.8)	2 (0.5)	11 (12.1)	<0.001
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18									
19	<i>Pericardial aspiration (n (%))</i>	3 (0.8)	0	3 (2.3)	0.065	3 (0.7)	0	3 (3.3)	<0.001
20									
21	<i>No flow (n (%))</i>	98 (24.7)	48 (18.2)	50 (37.9)	<0.001	84 (18.3)	55 (14.9)	29 (31.9)	<0.001
22									
23	<i>Coronary perforation (n (%))</i>	5 (1.3)	0	5 (3.8)	0.001	2 (0.4)	1 (0.3)	1 (1.1)	0.283
24									
25									
26	<i>Dissection (n (%))</i>	3 (0.8)	0	3 (2.3)	0.065	5 (1.1)	0	5 (5.5)	<0.001
27									
28	<i>Pericardial tamponade (n (%))</i>	9 (2.3)	0	9 (6.8)	<0.001	2 (0.4)	0	2 (2.2)	0.004
29									
30	<i>Acute HF (n (%))</i>	55 (13.9)	22 (8.3)	33 (25.0)	<0.001	52 (11.3)	30 (7.7)	22 (24.2)	<0.001
31									
32	<i>Bleeding (n (%))</i>	2 (0.5)	0	2 (1.5)	0.21	6 (1.3)	3 (0.8)	3 (3.3)	0.062
33									
34									
35	<i>Cardiac arrest (n (%))</i>	24 (6.1)	1 (0.4)	23 (17.4)	<0.001	14 (3.1)	6 (1.6)	8 (8.8)	<0.001
36									
37	<i>Recurrent MI (n (%))</i>	16 (4.0)	1 (0.4)	15 (11.4)	<0.001	7 (1.5)	2 (0.5)	5 (5.5)	0.001
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5	<i>Stent thrombosis (n (%))</i>	8 (2.0)	6 (2.3)	2 (1.5)	0.9	14 (3.1)	13 (3.5)	1 (1.1)	0.227
6									
7	<i>Type B2-C (n (%))</i>	309 (78.0)	213 (80.7)	96 (72.7)	0.094	277 (60.3)	230 (62.5)	47 (51.6)	0.058
8									
9	<i>TIMI flow grade 0-1 before PCI</i>								
10									
11	<i>(n (%))</i>	311 (78.5)	197 (74.6)	114 (86.4)	0.011	339 (73.9)	274 (74.5)	65 (71.4)	0.556
12									
13	<i>Use of GP IIb/IIIa inhibitors (n</i>								
14	<i>(%))</i>	92 (23.2)	54 (20.5)	38 (28.8)	0.064	107 (23.3)	80 (21.7)	27 (29.7)	0.109
15									
16	<i>multivessel CAD (n (%))</i>	316 (79.8)	207 (78.4)	109 (82.6)	0.33	373 (81.3)	296 (80.4)	77 (84.6)	0.36
17									
18	<i>LAD (n (%))</i>	149 (37.6)	85 (32.2)	64 (48.5)	0.002	209 (45.5)	177 (48.1)	32 (35.2)	0.027
19									
20	<i>LCX (n (%))</i>	59 (14.9)	39 (14.8)	20 (15.2)	0.921	64 (13.9)	46 (12.5)	18 (19.8)	0.072
21									
22	<i>RCA (n (%))</i>	101 (25.5)	101 (38.3)	40 (30.3)	0.119	144 (31.4)	120 (32.6)	24 (26.4)	0.251
23									
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26	<i>Biochemical markers</i>								
27									
28	<i>Hyperkalemia (n (%))</i>	36 (9.1)	3 (1.1)	33 (25.0)	<0.001	30 (6.5)	11 (3.0)	19 (20.9)	<0.001
29									
30	<i>Hyponatremia (n (%))</i>	29 (7.3)	12 (4.5)	19 (14.4)	0.001	37 (8.1)	31 (8.4)	6 (6.6)	0.566
31									
32	<i>Anemia (n (%))</i>	26 (6.6)	12 (4.5)	14 (10.6)	0.022	40 (8.7)	21 (5.7)	19 (20.9)	<0.001
33									
34	<i>Creatinine (median (IQR))</i>	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
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<i>N/L ratio (median (IQR))</i>	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
<i>HCT, % (median (IQR))</i>	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
<i>HGB, g/L (median (IQR))</i>	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
<i>PLT, ×10⁹/L (median (IQR))</i>	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
<i>Random blood glucose on admission, mmol/L (median (IQR))</i>	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
<i>EF after PCI (median (IQR))</i>	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								
<i>(n (%))</i>								
<i>Aspirin</i>	379 (95.7)	262 (99.2)	117 (88.6)	<0.001	404 (88.0)	332 (90.2)	72 (79.1)	0.004
<i>Ticagrelor/clopidogrel</i>	393 (99.2)	262 (99.2)	131 (99.2)	>0.999	418 (91.1)	332 (90.2)	86 (94.5)	0.199

	<i>Ticagrelor</i>	223 (56.3)	162 (61.4)	61 (46.2)		218 (47.5)	183 (49.7)	35 (38.5)	
	<i>clopidogrel</i>	170 (42.9)	100 (37.9)	70 (53.0)		200 (43.6)	149 (40.5)	51 (56.0)	
	<i>ACEI/ARB</i>	133 (33.6)	100 (37.9)	33 (25.0)	0.014	25 (5.4)	18 (4.9)	7 (7.7)	0.292
	<i>β-Blocker</i>	92 (23.2)	66 (25.0)	26 (19.7)	0.239	37 (8.1)	29 (7.9)	8 (8.9)	0.753
	<i>Statin</i>	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) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —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 <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	6
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —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) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	

		<i>Cross-sectional study</i> —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 (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	9
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	9
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time <i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure <i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	9
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 (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	9
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 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.