Development and validation of a prediction rule of major adverse cardiac and cerebrovascular event for high-risk STEMI patients after primary percutaneous coronary intervention

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Research

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Abstract

Background and Aims We aimed to develop a clinical prediction tool to improve the prognostication of major adverse cardiac and cerebrovascular events (MACCE) among high-risk myocardial infarction (MI) patients undergoing primary PCI.

Methods Among 4151 consecutive MI patients who underwent primary percutaneous coronary intervention (PPCI) from FuWai Hospital in BeiJing, China (January 2010 and June 2017), and a prediction rule was derived from derivation and internally validation cohort to predict MACCE after PPCI. Subject must have met at least one clinical criterion and at least one angiographic criterion to be eligible for treatment in the study. The predictive values of markers and clinical variables were assessed with least absolute shrinkage and selection operator (LASSO) regression. The most important variables were included in the score with weights proportional to the model coefficients.

Results The full model included 7 variables, and the risk score was total 160 points. The full model had similar discriminatory value across pre-specified subgroups and was well calibrated. Derivation cohort models predicting MACCE events had C statistics of 0.695 and 0.673, respectively. The areas under curve (AUC) of the survival receiver operator characteristic curve (ROC) were 0.991 and 0.883 in derivation and validation cohort among 3-year follow-up for predicting the MACCE events. The relative high risk group was observed to have significantly greater likelihood of occurrence of all-caused death, recurrence MI, heart failure, ischemic stroke, hemorrhagic stroke and revascularization compared with the low risk group ($p<0.05$ respectively).

Conclusion The predicted model was internally validated and calibrated in large cohorts of patients with high risk MI receiving primary PCI therapy to predict the MACCE event and showed modest accuracy in derivation and validation cohorts.

Introduction

Early primary percutaneous coronary intervention (PPCI) has now been set up as the first-line treatment for subjects who has acute myocardial infarction (MI) [1]. A randomized trial of moderate size [2-7] showed there is a significant increase in major adverse cardio-cerebral events (MACCE) after undergoing the PPCI. Indeed, in high-risk patients and lesion subsets, including those older than 65 years old, with renal dysfunction, diabetes mellitus (DM), thrombotic target lesion and multi-vessel disease residual athero-thrombotic risk remains substantial. Framingham Heart Study investigators have developed various cardiovascular disease risk prediction project which identified high-risk patients more precise than the conventional classification. It is beneficial and effective that pretreatment risk factors to reduce the risk of cardiovascular disease within patients who are evaluated as high-risk with multivariable prediction equations than treating patients with high levels of single risk factors [8, 9]. However, few tools are provided to assess the incidence of MACCE events among high-risk MI subjects undergoing primary PCI to guide long-term risk management. Using these specific data elements, a new risk score project was

created, with which we sought to: 1) define major independent predictors of MACCE among MI patients with high-risk after undergoing PPCI; and 2) develop and validate a full pre-procedure risk prediction model which adapted to individuals based on precision medicine, healthcare decisions. We present the following article in accordance with the TRIPOD reporting checklist (Appendix file)[1].

[1] The authors have completed the TRIPOD reporting checklist

Material And Methods

Study population – enrollment and randomization

This observational, retrospective cohort study analyzed data from Fuwai Hospital, National Center for Cardiovascular Diseases, Peking Union Medical College & Chinese Academy of Medical Sciences from a total of 4151 consecutive MI patients who underwent primary PCI at FuWai Hospital in BeiJing, China, between January 2010 and June 2017, were enrolled. 48 patients without follow-up data were excluded from the study. Enrollment into the study will require meeting at least one of the clinical inclusion criteria and one of the angiographic inclusion criteria but none of the exclusion criteria, as shown in figure 1. Clinical criteria included: 1) adult patients ≥65 years of age; 2) female gender; 3) documented PAD or CAD/PAD revascularization; 4) diabetes mellitus; 5) chronic kidney disease;6) troponin positive. The angiographic criteria included: 1) multi-vessel coronary artery disease; 2) target lesion requiring total stent length>30 mm; 3) thrombotic target lesion; 4) bifurcation lesions; 5) left main (≥50%) or proximal LAD (≥70%) lesion; 6) calcified target lesion. These pre-specified criteria were chosen to enroll STEMI patients at high risk for MACCE complications after PCI. Elements are included in validated risks score-projects for either ischemic, bleeding or both types of complications after PCI [10-18]. The R software was used to divide the derivation cohort and the validation cohort randomly and proportionally (70%:30%). All patients were referred to the coronary catheterization center with the diagnosis of MI fulfilling the criteria for PPCI according to the guidelines [19, 20]. The study was approved by the Ethics Committee of Fuwai Hospital, and all patients enrolled will require providing written informed consent for coronary angiography and PPCI. Patient records, including demographics, medical history, physical examination, blood test results, electrocardiography (ECG), echocardiography data, and discharge medication regimen was reviewed. Blood testing was performed at the clinical laboratory in Fuwai Hospital. Experimental protocols and the process for obtaining informed consent were approved by the appropriate by Fuwai hospital institutional review committee. This investigation conformed to the principles outlined in the Declaration of Helsinki. We stated that informed written consent was given prior to the inclusion of subjects in the study.

Definitions and primary outcome

The primary outcome for this analysis was MACCE which defined as the composite of all-cause death, recurrence myocardial infarction, stroke (including ischemic stroke and hemorrhagic stroke), heart failure or target-vessel revascularization. Hypertension was defined as blood pressure ≥140/90 mmHg in three occasions at rest or previous diagnosis of hypertension and current use of antihypertensive drugs.

Diabetes mellitus (DM) was defined according to the 75-g oral glucose tolerance test (OGTT), that is, patients were diagnosed with DM if they met one of the following criteria: (i) fasting plasma glucose level of ≥7.0 mmol/L, (ii) 2-h value of ≥11.1 mmol/L in 75-g OGTT, and (iii) casual plasma glucose level of ≥ 11.1 mmol/L. Dyslipidemia was defined by any of the following parameters: total cholesterol (TC) 5.0 mmol/L, low-density lipoprotein cholesterol (LDL-C) ≥3.0 mmol/L, triglycerides (TG) ≥1.7 mmol/L, high-density lipoprotein cholesterol (HDL-C) ≥ 1.2 mmol/L (women) or ≥ 1.0 mmol/L (men), or statin treatments. Height and weight were measured by trained medical staff; body mass index was calculated by weight (kg)/height squared (m^2). No-reflow phenomenon was defined as thrombolysis in myocardial infarction (TIMI) flow grade <3 after PPCI. Stroke is defined by the World Health Organization (WHO) Multinational Monitoring of Trends and Determinants in Cardiovascular diseases (MONICA) standard. Stroke is defined as a rapidly developing focal or general brain dysfunction which lasts for more than 24 hours or causes death excluding non-vascular causes (such as trauma, metabolic disorders, tumors and any neurological abnormalities caused by CNS infection). According to the imaging examination in the first week of onset, the neurologist diagnosed stroke included subarachnoid hemorrhage, intracranial hemorrhage, cerebral thrombosis and cerebral embolism. Hemorrhagic stroke includes subarachnoid hemorrhage and intracranial hemorrhage. Furthermore, ischemic stroke includes cerebral thrombosis and cerebral embolism. Transient ischemic attack (TIA) and chronic cerebrovascular disease are not included. The outcome of this study included only initial stroke. Investigators collected data including head CT, head MRI, hospital records from patients during their hospitalization. The STROBE checklist has been provided as a supplementary figure.

Statistical analysis

The normal distribution of outcome variables was confirmed by Kolmogorov–Smirnov tests. Categorical variables are summarized as frequencies (percentages) and compared with person chi-square tests. Continuous variables are presented as the median and compared using independent t-test. Characteristic of the derivation cohort and validation cohort are showed in table 1. The study population was randomly split into a development sample consisting of 70% of admissions and a validation sample consisting of the remaining 30% of admissions. Baseline patient characteristics and variables from coronary angiography and diagnostic catheterization were considered candidate variables and all prespecified. Candidate variables had <1.8% missing data except for the use of IABP (27%), ApoA (29.2%) and uric acid (12.6%). The variables included in the least absolute shrinkage and selection operator (LASSO) regression were showed in the appendix table 1 and it was used to screen the independent variables to draw the corresponding nomogram model.

We developed a predicting model using all potential predictive variables selected by LASSO regression. We also developed a risk prediction score by taking the regression coefficients from the pre-procedure model and assigning them an integer weighted associated with the risk factors. The corresponding nomogram model is drawn according to the regression coefficient of the selected independent variables. For the variables selected in the nomogram model, the values of different variables can correspond to different scores on the integral line at the top of the nomogram (the score range is 0-160 points) through

the projection of the vertical line, and the total score can be obtained by adding up the scores corresponding to the values of each variable. The cumulative occurrence probability of MACCE events in 3 and 5 years can be obtained from the total score on the prediction line at the bottom of the nomogram.

In order to reduce the over-fitting bias, the self - sampling method is used to verify the nomogram model. The Harrell's C-statistic was used to compare discrimination between derivation cohort and validation cohort including 3-year and 5-year. Calibration plots were used to access goodness of fit. We draw the survival receiver operator characteristic curve (survival ROC curve) by R language. Survival ROC curves export the best cut-off values and divided into low risk group and high risk group by R language. We conducted the K-M survival analysis between two groups and export the discrepancy result of the analysis. The subgroup of the K-M curves included the all-caused death, recurrence MI and stroke during 3 and 5 years. LASSO method adopts glmnet package of R language for variable selection, and RMS package of the R language for drawing and internal verification of nomogram (c-index and calibration chart). The cox regression analysis was performed using the survival package. The main statistical analysis software used in this study is the R language version I 386 3.6.2. Other analyses were performed with SPSS version 20.0 statistical software (SPSS, Inc., Chicago, IL.). A p value <0.05 was considered statistically significant. All statistical tests were 2 sided.

Performance and internal validation of new risk prediction equations

The baseline survival probabilities of each model were obtained by the R language version I 386 3.6.2 commands that were utilized to fit the models. Calibration performance was assessed graphically to predict 3-year and 5-year MACCE events risk and to plot 3-year and 5-year predicted risk against observed 3-year and 5-year risk. A diagonal line with a slope of 1 represents perfect calibration. Observed 3-year and 5-year risk was obtained by the Kaplan-Meier method, and the slopes of regression lines comparing predicted versus observed 5-year risk were calculated. Standard statistical metrics of model and discrimination performance (R^2, Harrell's C statistic) were calculated. The calibration and discrimination performance of equations developed in the derivation sub-cohort was assessed in the validation sub-cohort and compared with the performance of models developed in the entire cohort; baseline survival functions and hazard ratios were also compared. Indicators of internal verification include c-index and calibration degree, which respectively represents the prediction accuracy and prediction consistency of the nomogram prediction model. The degree of calibration is represented by a calibration graph. ROC plotting was used for the survival roc package.

Results

Patient demographics of derivation and validation cohort

Between Jan 1, 2010, and Jun 30, 2017, the study population included 4151 men and women and excluded 48 people without following up. After applying inclusion criteria, 3404 high-risk MI subjects remained. The average follow up time was 3 year. Subject must have met at least one clinical and at least one angiographic criteria to be eligible for treatment in the study. 2384 people constituted the derivation

cohort and 1020 cases consisted of validation cohort used in these analyses by random allocation (figure 1). Candidate variables had <1.8% missing data except for the use of IABP (27%), ApoA (29.2%) and uric acid (12.6%). Table 1 displays the baseline patient, procedure, and hospital characteristics of the development and validation samples. There were 578 high-risk MI subjects that had MACCE events in derivation cohort after undergoing PPCI procedures, yielding a MACCE event rate of 24.24%. Of these events, 25.09% were all-caused death; whereas 14.09% were detected due to recurrence MI, 60.07% by revascularization, 3.99% by heart failure, 8.15% by ischemic stroke and 1.39% were hemorrhagic stroke.

Screening risk factors for MACCE by LASSO method

Baseline patient characteristics and variables from coronary angiography and diagnostic catheterization were considered candidate variables and all prespecified (appendix table 1). These variables were filtered by the method of LASSO regression. The filtering and cross-validation processes of independent variables are shown in figure 2A1 and 2A2 respectively. Lambda.1se is the lambda value of the optimal efficiency model in the standard error range which gives a model with excellent performance.

The establishment of risk prediction model

At this time, a total of 7 independent variables (the subgroup of age, Killip classification, ejection fraction, history of CABG, type of lesions, complete revascularization at admission and multi-vessel disease of coronary artery) were included in the predictive model. The forest plot of the variables which conducted by the multivariate cox regression was shown in the figure 2B and the binary decision diagram of the variables was shown in figure 2C. It is necessary to make the classification variables into factorization and then use the as.matrix() function to convert the data from the non-matri x format to the matrix format before the R language "glmet" package can call the data. According to the nomogram model (figure 2D), the score predicting project included 7 variables as the variables of predictive factors.

Clinical Prediction Score

A simplified risk score was generated to predict MACCE events. The score, ranging from 0 to 160, assigned points as follows: for patients younger than 40 years, 100 points; for age 40 to younger than 50 years, 80 points; for age 50 to younger than 60 years, 60 points; for age 60 to younger than 70 years, 40 points; for age 70 to younger than 80 years, 20 points; for patients 80 years or older,0; for Killip II, 7.68; for Killip III, 15.36; for Killip IV, 23.03; for EF at admission≦50%, 4.62; for previous history of CABG, 20; for in-stent restenosis, 4.81; for stent thrombosis, 9.62; for without complete revascularization, 3.45; for multi-vessel lesion, 18 (Figure2E). The elements of clinical prediction score and distribution of score among high-risk MI patients who undergent PPCI was shown in figure 2E.

The performance of risk score project

The MACCE predicting risk model had good discrimination in both the development and validation samples (c-index, development sample 0.695; validation sample 0.673). The model calibration plot for the full model is shown in Figure 3A-D. There was high concordance between the risk predicted by the

models and the observed MACCE events. Calibration is indicated by the estimated risk against survival from Kaplan- Meier analysis. Gray line represents perfect calibration. Figure 3E-H shows survival (time-dependent) ROC curves for the discriminatory value of the 3–year and 5-year evaluation performance of the risk prediction model. The cutoff points of 3-year and 5-year survival ROC curves were 0.22663, 0.09733 and the area under curve (AUC) were 0.991 and 0.931 in the derivation cohort. On the other hand, the cutoff points of 3-year and 5-year survival ROC curves were -0.35597, -0.35597 and AUC were 0.883 and 0.883 in the validation cohort in 3-year and 5-year survival ROC curves. Appendix Figure 1A-D showed the decision curve analysis of 3-year and 5-year in the derivation and validation cohort.

Survival ROC curves export the best cut-off values and divided into relative low risk group and high risk group by R language. We conducted the K-M survival analysis (Figure 4A-P) and export the discrepancy result of the analysis. In the group of predicting MACCE events, the two groups displayed significant difference in both derivation cohort ($p<0.001$) and validation cohort ($p<0.001$) shown in figure 4A-D. In the subgroup of predicting all caused death, it is remarkable difference ($p<0.001$) between the high risk group and relative low risk group in both development and validation group (figure 4E-H). Furthermore, when the endpoint was recurrence MI, the logrank p value was less than 0.02 in the 3-year derivation cohort and p less than 0.01 in the 5-year K-M curve in derivation cohort (figure 4I-L). Finally, we also found distinct discrepancy in predicting the stroke ($p<0.05$) (figure4 M-P) events in 3-year and 5-year development and validation cohort.

Discussion

This study developed a clinical prediction score based on clinical and coronary angiology index to help predicting the incidence of long-term MACCE events among MI patients with greater risk factors underwent primary PCI. The MACCE predicting risk model had good discrimination in both the development and validation samples (c-index, validation sample 0.673; development sample 0.695). For patients who divided into relative low risk group and high risk group by best cut-off values in the prediction model study (derivation cohort), the relative high risk group was observed to have significantly greater likelihood of occurrence of all-caused death, recurrence MI, heart failure, ischemic stroke, hemorrhagic stroke and revascularization compared with the low risk group. These results suggest that it may be possible to identify individual patients with discordant the incidence of MACCE. Although prediction score project is expected to be applied to the subjects represented by enrollment criteria, inconsistent in setting up treatment risks and benefits, adjusting treatment according to personal data, provides opportunities for further optimization results in order to maximize benefits and reduce harm. Yet few equivalent scores are available for use in high-risk patients with acute myocardial infarction undergoing primary PCI to predict the MACCE events. For these patients, cardiac imaging, coronary angiography and advanced biomarkers are routinely available at admission period, so it is convenient to include them in a score for this setting for long- term management.

The thing that matters, a lot of patient characteristics were correlated with long-term of the incidence of MACCE. Many of the predictive elements which we have identified have been shown in many other

studies to be predictive of MACCE events. For instance, age is consistently associated with an increased risk of the incidence of MACCE [21], as are other variable like killip classification, EF at admission, history of CABG and multi-vessels lesion of coronary artery [22]. In addition to these factors, we also identified unique variables not present in other predicting models, such as the complete revascularization and the type of lesion detected by the coronary angiography. The addition of such forecasting factors is a noteworthy superiority where the acuity of clinical presentation is generally not as severe compared with previous models that merely included clinical characteristics. It is conspicuous to minimize the risk of the inappropriate care and management for MI patients with high-risk characteristics who undergoing primary PCI by including these factors. Bleeding complications including hemorrhagic stroke after primary PCI are not rare and it is correlated with an increased short-term and long-term risk of mortality [23, 24]. It has been proposed to drop the hemorrhage among higher-risk patient subjects by the using of vascular closure devices, bivalirudin and radial approach which called bleeding avoidance strategies [25-28]. Therefore, this model can be used to predict the long-term incidence of MACCE events for the high-risk MI subjects' post-PCI, identify leaders and laggards, and ultimately improve the long-term prognostic of primary PCI by making healthcare decisions in the follow-up and encouraging the adoption of taking corresponding measures at admission.

According to the present model, the score predicting project included 7 variables (age, Killip classification, ejection fraction, history of CABG, type of lesions, complete revascularization at admission and multi-vessel disease of coronary artery) as the variables of predictive factors. Previous analyses [29, 30] have also identified that the risk factors including age, atrial fibrillation, female sex, killip classification, as well as chronic disease could predict the incidence of stroke within 12-months of PCI which are generally accordance with classic risk variables in the general population. Stroke including ischemic and hemorrhagic are devastating complications with high MACE rates and mortality following PCI. Similarly database derived from the British Cardiovascular Intervention Society (BCIS) has reported ischemic stroke was independently associated with both 30-day mortality and in-hospital MACE by following adjustment for baseline clinical and procedural demographics [31]. Previously, Luke P et al [32] demonstrated that the incidence of stroke among outpatients following percutaneous coronary intervention are higher for younger instead of older comparing to the general population. It is coincident with our score projection that age less than 40 years old contributed the greater weight compared with other groups of age. Furthermore, during the beginning period of cardiac catheterization (1970-1980s), the incidence of cerebrovascular events was ranged from 0.03% to 0.06% [33] comparing to 0.18%–0.44% during the following years. The increasing in the incidence of stroke-complicating PCI might account for extended use of PCI and coronary angiography especially among subjects with severe vascular calcification [34]. The time of risk assessment post-event and cardiovascular disease is both the main factors to evaluate the performance of the risk score for secondary prevention. The research of CALIBER [35] enrolled 102 023 stable CAD subjects and developed a risk score for people with stable CAD to identify patients at high risk and stand by a management decision.

Study Limitation

Several limitations of our study should be considered in interpreting these results. On the basis of the clinical and angiography inclusion and exclusion criteria of the trial, as well as the single-center and retrospective study design, score project of model should be interpreted with the understanding that patients enrolled in clinical trials may not be completely representative of those cared for in routine practice of primary PCI. The analysis ought to be regarded as exploratory despite the predetermination of the score variables. Therefore, the predictive score should be used with circumspection until further external validation is carried on. Optimal and suitable long-term management of procedural and care should be administered independent of the patient's score to reduce overall MACCE events. Furthermore, the extent and severity of granular measures of atherosclerosis were not available and the situation of receiving ticagrelor or other antiplatelet combinations may in part make a difference to the discrimination of the cohort and have a different risk benefit relationship [36]. Finally, cerebrovascular events are determined by contacting the subjects followed by validation through medical records. In spite of it is probably to cover almost all hemorrhagic stroke and ischemic strokes, it may undervalue stroke incidence if the patients were asymptomatic and not admitted to hospital.

Conclusion

In summary, we developed a risk predicted model for estimating long-term (3-year and 5-year) incidence of MACCE based on clinical parameters and indexes of coronary angiography which suit for high-risk subjects with MI who underwent primary PCI. The score project can be implemented alongside further medical investigations to support therapeutic decision making. This project requires further prospective assessment to evaluate potential impacts on subjects' management, as well as external validation in other cohorts.

Abbreviations

I, myocardial infarction	HDL-C, high-density lipoprotein cholesterol
PCI, primary percutaneous coronary tervention	TIMI, thrombolysis in myocardial infarction
ASSO, least absolute shrinkage and selection perator	WHO, World Health Organization
F, atrial fibrillation	SBP, systolic blood pressure
UC, areas under curve	TIA, Transient ischemic attack
OC ,survival receiver operator characteristic urve	SE, standard error
CG , electrocardiography	CABG, history of coronary artery bypass grafting
M, Diabetes mellitus	Crea, creatinine
GTT, oral glucose tolerance test	eGFR, estimated glomerular rate
C, total cholesterol	LPA, lipse activator
DL-C, low-density lipoprotein cholesterol	BMI, body mass index
G, triglycerides	PTCA, Percutaneous transluminal coronary angioplasty
BP, diastolic blood pressure	MACCE, major adverse cardiac cerebrovascular events

Declarations

Ethics approval and consent to participate:

It is from the ethics committee of the department of Cardiology, Fuwai Hospital, National Center for Cardiovascular Diseases, Peking Union Medical College, China.

Consent for publication

Written informed consent for publication was obtained from all participants.

Data Availability

Data have been provided in the supplementary information files that submit alongside the manuscript.

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Competing interests

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2. Non-financial competing interests.

3. Non-financial competing interests include family associations, political, religious, academic or any other.

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Disclosures

No conflicts of interest, financial or otherwise, are declared by the authors.

References

[1] Borja Ibanez, Stefan James, Stefan Agewall, Manuel J Antunes, Chiara Bucciarelli-Ducci, Héctor Bueno, Alida L P Caforio, Filippo Crea, John A Goudevenos, Sigrun Halvorsen, Gerhard Hindricks, Adnan Kastrati, Mattie J Lenzen, Eva Prescott, Marco Roffi, Marco Valgimigli, Christoph Varenhorst, Pascal Vranckx, Petr Widimský. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with STsegment elevation: the task force for the management of acute myocardial

infarction in patients presenting with STsegment elevation of the European Society of Cardiology (ESC). Eur Heart J, 2018; 39: 11977.

[2] Stuart J Head, Milan Milojevic, Joost Daemen, Jung-Min Ahn, Eric Boersma, Evald H Christiansen, Michael J Domanski, Michael E Farkouh, Marcus Flather, Valentin Fuster, Mark A Hlatky, Niels R Holm , Whady A Hueb, Masoor Kamalesh, Young-Hak Kim, Timo Mäkikallio , Friedrich W Mohr, Grigorios Papageorgiou, Seung-Jung Park, Alfredo E Rodriguez, Joseph F Sabik 3rd, Rodney H Stables, Gregg W Stone, Patrick W Serruys, A Pieter Kappetei. Stroke Rates Following Surgical Versus Percutaneous Coronary Revascularization [J]. J. Am. Coll. Cardiol, 2018, 72(4):386-398.

[3] Pieter J Vlaar, Tone Svilaas, Iwan C van der Horst, Gilles F H Diercks, Marieke L Fokkema, Bart J G L de Smet, Ad F M van den Heuvel, Rutger L Anthonio, Gillian A Jessurun, Eng-Shiong Tan, Albert J H Suurmeijer, Felix Zijlstra. Cardiac death and reinfarction after 1 year in the thrombus aspiration during percutaneous coronary intervention in acute myocardial infarction Study (TAPAS): a 1-year follow-up study. Lancet 2008; 371:1915–1920.

[4] Ph Gabriel Steg, Stefan K James, Dan Atar, Luigi P Badano, Carina Blömstrom-Lundqvist, Michael A Borger, Carlo Di Mario, Kenneth Dickstein, Gregory Ducrocq, Francisco Fernandez-Aviles, Anthony H Gershlick, Pantaleo Giannuzzi, Sigrun Halvorsen, Kurt Huber, Peter Juni, Adnan Kastrati, Juhani Knuuti, Mattie J Lenzen, Kenneth W Mahaffey, Marco Valgimigli, Arnoud van 't Hof, Petr Widimsky, Doron Zahger. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Eur Heart J 2012; 33:2569–2619.

[5] Tim Kinnaird, Thomas Johnson , Richard Anderson, Sean Gallagher, Alex Sirker, Peter Ludman , Mark de Belder, Samuel Copt, Keith Oldroyd , Adrian Banning, Mamas Mamas, Nick Curzen. Intravascular imaging and 12-month mortality after unprotected left main stem PCI: An analysis From the British Cardiovascular Intervention Society Database[J]. JACC. Cardiovascular Interventions, 2020, 10;13(3):346-357.

[6] Anna V Kontsevaya, Katie Bates, Henrik Schirmer, Natalia Bobrova David Leon, Martin McKee. Management of patients with acute ST-segment elevation myocardial infarction in Russian hospitals adheres to international guidelines[J]. Open Heart, 2020, 23;7(1):e001134.

[7] Mitsuhiro Takeuchi, Manabu Ogita , Hideki Wada , Daigo Takahashi, Yui Nozaki, Ryota Nishio, Kentaro Yasuda, Norihito Takahashi , Taketo Sonoda, Shoichiro Yatsu, Jun Shitara, Shuta Tsuboi, Tomotaka Dohi, Satoru Suwa, Katsumi Miyauchi, Hiroyuki Daida. Comparison of long-term mortality between living alone patients vs. living together patients with acute coronary syndrome treated with percutaneous coronary intervention[J]. Eur Heart J Qual Care Clin Outcomes. 2020

[8] B Mihaylova, J Emberson, L Blackwell, A Keech, J Simes, E H Barnes, M Voysey, A Gray, R Collins, C Baigent. The effects of lowering LDL cholesterol with statin therapy in people at low risk of vascular disease: meta-analysis of individual data from 27 randomised trials. Lancet 2012; 380: 581–90.

[9] Sundström J, Jackson R, Neal B, for the BPLTTC. Blood pressure-lowering treatment based on cardiovascular risk: a meta-analysis of individual patient data. Lancet 2014; 384: 591–98.

[10] Si-Hyuck Kang, Keun Ho Park, Hyo-Suk Ahn, Kyung Woo Park, Young Joon Hong, Bon-Kwon Koo, Myung Ho Jeong, Hyo-Soo Kim. Everolimus-eluting versus sirolimus-eluting coronary stents in patients with and without diabetes mellitus. EuroIntervention 2014;10(1):74-82.

[11] Somjot S Brar, John Kim, Simerjeet K Brar, Ray Zadegan, Michael Ree, In-Lu A Liu, Prakash Mansukhani, Vicken Aharonian, Ric Hyett, Albert Yuh-Jer Shen. Long-term outcomes by clopidogrel duration and stent type in a diabetic population with de novo coronary artery lesions. J Am Coll Cardiol 2008; 51(23):2220-7.

[12] Usman Baber, Jeffrey Bander, Rucha Karajgikar, Kapil Yadav, Ali Hadi, Kleanthis Theodoropolous, Nilusha Gukathasan, Swathi Roy, Swapna Sayeneni, Stuart A Scott, Jason C Kovacic, Jennifer Yu, Samantha Sartori, Roxana Mehran, Jaime Uribarri, Juan J Badimon, Paul Muntner, Pedro Moreno, Annapoorna S Kini, Samin K Sharma. Combined and independent impact of diabetes mellitus and chronic kidney disease on residual platelet reactivity. Thromb Haemost 2013;110(1):118-23.

[13] Usman Baber, Roxana Mehran, Ajay J Kirtane, Paul A Gurbel , Georgios Christodoulidis , Akiko Maehara, Bernhard Witzenbichler, Giora Weisz, Michael J Rinaldi, D Christopher Metzger , Timothy D Henry , David A Cox, Peter L Duffy, Ernest L Mazzaferri Jr , Ke Xu, Helen Parise 1 , Bruce R Brodie , Thomas D Stuckey , Gregg W Stone. Prevalence and Impact of High Platelet Reactivity in Chronic Kidney Disease: Results From the Assessment of Dual Antiplatelet Therapy With Drug-Eluting Stents Registry. Circ Cardiovasc Interv 2015;8(6):e001683.

[14] Dominick J Angiolillo, Esther Bernardo, Davide Capodanno, David Vivas, Manel Sabaté, José Luis Ferreiro, Masafumi Ueno, Pilar Jimenez-Quevedo, Fernando Alfonso, Theodore A Bass, Carlos Macaya, Antonio Fernandez-Ortiz. Impact of chronic kidney disease on platelet function profiles in diabetes mellitus patients with coronary artery disease taking dual antiplatelet therapy. J Am Coll Cardiol 2010;55(11):1139-46.

[15] Morrow DA. Cardiovascular risk prediction in patients with stable and unstable coronary heart disease. Circulation 2010;121(24):2681-91.

[16] George D Dangas 1 , Bimmer E Claessen, Roxana Mehran, Ke Xu, Martin Fahy, Helen Parise, José P S Henriques, E Magnus Ohman, Harvey D White, Gregg W Stone. Development and validation of a stent thrombosis risk score in patients with acute coronary syndromes. JACC Cardiovasc Interv 2012;5(11): 1097-105.

[17] Sunil V Rao, Lisa A McCoy, John A Spertus, Ronald J Krone, Mandeep Singh, Susan Fitzgerald, Eric D Peterson. An updated bleeding model to predict the risk of post-procedure bleeding among patients undergoing undergoing percutaneous coronary intervention: a report using an expanded bleeding

definition from the National Cardiovascular Data Registry CathPCI Registry. JACC Cardiovasc Interv 2013;6(9): 897-904.

[18] Roxana Mehran, Usman Baber, Samin K Sharma, David J Cohen, Dominick J Angiolillo, Carlo Briguori, Jin Y Cha, Timothy Collier, George Dangas , Dariusz Dudek , Vladimír Džavík , Javier Escaned, Robert Gil , Paul Gurbel, Christian W Hamm, Timothy Henry, Kurt Huber, Adnan Kastrati , Upendra Kaul, Ran Kornowski, Mitchell Krucoff, Vijay Kunadian, Steven O Marx, Shamir R Mehta, David Moliterno, E Magnus Ohman, Keith Oldroyd, Gennaro Sardella, Samantha Sartori, Richard Shlofmitz, P Gabriel Steg, Giora Weisz, Bernhard Witzenbichler, Ya-Ling Han, Stuart Pocock, C Michael Gibson. Ticagrelor with or without aspirin in high-risk patients after PCI. N Engl J Med, 2019, 381(21): 2032-2042.

[19] Ph Gabriel Steg, Stefan K James, Dan Atar, Luigi P Badano, Carina Blömstrom-Lundqvist, Michael A Borger, Carlo Di Mario, Kenneth Dickstein, Gregory Ducrocq, Francisco Fernandez-Aviles, Anthony H Gershlick, Pantaleo Giannuzzi, Sigrun Halvorsen, Kurt Huber, Peter Juni, Adnan Kastrati, Juhani Knuuti, Mattie J Lenzen, Kenneth W Mahaffey, Marco Valgimigli, Arnoud van 't Hof, Petr Widimsky, Doron Zahger. ESC guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Eur Heart J 2012; 33:2569-2619.

[20] Patrick T O'Gara, Frederick G Kushner, Deborah D Ascheim, Donald E Casey Jr, Mina K Chung, James A de Lemos, Steven M Ettinger, James C Fang, Francis M Fesmire, Barry A Franklin, Christopher B Granger, Harlan M Krumholz, Jane A Linderbaum, David A Morrow, L Kristin Newby, Joseph P Ornato, Narith Ou, Martha J Radford, Jacqueline E Tamis-Holland, Jacqueline E Tommaso, Cynthia M Tracy, Y Joseph Woo, David X Zhao. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: executive summary: a report of the American College of Cardiology Foundation/American Heart Association task force on practice guidelines. Circulation 2013; 127: 529-55.

[21] Ce Zhang, Lin Jiang, Lianjun Xu, Jian Tian, Junhao Liu, Xueyan Zhao, Xinxing Feng, Dong Wang, Yin Zhang, Kai Sun, Bo Xu, Wei Zhao, Rutai Hui, Runlin Gao, Jinqing Yuan, Lei Song. Implications of N-terminal pro-B-type natriuretic peptide in patients with three-vessel disease[J]. European Heart Journal (41):40. 3397–3405,

[22] Chengchun Tan, Erfei Luo, Dong Wang, Gaoliang Yan, Yong Qiao, Boqian Zhu, Bo Liu, Jiantong Hou. Usefulness of Haemoglobin Level Combined with CAMI-STEMI Score for Predicting MACCE in Patients with Acute ST-Elevation Myocardial Infarction after PCI[J]. BioMed Research International, 2019, 2019(8):1-8.

[23]Doyle BJ, Rihal CS, Gastineau DA, Holmes DR Jr. Bleeding, blood transfusion, and increased mortality after percutaneous coronary intervention: implications for contemporary practice. J Am Coll Cardiol, 2009;53:2019–27.

[24] Sunil V Rao, Padma R Kaul, Lawrence Liao, Paul W Armstrong, E Magnus Ohman, Christopher B Granger, Robert M Califf, Robert A Harrington, Eric L Eisenstein, Daniel B Mark. Association between

bleeding, blood transfusion, and costs among patients with non-ST-segment elevation acute coronary syndromes. Am Heart J 2008;155:369–74.

[25]Sherev DA, Shaw RE, Brent BN. Angiographic predictors of femoral access site complications: implication for planned percutaneous coronary intervention. Catheter Cardiovasc Interv 2005;65:196–202.

[26] Ajay J Kirtane, Gregory Piazza, Sabina A Murphy, Daniela Budiu, David A Morrow, David J Cohen, Eric Peterson, Nasser Lakkis, Howard C Herrmann, Theresa M Palabrica, C Michael Gibson. Correlates of bleeding events among moderate- to high-risk patients undergoing percutaneous coronary intervention and treated with eptifibatide: observations from the PROTECT-TIMI-30 trial. J Am Coll Cardiol 2006; 47:2374–9.

[27] Freek W A Verheugt, Steven R Steinhubl, Martial Hamon, Harald Darius, Philippe Gabriel Steg, Marco Valgimigli, Steven P Marso, Sunil V Rao, Anthony H Gershlick, A Michael Lincoff, Roxana Mehran, Gregg W Stone. Incidence, prognostic impact, and influence of antithrombotic therapy on access and nonaccess site bleeding in percutaneous coronary intervention. J Am Coll Cardiol Intv 2011;4:191–7.

[28] Sunil V Rao, Fang-Shu Ou, Tracy Y Wang, Matthew T Roe, Ralph Brindis, John S Rumsfeld, Eric D Peterson. Trends in the prevalence and outcomes of radial and femoral approaches to percutaneous coronary intervention: a report from the national cardiovascular data registry. J Am Coll Cardiol Intv 2008;1:379–86.

[29] Emelia J Benjamin, Michael J Blaha, Stephanie E Chiuve, Mary Cushman, Sandeep R Das, Rajat Deo, Sarah D de Ferranti, James Floyd, Myriam Fornage, Cathleen Gillespie, Carmen R Isasi, Monik C Jiménez, Lori Chaffin Jordan, Suzanne E Judd, Daniel Lackland, Judith H Lichtman, Lynda Lisabeth, Simin Liu, Chris T Longenecker, Rachel H Mackey, Kunihiro Matsushita, Dariush Mozaffarian, Michael E Mussolino, Khurram Nasir, Robert W Neumar, Latha Palaniappan, Dilip K Pandey, Ravi R Thiagarajan, Mathew J Reeves, Matthew Ritchey, Carlos J Rodriguez, Gregory A Roth, Wayne D Rosamond, Comilla Sasson, Amytis Towfighi, Connie W Tsao, Melanie B Turner, Salim S Virani, Jenifer H Voeks, Joshua Z Willey, John T Wilkins, Jason Hy Wu, Heather M Alger, Sally S Wong, Paul Muntner. Heart disease and stroke statistics-2017 update: a report from the American Heart Association. Circulation 2017; 135: e146–e603.

[30] Martin J O'Donnell, Siu Lim Chin , Sumathy Rangarajan, Denis Xavier, Lisheng Liu, Hongye Zhang, Purnima Rao-Melacini, Xiaohe Zhang, Prem Pais, Steven Agapay, Patricio Lopez-Jaramillo, Albertino Damasceno, Peter Langhorne, Matthew J McQueen , Annika Rosengren, Mahshid Dehghan, Graeme J Hankey, Antonio L Dans , Ahmed Elsayed, Alvaro Avezum, Charles Mondo, Hans-Christoph Diener, Danuta Ryglewicz, Anna Czlonkowska, Nana Pogosova, Christian Weimar, Romaina Iqbal, Rafael Diaz , Khalid Yusoff , Afzalhussein Yusufali , Aytekin Oguz , Xingyu Wang , Ernesto Penaherrera, Fernando Lanas, Okechukwu S Ogah, Adesola Ogunniyi, Helle K Iversen, German Malaga, Zvonko Rumboldt, Shahram Oveisgharan, Fawaz Al Hussain, Daliwonga Magazi , Yongchai Nilanont , John Ferguson , Guillaume

Pare, Salim Yusuf. Global and regional effects of potentially modifiable risk factors associated with acute stroke in 32 countries (interstroke): a case-control study. Lancet 2016; 388: 761–775.

[31] Chun Shing Kwok, Evangelos Kontopanteli , Phyo K Myint, Azfar Zaman , Colin Berry , Bernard Keavney, Jim Nolan , Peter F Ludman, Mark A de Belder , Iain Buchan, Mamas A Mamas. Stroke following percutaneous coronary intervention: type-specific incidence, outcomes and determinants seen by the British Cardiovascular Intervention Society 2007–12[J]. European Heart Journal, 2015, 36, 1618–1628.

[32] Luke P Dawson, Justin A Cole, Terase F Lancefield, Andrew E Ajani, Nick Andrianopoulos , Amanda G Thrift, David J Clark, Angela L Brennan, Melanie Freeman , Jessica O'Brien, Martin Sebastian, William Chan, James A Shaw , Diem Dinh, Christopher M Reid, Stephen J Duffy. Lancefield Incidence and risk factors for stroke following percutaneous coronary intervention. International Journal of Stroke, 2020(0) 1–14.

[33]Bredlau CE, Roubin GS, Leimgruber PP, Douglas JS, King SB, Gruentzig AR. In-hospital morbidity and mortality in patients undergoing elective coronary angioplasty.Circulation. 1985; *72*:1044–1052.

[34] Hoffman SJ, Routledge HC, Lennon RJ, Mustafa MZ, Rihal CS, Gersh BJ, Holmes DR, Gulati R. Procedural factors associated with percutaneous coronary intervention-related ischemic stroke.JACC Cardiovasc Interv. 2012; *5*:200–206

[35] Eleni Rapsomaniki, Anoop Shah, Pablo Perel, Spiros Denaxas, Julie George, Owen Nicholas, Ruzan Udumyan, Gene Solomon Feder, Aroon D Hingorani, Adam Timmis, Liam Smeeth, Harry Hemingway. Prognostic models for stable coronary artery disease based on electronic health record cohort of 102 023 patients. Eur Heart J 2014; 35:844–52.

[36] Robert W Yeh, Eric A Secemsky, Dean J Kereiakes, Sharon-Lise T Normand, Anthony H Gershlick, David J Cohen, John A Spertus , Philippe Gabriel Steg , Donald E Cutlip, Michael J Rinaldi, Edoardo Camenzin, William Wijns, Patricia K Apruzzese , Yang Song, Joseph M Massaro, Laura Mauri. Development and validation of a prediction rule for benefit and harm of dual antiplatelet therapy beyond 1 year after percutaneous coronary intervention.[J]. JAMA, 2016, 315(16):1735-1749.

Table

Table 1 The characteristic of derivation cohort and validation cohort

Variables	Derivation cohort (n=2384)			Validation cohort (n=1020)		
	MACCE (n=578)	No MACCE (n=1806)	P value	MACCE (n=251)	No MACCE (n=769)	P value
Age (years)	65.1246	58.8632	<0.0001	64.7331	58.6736	<0.0001
Male [%(n)]	405 (70.07%)	1412 (78.18%)	<0.0001	177 (70.52%)	577 (75.03%)	0.1572
Height (cm)	167.7623	168.4187	0.0718	168.0256	168.2891	0.6317
Weight (kg)	73.1232	73.8718	0.2545	73.6537	73.5102	0.8778
BMI (kg/m□)	25.8476	25.9597	0.5528	25.9623	25.8643	0.7119
Heart rate (beats per minute)	79.5655	77.3499	0.0033	80.5840	76.1917	0.0001
SBP (mmHg)	124.6982	124.3561	0.7031	121.6345	126.1836	0.1725
DBP(mmHg)	73.0745	74.4174	0.0315	72.3109	74.2051	0.0470
Hypertension[%(n)]	385 (66.61%)	1069 (59.19%)	0.0015	172 (68.53%)	465 (60.47%)	0.0221
Diabetes[%(n)]	234 (40.48%)	677 (37.49%)	0.1966	98 (39.04%)	277 (36.02%)	0.3884
Hyperlipidemia[%(n)]	515 (89.10%)	1672 (92.58%)	0.0082	226 (90.04%)	727 (94.54%)	0.0125
Smoking[%(n)]	342 (62.75%)	1083 (66.08%)	0.1580	149 (63.14%)	455 (65.56%)	0.4998
Previous PCI[%(n)]	98 (16.96%)	273 (15.12%)	0.2885	44 (17.53%)	131 (17.04%)	0.8567
Previous CABG[%(n)]	11 (1.90%)	19 (1.05%)	0.1101	8 (3.19%)	6 (0.78%)	0.0044
Atrial fibrillation[%(n)]	48 (8.30%)	85 (4.71%)	0.0010	28 (11.16%)	41 (5.33%)	0.0014
CKD[%(n)]	64 (11.07%)	146 (8.08%)	0.0274	36 (14.34%)	59 (7.67%)	0.0016
Laboratory examinations						
HDL-cholesterol (mg/dl)	1.6936	1.7091	0.7880	1.6525	1.7000	0.5692
LDL-cholesterol (mg/dl)	2.6939	2.7461	0.2561	2.7078	2.7219	0.8267
Triglycerides (mg/dl)	1.0528	1.0565	0.7904	1.0606	1.0419	0.3483
LPA (g/L)	272.53	265.12	0.5234	262.53	255.06	0.6753
hs-CRP	7.9750	7.6508	0.1712	8.5646	7.1744	0.0001
D-dimer	0.8345	0.5736	0.0009	1.0090	0.6265	0.0122
Crea	85.5148	81.4937	0.0005	87.459	80.507	0.0006
eGFR	87.7076	90.0583	0.5702	96.147	92.221	0.5744
Discharge medication regimen						
Statin[%(n)]	533 (95.01%)	1682 (93.86%)	0.3128	221 (90.57%)	711 (92.70%)	0.2814
Aspirin[%(n)]	554 (98.75%)	1782 (99.44%)	0.0923	237 (97.13%)	759 (98.96%)	0.0399
Clopidogrel	493 (87.88%)	1353 (75.50%)	<0.0001	205 (84.02%)	575 (74.97%)	0.0034
Ticagrelor[%(n)]	65 (11.84%)	426 (23.81%)	<0.0001	37 (15.48%)	184 (24.02%)	0.0054
ACEI [%(n)]	304 (54.19%)	1134 (63.28%)	0.0001	137 (56.15%)	501 (65.32%)	0.0097
ARB[%(n)]	54 (9.63%)	165 (9.21%)	0.7661	18 (7.38%)	52 (6.78%)	0.7488
Beta-Blockers[%(n)]	479 (85.38%)	1574 (87.83%)	0.1287	211 (86.48%)	681 (88.79%)	0.3290
Diuretic[%(n)]	197 (35.12%)	531 (29.63%)	0.0142	96 (39.34%)	193 (25.16%)	<0.0001
Spironolactone[%(n)]	142 (25.31%)	407 (22.71%)	0.2039	61 (25.00%)	151 (19.69%)	0.0758
P2Y12 inhibitors	558 (99.47%)	1778 (99.22%)	0.5474	242 (99.18%)	759 (98.96%)	0.7588
Endpoint events						
All caused death [%(n)]	145 (25.09%)	0 (0.00%)	<0.0001	68 (27.09%)	0 (0.00%)	<0.0001
Recurrent MI [%(n)]	81 (14.09%)	0 (0.00%)	<0.0001	37 (14.74%)	0 (0.00%)	<0.0001
revascularization [%	346	0 (0.00%)	<0.0001	144	0 (0.00%)	<0.0001

(n)]	(60.07%)			(57.37%)		
heart failure [%(n)]	23 (3.99%)	0 (0.00%)	<0.0001	11 (4.40%)	0 (0.00%)	<0.0001
ischemic stroke [%(n)]	47 (8.15%)	0 (0.00%)	<0.0001	19 (7.60%)	0 (0.00%)	<0.0001
hemorrhagic stroke [%(n)]	8 (1.39%)	0 (0.00%)	<0.0001	3 (1.20%)	0 (0.00%)	<0.0001
Coronary angiography						
Bifurcation lesion [%(n)]	189 (33.69%)	630 (35.16%)	0.5246	74 (30.33%)	272 (35.46%)	0.1409
Muli-vessel lesions [%(n)]	487 (86.81%)	1339 (74.72%)	<0.0001	218(89.35)	559(72.99)	<0.0001
LM lesion [%(n)]	58 (10.34%)	104 (5.80%)	0.0002	23 (9.43%)	48 (6.26%)	0.0916
PTCA	504 (89.84%)	1566 (87.39%)	0.1193	215 (88.11%)	681 (88.79%)	0.7731
Thrombus aspiration	208 (37.08%)	784 (43.75%)	0.0052	100 (40.98%)	323 (42.11%)	0.7556
Coronary stent implantation	484 (86.27%)	1593 (88.90%)	0.0923	207 (84.84%)	680 (88.66%)	0.1130
The use of IABP	74 (13.19%)	168 (9.38%)	0.0094	35 (14.34%)	68 (8.87%)	0.0137

Continuous data are presented as mean, categorical variables are presented as % (n). BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; CKD, chronic kidney disease; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglyceride; LPA, lipse activator; hs-CRP, high sensitive C-reactive protein; eGFR, estimated glomerular filtration rate; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; MACCE, major adverse cardiovascular cerebrovascular event

Figures

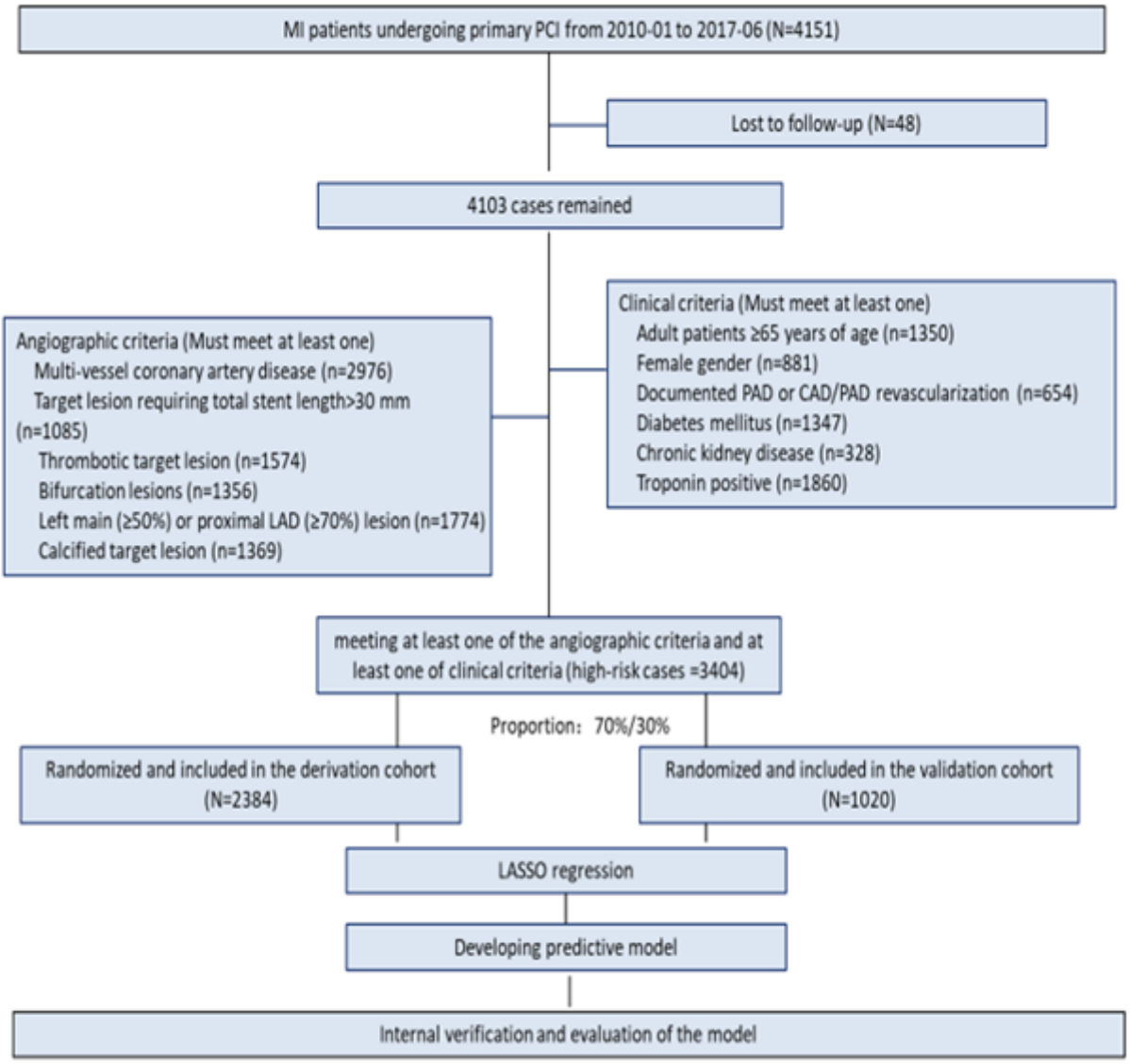


Figure 1 Study Sample Selection Flow Diagram

Figure 1

Study Sample Selection Flow Diagram

Figure 2 A1 Least absolute shrinkage and selection operator (LASSO) regression

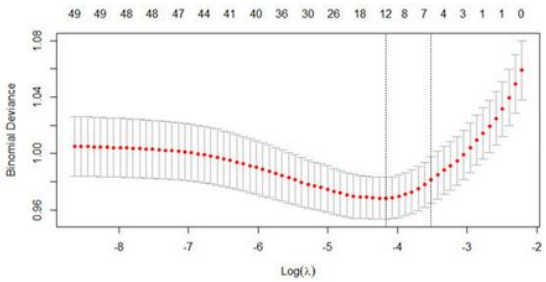
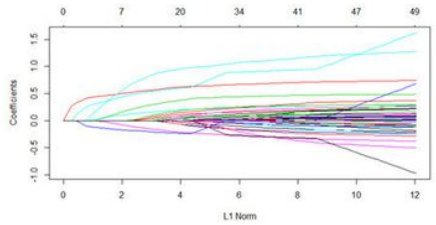
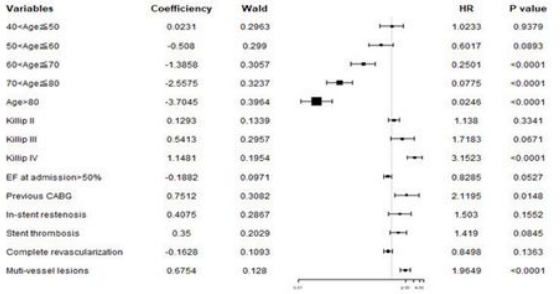


Figure 2 A2 Least absolute shrinkage and selection operator (LASSO) regression



The filtering and cross-validation processes of independent variables are shown in figure 2A1 and 2A2 respectively. Lambda.1se is the lambda value of the optimal efficiency model in the standard error range which gives a model with excellent performance.

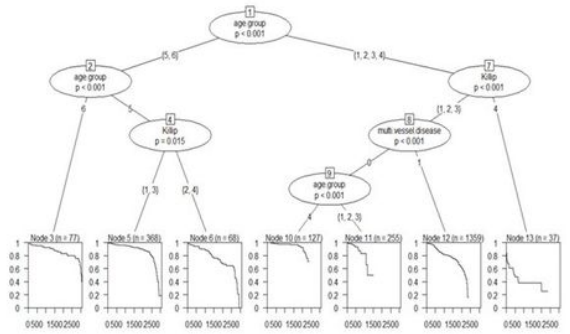
Figure 2 B Forest plot by using the multivariable COX regression



Variables	Coefficiency	Wald	HR	P value
40<Age≦50	0.0231	0.2963	1.0233	0.9379
50<Age≦60	-0.508	0.299	0.6017	0.0893
60<Age≦70	-1.3858	0.3057	0.2501	<0.0001
70<Age≦80	-2.5575	0.3237	0.0775	<0.0001
Age>80	-3.7045	0.3964	0.0246	<0.0001
Killip II	0.1293	0.1339	1.138	0.3341
Killip III	0.5413	0.2957	1.7183	0.0671
Killip IV	1.1481	0.1954	3.1523	<0.0001
EF at admission>50%	-0.1882	0.0971	0.8285	0.0527
Previous CABG	0.7512	0.3082	2.1195	0.0148
In-stent restenosis	0.4075	0.2867	1.503	0.1552
Stent thrombosis	0.35	0.2029	1.419	0.0845
Complete revascularization	-0.1628	0.1093	0.8498	0.1363
Muti-vessel lesions	0.6754	0.128	1.9649	<0.0001

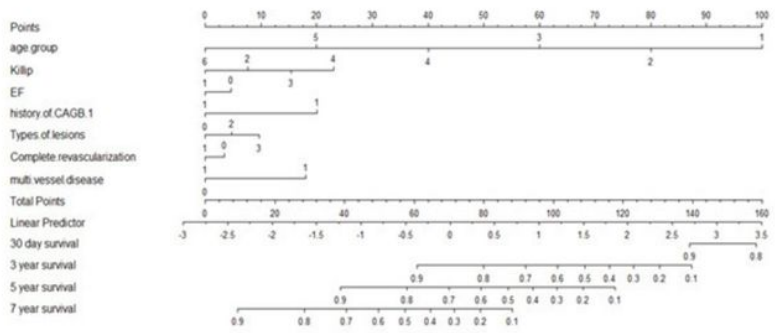
Forest plot by using the multivariable COX regression; HR, hazard ratio; CABG, coronary artery bypass grafting

Figure 2 C Decision tree flow diagram



The binary decision diagram of the variables was shown in figure 2C.

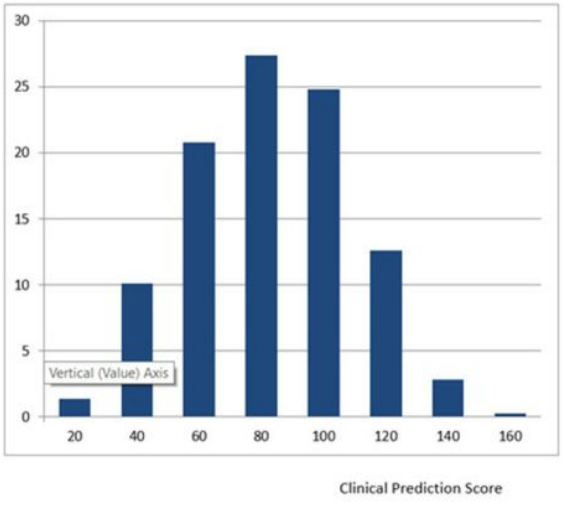
Figure 2D the risk score nomogram.



The score, ranging from 0 to 160, assigned points as follows: for patients younger than 40 years=1, 100 points; for age 40 to younger than 50 years=2, 80 points; for age 50 to younger than 60 years=3, 60 points; for age 60 to younger than 70 years=4, 40 points; for age 70 to younger than 80 years=5, 20 points; for patients 80 years or older=6,0; for Killip II, 7.68; for Killip III, 15.36; for Killip IV, 23.03; for EF at admission ≦ 50%, 4.62; for previous history of CABG, 20; for in-stent restenosis, 4.81; for stent thrombosis, 9.62; for without complete revascularization, 3.45; for multi-vessel lesion, 18. Age group, 1 stand for age less than 40 years/ 2 stand for age range from 40 to 50 years/ 3 stand for age range from 50 to 60 years/4 stand for age range from 60 to 70 years/ 5 stand for age range from 70 to 80 years/ 6 age stand for age more than 80 years. Killip classification, 1= Killip I, 2= Killip II, 3= Killip III, 4=Killip IV. EF, 0 stands for >50%, 1 stands for less than 50%. History of CABG, 1=with, 0=without; type of lesion, 1= Denovo lesion, 2=restenosis, 3= stent thrombosis; complete revascularization, 0=without, 1=with; mutivessel disease, 1=with, 0=without.

Figure 2 E the internal validation of the model

Clinical prediction score variable	Points
Age, y	
Age ≦ 40 ----------1	100
40<Age ≦ 50 ----------2	80
50<Age ≦ 60 ----------3	60
60<Age ≦ 70----------4	40
70<Age ≦ 80----------5	20
Age>80----------6	0
Killip II----------2	7.68
Killip III----------3	15.36
Killip IV----------4	23.03
EF at admission ≦ 50%-0	4.62
Previous CABG----------1	20
In-stent restenosis--------2	4.81
Stent thrombosis---------3	9.62
Without complete revascularization----------0	3.45
Multi-vessel lesions--------1	18
Total score range: 0 to 160	



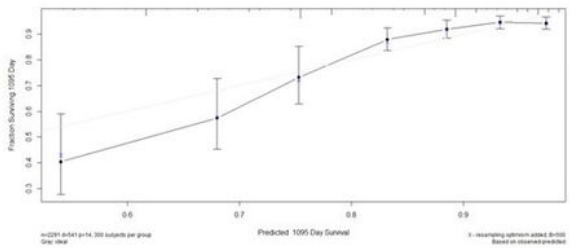
The left side has shown the clinical prediction score variable and corresponding points. The right side has shown the graph of distribution of the clinical prediction score.

Figure 2

The establishment procedure of the model Figure 2A1, A2 Least absolute shrinkage and selection operator (LASSO) regression. The filtering and cross-validation processes of independent variables are shown in figure 2A1 and 2A2 respectively. Lambda.1se is the lambda value of the optimal efficiency model in the standard error range which gives a model with excellent performance. Figure 2B, Forest plot by using the multivariable COX regression; HR, hazard ratio; CABG, coronary artery bypass grafting Figure 2C, Decision tree flow diagram. The binary decision diagram of the variables was shown in figure 2C.

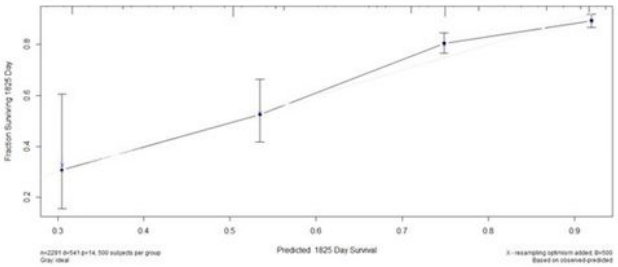
Figure 2D, the risk score nomogram. The score, ranging from 0 to 160, assigned points as follows: for patients younger than 40 years, 100 points; for age 40 to younger than 50 years, 80 points; for age 50 to younger than 60 years, 60 points; for age 60 to younger than 70 years, 40 points; for age 70 to younger than 80 years, 20 points; for patients 80 years or older,0; for Killip II, 7.68; for Killip III, 15.36; for Killip IV, 23.03; for EF at admission≦50%, 4.62; for previous history of CABG, 20; for in-stent restenosis, 4.81; for stent thrombosis, 9.62; for without complete revascularization, 3.45; for multi-vessel lesion, 18. Age group, 1 stand for age less than 40 years/ 2 stand for age range from 40 to 50 years/ 3 stand for age range from 50 to 60 years/4 stand for age range from 60 to 70 years/ 5 stand for age range from 70 to 80 years/ 6 age stand for age more than 80 years. Killip classification, 1= Killip I, 2= Killip II, 3= Killip III, 4=Killip IV. EF, 0 stands for >50%, 1 stands for less than 50%. History of CABG, 1=with, 0=without; type of lesion, 1= Denovo lesion, 2=restenosis, 3= stent thrombosis; complete revascularization, 0=without, 1=with; mutivessel disease, 1=with, 0=without. Histogram refers to the score distribution in the derivation cohort. For the variables selected in the nomogram model, the values of different variables can correspond to different scores on the integral line at the top of the nomogram (the score range is 0-160 points) through the projection of the vertical line, and the total score can be obtained by adding up the scores corresponding to the values of each variable. The cumulative occurrence probability of MACCE in 30 days, 3 year, 5 year and 7 years can be obtained from the total score on the prediction line at the bottom of the nomogram. Figure 2E, Elements of clinical prediction score and distribution of score among high-risk MI patients who undergent PPCI Figure 2D, The left side has shown the clinical prediction score variable and corresponding points. The right side has shown the graph of distribution of the clinical prediction score.

Figure 3A



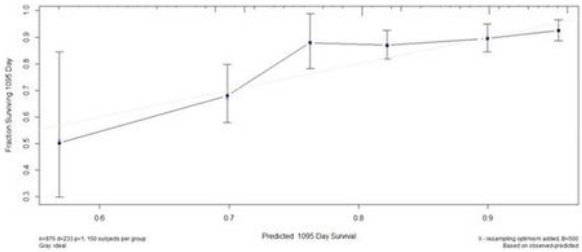
risk score calibration in the derivation cohort and the internal validation cohort; the stroke events risk score of 3-year

Figure 3B



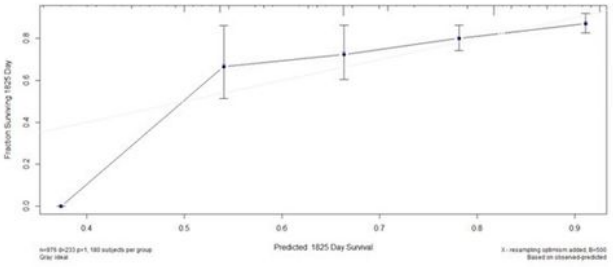
risk score calibration in the derivation cohort and the internal validation cohort; the stroke events risk score of 5-year

Figure 3C



risk score calibration in the validation cohort and the internal validation cohort; the stroke events risk score of 3-year

Figure 3D



risk score calibration in the validation cohort and the internal validation cohort; the stroke events risk score of 5-year

Figure 3E ROC curve of derivation cohort

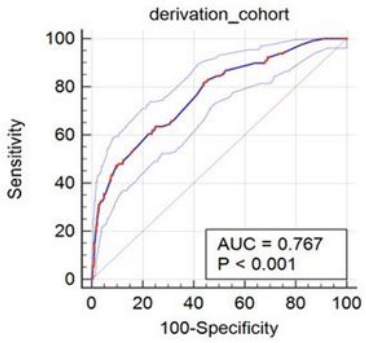


Figure 3E showed the survival ROC curve of derivation cohort (AUC=0.767, p<0.001). AUC, area under the curve; ROC, survival receiver operating characteristic; TP, true positive; FP, false positive.

Figure 3 F ROC curve of validation cohort

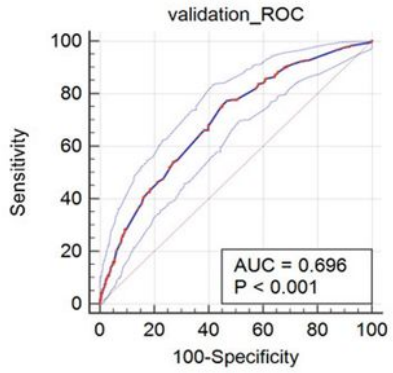


Figure 3F showed the survival ROC curve of validation cohort (AUC=0.696, p<0.001). AUC, area under the curve; ROC, survival receiver operating characteristic; TP, true positive; FP, false positive.

Figure 3

The internal validation of the model Figure 3A-D, risk score calibration in the derivation cohort and the internal validation cohort; the stroke events risk score of 3-year (A) 5-year (B) in the derivation cohort and 3-year (C) 5-year (D) in the validation cohort. Calibration is shown as the estimated risk against survival from Kaplan- Meier analysis. Gray line=perfect calibration. Figure 3E showed the survival ROC curve of derivation cohort (AUC=0.767, p<0.001). Figure 3F showed the survival ROC curve of validation cohort

(AUC=0.696, p<0.001). AUC, area under the curve; ROC, survival receiver operating characteristic; TP, true positive; FP, false positive.

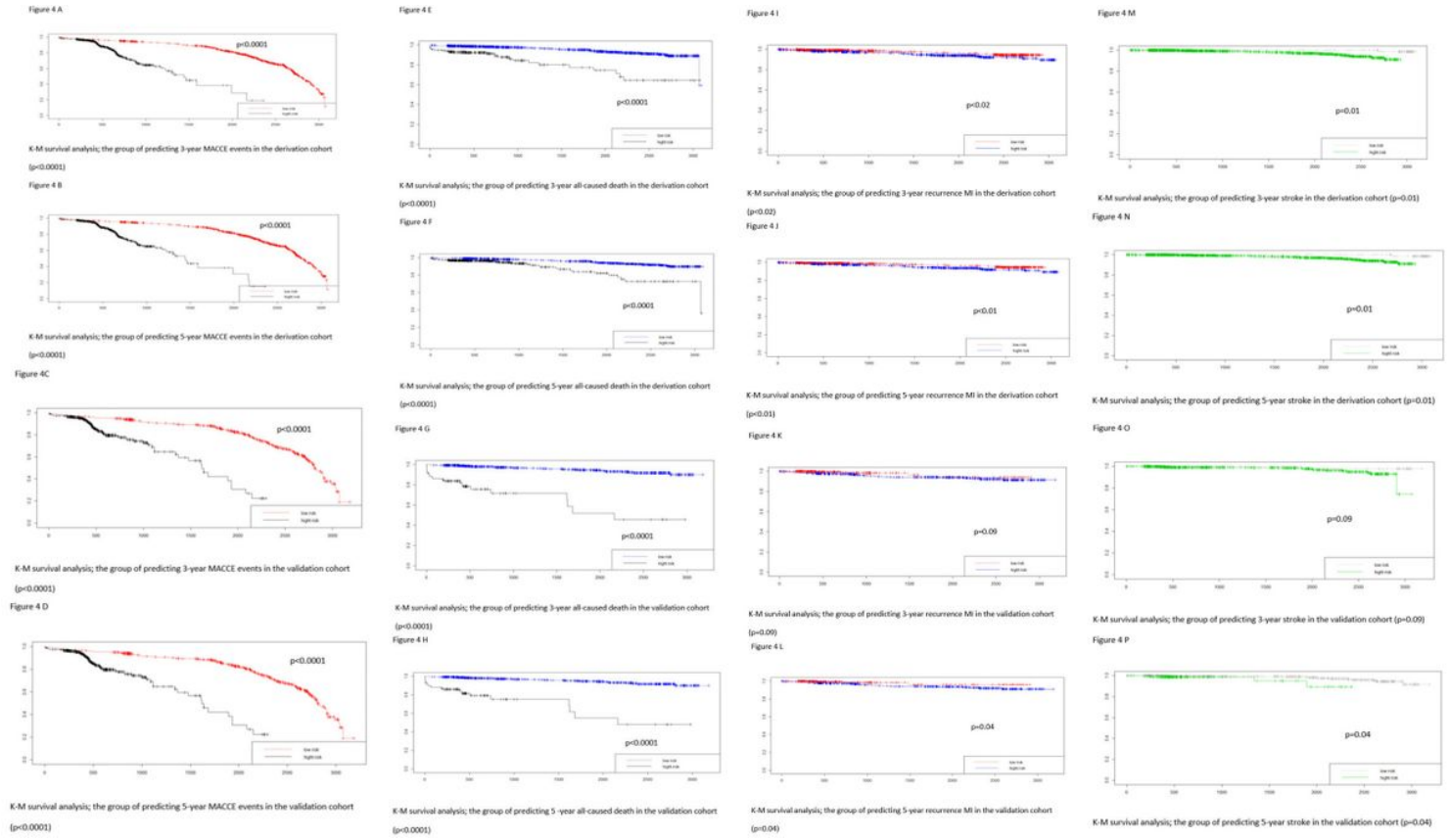


Figure 4

K-M survival analysis; In the group of predicting MACCE events, the two groups displayed significant difference in both derivation cohort (p<0.001) and validation cohort (p<0.001) shown in figure 4A-D. In the subgroup of predicting all caused death, it is remarkable difference (p<0.001) between the high risk group and relative low risk group in both development and validation group (figure 4E-H). Furthermore, when the endpoint was recurrence MI, the longrank p was less than 0.02 in the 3-year derivation cohort and p less than 0.01 in the 5-year K-M curve in derivation cohort (figure 4I-L). Finally, we also found distinct discrepancy in predicting the stroke (p<0.05) (figure4 M-P) events in 3-year and 5-year development and validation cohort.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- 20200702TripodChecklistPredictionModelDevelopmentMACCE.pdf
- Supplement.docx