



# Identifying patients with refusal of percutaneous coronary intervention for acute myocardial infarction: a classification and regression tree analysis

Manyan Wu<sup>1</sup> · Long Li<sup>1</sup> · Sufang Li<sup>1</sup> · Yuxia Cui<sup>1</sup> · Dan Hu<sup>1</sup> · Junxian Song<sup>1</sup> · Chongyou Lee<sup>1</sup> · Hong Chen<sup>1</sup>

Received: 28 January 2019 / Accepted: 20 March 2019 / Published online: 4 April 2019  
© Società Italiana di Medicina Interna (SIMI) 2019

## Abstract

The purpose of the present study is to develop and validate a prediction tool to identify patients who refuse to receive percutaneous coronary intervention (PCI) rapidly. We developed a risk stratification model using the derivation cohort of 288 patients with ST segment elevation myocardial infarction (STEMI) in our hospital and validated it in a prospective cohort of 115 patients. There were 52 (18.1%) patients and 18 (15.7%) patients who refused PCI among derivation and validation cohort, respectively. A classification and regression tree (CART) analysis and multivariate logistic regression were used for statistical analysis. The decision-making factors for refusal of PCI were also investigated. The CART analysis and logistic regression both showed that self-rated mild symptom was the most significant predictor of not choosing PCI. The model generated three risk groups. The high-risk group included: self-rated mild symptoms; self-rated severe symptom, glomerular filtration rate < 60 ml/min/1.73m<sup>2</sup>. The intermediate-risk group included: self-rated severe symptom, glomerular filtration rate ≥ 60 ml/min/1.73m<sup>2</sup> and age ≥ 75 years. The low-risk group included: self-rated severe symptom, glomerular filtration rate ≥ 60 ml/min/1.73m<sup>2</sup> and age < 75 years. The prevalence for refusal of PCI of the three groups were 45%–44%, 18% and 4%, respectively. The sensitivity was 88% and the negative predictive value was 96%. And similar results were obtained when this prediction tool was applied prospectively to the validation cohort. Patients at low and high risk can be easily identified for refusal of PCI by the prediction tool using common clinical data. This practical model might provide useful information for rapid recognition and early response for this kind of crowd.

**Keywords** Acute myocardial infarction · Percutaneous coronary intervention · Clinical prediction rule

## Introduction

Coronary vascular diseases (CVD) remain the leading cause of death worldwide [1]. Acute myocardial infarction (AMI) is the most serious type of CVD with significant high rate of

disability and mortality [2]. Effective and timely reperfusion of the infarct-related coronary artery is crucial for patients with ST segment elevation myocardial infarction (STEMI) [3]. Current guidelines highly recommend that primary percutaneous coronary intervention (PCI) should be suggested for STEMI patients with ischemic symptoms of less than 12 h duration, and that first medical-contact-to-device time should be controlled within 90 min in PCI-capable hospitals [4, 5].

However, a substantial proportion of patients with STEMI in China, who are eligible for reperfusion therapies, refuse or do not receive primary PCI [6–8]. Previous study showed PCI was refused by almost one quarter of eligible elderly Chinese patients with a first STEMI. And older age, symptom severity and trust in physician were independent predictors associated with the use of PCI in elderly patients [9]. However, these factors were not validated by other cohorts,

---

Manyan Wu and Long Li contributed equally to this work.

**Electronic supplementary material** The online version of this article (<https://doi.org/10.1007/s11739-019-02079-3>) contains supplementary material, which is available to authorized users.

✉ Hong Chen  
chenhongbj@medmail.com.cn

<sup>1</sup> Department of Cardiology, Beijing Key Laboratory of Early Prediction and Intervention of Acute Myocardial Infarction, Center for Cardiovascular Translational Research, Peking University People's Hospital, Xizhimen South Rd No.11, Xicheng District, Beijing 100044, China

nor did they be integrated into a risk stratification model for clinical use.

The Classification and regression tree (CART) analysis is well suited to develop a simple and user-friendly clinical prediction tool [10, 11]. Unlike the clinical model and score generated by logistic or Cox regression, the CART analysis used a very intuitive diagram to represent risk prediction without complicated calculation [12]. The CART analysis has been explored its potential use in many clinical conditions, such as acute myocardial infarction [13] and antiplatelet effects of clopidogrel [14]. Therefore, the aim of this study is to develop and validate a simple and practical tool to identify potential patients with refusal of PCI.

## Materials and methods

### Study population and data collection

After receiving approval from the institutional review board at our hospital, we retrospectively reviewed the medical records of consecutive patients presented with chest pain suggestive of AMI to the emergency department (ED) of Peking University People's Hospital from August 2014 to April 2016. Among them, those finally diagnosed STEMI within 12 h from the onset of symptoms eligible for PCI were included. Twenty-three patients who received primary PCI in other acute-care hospital, 48 had contraindications to PCI because of intracranial neoplasm, active bleeding, or suspected or documented aortic dissection, 4 died before decision were excluded. Finally, 288 patients were included in the final analysis (Supplementary Fig. 1).

The routine clinical assessment was performed on every patient in the ED, including history, physical examination, serial 12-lead ECG monitoring and other laboratory examinations. Time of hospital arrival was classified on the basis of those who presented during “regular” working hours (weekdays between 8 a.m. and 6 p.m.) and those who presented during off-hours. The final diagnosis of STEMI was made according to the 2012 ESC/AHA/ACC guideline [15]. Briefly, that is a rise and fall of cardiac biomarker (preferably troponin) with at least one value above the 99th percentile of upper reference limit, lasting ischemic symptoms ( $> 30$  min), and new ST elevation at the J point in at least two contiguous leads of  $\geq 2$  mm (0.2 mV) in men or  $\geq 1.5$  mm (0.15 mV) in women in leads V2–V3 and/or of  $\geq 1$  mm (0.1 mV) in other contiguous chest leads or the limb leads. The visual analog scale (VAS) often considered the gold standard in pain, ranging from zero to ten [16]. A point of VAS  $\geq 7$  was considered the self-rated severe symptom and thus a point of VAS  $< 7$  was considered the self-rated mild symptom in this study. Renal insufficiency was defined as glomerular filtration rate  $< 60$  ml/min/1.73m<sup>2</sup>.

Patients prospectively enrolled from April 2016 to February 2017 were used for model validation. Moreover, we prospectively collected patient decision-making information. A staff will be present during the communication between cardiologists and patients. The staff was trained to identify and record the seven elements of informed decision making, using the framework of Braddock et al. [17]. These elements included (1) discussion of the patient's role in decision making, (2) discussion of the clinical issue or nature of the decision, (3) discussion of the alternatives, (4) discussion of the pros and cons of the alternatives, (5) discussion of the uncertainties associated with the decision, (6) assessment of the patient's understanding, and (7) exploration of patient preference.

Our center was a tertiary care and one of affiliated hospitals of Peking University, which was the first chest pain unit in China certified by the Society of Cardiovascular Patient Care (now called ACC Accreditation Services). It provided 24/7 primary PCI and interventional cardiac care with annual PCI volume  $\geq 800$  and annual primary PCI volume  $\geq 50$ . The protocol of primary PCI for STEMI adopted by our center represents the practice at PCI-capable hospitals in China as previously described [18]. The protocol of the study was approved by the Medical Ethics Committee of our hospital according to the principles of the Declaration of Helsinki, and written informed consent was obtained from each patient.

### Statistical analysis

Continuous variables were represented as mean  $\pm$  standard deviation (SD) or median (interquartile range, IQR). Categorical variables were represented as numbers and percentage. Quantitative data were analyzed using Student's *t* test or one-way ANOVA ( $> 2$  groups) followed by the Bonferroni's multiple comparisons if fulfilled normally distributed. Otherwise, for comparing between groups, Mann–Whitney *U* test or Kruskal–Wallis test ( $> 2$  groups) was used. For categorical variables, the Chi-square method was used for analysis.

Patients were divided into consent to PCI group and refusal of PCI group. We use CART analysis to generate a simple and practical clinical decision rule. Every value of each variable is considered as a potential split (parent nodes), and the CART method divides a selected range of variables to obtain an optimal binary split into two subgroups (child nodes). Impurity criterion is adopted as the node splitting rule. From this, CART analysis generates a classification tree and numerical rank for each input used to build the tree by relative importance. The deviation cohort was used for model development and we grouped the four terminal nodes into three risk levels (high-, intermediate- and low-risk groups) based on the prevalence of refusal of

PCI. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were used to evaluate the accuracy of the novel predictive rule. The model was validated in the prospective cohort. Prevalence of not choosing PCI between all groups and the index of accuracy were compared with those of the derivation cohort.

Finally, a multivariate logistic regression model was constructed from the derivation cohort. To avoid overfitting, a predefined ratio of predictive variables to the number of observed events was set at 1:10. Especially, the CART analysis identify the cutoff points of age of 75 years, and the dichotomy of age  $\geq 75$  years were used as a variable.  $P < 0.05$  was considered as statistical significance. Statistical analysis was performed using SPSS Statistics (version 20; SPSS, Inc., Chicago, IL) and CART Pro software (version 6.0, Salford systems, San Diego, CA).

## Results

### Characteristics of deviation cohort

In retrospective deviation cohort, a total of 436 patients with acute STMI were admitted to our hospital during the study period, of which 288 met the inclusion and exclusion criteria. The overall median age of the population was 62.8 (52.0, 75.0) years. Two hundred and thirteen (74.0%) were men and 263 (91.3%) had medical insurance. PCI was accepted by 236 patients (81.9%) and refused by 52 patients (18.1%). Table 1 displayed the baseline clinical characteristics of the deviation cohort. For finding out the factors associated with refusal of PCI, patients were divided into consent group and refusal group. Primary PCI was accepted more frequently in patients who were on the job, current smokers, and had medical insurance, with self-rated severe symptoms. Primary PCI was refused more likely by patients who were older, outlander, had a prior history of myocardial infarction, diabetes mellitus, ischemic stroke, and renal insufficiency and positive troponin result on admission.

### Model development for refusal of PCI

The CART analysis showed that the best discriminator for refusal of PCI was self-rated mild symptom. The other significant predictors were renal insufficiency (glomerular filtration rate  $< 60$  ml/min/1.73m<sup>2</sup>) and older age (age  $\geq 75$  years). Figure 1 showed the optimal tree generated by this analysis. The tree had three splits and produced four terminal nodes (TNs). The high-risk group included: self-rated mild symptom (TN 1); self-rated severe symptom, glomerular filtration rate  $< 60$  ml/min/1.73m<sup>2</sup> (TN 2). The intermediate-risk group: self-rated severe symptom, glomerular filtration rate  $< 60$  ml/min/1.73m<sup>2</sup> and

age  $\geq 75$  years (TN 3). The low-risk group: self-rated severe symptom, glomerular filtration rate  $< 60$  ml/min/1.73m<sup>2</sup> and age  $< 75$  years (TN 4). The prevalence for refusal of PCI of these four TNs was 45%, 44%, 18% and 4%, respectively. Table 2 showed the performance of the model for refusal of PCI. The sensitivity was 88%, and the negative predictive value was 96%.

After adjustment of significant variables in univariate analysis, multivariate logistic regression identified the same important predictors as the CART analysis (Table 3). As it showed, self-rated severe symptom (OR 0.13, 95% CI 0.05–0.33,  $P < 0.001$ ) was the most powerful and significantly independent predictor of consent to primary PCI. Besides, glomerular filtration rate  $< 60$  ml/min/1.73m<sup>2</sup> (OR 8.97, 95% CI 3.15–25.50,  $P < 0.001$ ) and age  $\geq 75$  years (OR 5.03, 95% CI 1.65–15.30,  $P = 0.004$ ) were the next two discriminators of refusal of primary PCI. And prior history of myocardial infarction (OR 3.15, 95% CI 1.09–9.05,  $P = 0.034$ ) and outlander (OR 4.41, 95% CI 1.10–17.65,  $P = 0.036$ ) were also associated with refusal of primary PCI.

### Model validation for refusal of PCI

The decision tree generated by CART analysis of the derivation cohort was tested for its ability to stratify the risk of patients in the validation cohort. Table 4 showed the baseline characteristics of this population. The derivation cohort and validation cohort were similar with respect to age, medical history and situation at admission. The prevalence of not consent to PCI in the derivation cohort and validation cohort was 18.1 and 15.7, respectively.

The CART analysis was applied to divide the patients in the validation cohort into high, intermediate, and low risk. The prevalence for refusal of PCI of the three risk groups were 36%–50%, 23% and 7%, respectively. Table 2 also showed the performance of the model validation for refusal of PCI. The sensitivity was 72% and the negative predictive value was 93%, which is slightly lower than that in the derivation cohort.

### Decision-making factors for refusal of PCI

There were 115 conversations conducted by nine cardiologists, of whom four were male. The median age of them was 30 (IQR 26–34) years, and the median resident time of them was 5 (IQR 3–7) years. Besides, most of them were chief resident doctors. Interestingly, the majority of the consent signers were not the patients themselves but their relatives (Supplementary Table 1). Among them, 9 (7.8%) were their mate, 94 (81.7%) were their children and only 12 (20.4%) were patients themselves. And when these conversations were divided into two groups by consent to PCI, the proportion of signers between groups ( $P = 0.674$ ) was similar.

**Table 1** Baseline characteristics of derivation cohort by consent to PCI

| Patient characteristics        | All<br>( <i>n</i> = 288) | Consent to PCI           |                        | <i>P</i> |
|--------------------------------|--------------------------|--------------------------|------------------------|----------|
|                                |                          | Yes<br>( <i>n</i> = 236) | No<br>( <i>n</i> = 52) |          |
| Demographic characteristics    |                          |                          |                        |          |
| Age, years                     | 62.8 ± 13.9              | 61.4 ± 13.0              | 69.2 ± 16.1            | < 0.001  |
| Male                           | 213 (73.9)               | 174 (73.7)               | 39 (75.0)              | 0.850    |
| Living with mate               | 243 (84.3)               | 202 (85.7)               | 41 (78.8)              | 0.225    |
| On the job                     | 107 (37.1)               | 96 (40.7)                | 11 (21.2)              | 0.008    |
| Outlander                      | 36 (12.5)                | 24 (10.2)                | 12 (23.1)              | 0.011    |
| Medical insurance              | 263 (91.3)               | 220 (93.2)               | 43 (82.7)              | 0.030    |
| Medical history                |                          |                          |                        |          |
| Hyperlipemia                   | 87 (30.2)                | 74 (31.4)                | 13 (25.0)              | 0.366    |
| Hypertension                   | 186 (64.5)               | 143 (60.6)               | 34 (65.4)              | 0.520    |
| Diabetes mellitus              | 79 (27.4)                | 59 (25.0)                | 20 (38.5)              | 0.049    |
| Current smoking                | 132 (45.8)               | 119 (50.4)               | 13 (25.0)              | 0.001    |
| Renal insufficiency*           | 31 (10.7)                | 14 (5.9)                 | 17 (32.7)              | < 0.001  |
| Ischemic stroke                | 35 (12.1)                | 23 (9.7)                 | 12 (23.1)              | 0.008    |
| Family history of CAD          | 66 (22.9)                | 58 (24.6)                | 8 (15.4)               | 0.153    |
| History of CAD                 |                          |                          |                        |          |
| Prior CAD                      | 61 (21.1)                | 46 (19.4)                | 15 (28.8)              | 0.135    |
| Prior MI                       | 41 (14.2)                | 29 (12.3)                | 12 (23.1)              | 0.044    |
| Prior PCI                      | 36 (12.5)                | 29 (12.3)                | 7 (13.5)               | 0.817    |
| Prior CABG                     | 4 (1.3)                  | 2 (0.8)                  | 2 (3.8)                | 0.151    |
| Situation on admission         |                          |                          |                        |          |
| Heart rate, beats/min          | 77.8 ± 17.2              | 77.3 ± 16.6              | 80.2 ± 15.6            | 0.891    |
| SBP, mmHg                      | 126.2 ± 29.1             | 125.7 ± 29.7             | 130.2 ± 28.4           | 0.316    |
| DBP, mmHg                      | 75.3 ± 18.7              | 77.0 ± 17.3              | 74.8 ± 19.1            | 0.506    |
| Cardiogenic shock              | 16 (5.5)                 | 15 (6.4)                 | 1 (1.9)                | 0.353    |
| Killip ≥ 2                     | 73 (25.3)                | 58 (24.5)                | 15 (28.8)              | 0.522    |
| Self-rated severe symptoms     | 228 (79.1)               | 203 (86.0)               | 25 (48.1)              | < 0.001  |
| ST elevation of first ECG      | 234 (81.2)               | 195 (82.6)               | 39 (75.0)              | 0.202    |
| Positive troponin on admission | 174 (60.4)               | 136 (57.6)               | 38 (73.0)              | 0.039    |
| EMS transportation             | 70 (24.3)                | 56 (23.7)                | 14 (26.9)              | 0.627    |
| Pre-hospital delay > 4 h       | 129 (44.7)               | 101 (42.8)               | 28 (53.8)              | 0.147    |
| Off-hours arrival              | 218 (75.6)               | 177(75.0)                | 41 (78.8%)             | 0.558    |

Data are presented as mean ± SD or *n* (%)

CAD coronary artery disease, MI myocardial infarction, PCI percutaneous coronary intervention, CABG coronary artery bypass graft, SBP systolic blood pressure, DBP diastolic blood pressure, EMS emergency medical service

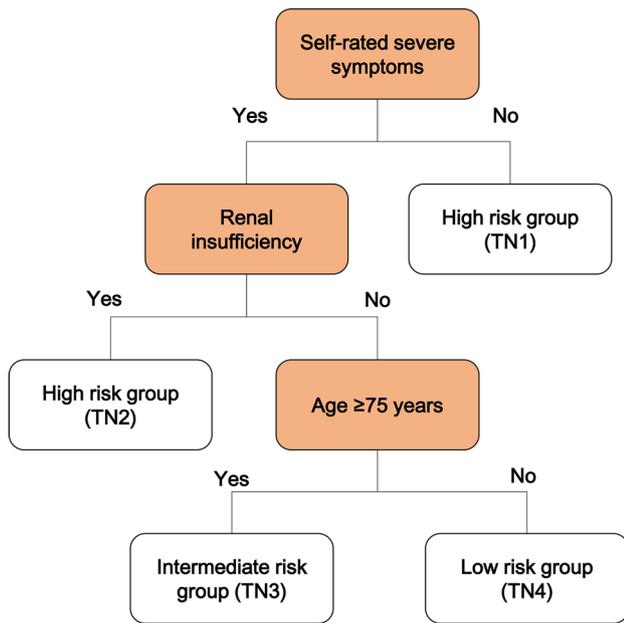
\*Renal insufficiency, glomerular filtration rate < 60 ml/min/1.73m<sup>2</sup>

Also, we found that the patient himself was usually older and was not willing to make his own decision but to pay attention to family's opinions. Hence, the percentage of patients presented with their relatives was higher in the shorter consent time group (75.2% vs 57.8%, *P* = 0.019), this maybe for saving the time of waiting for their family members. Among the classic seven elements of informed decision making, cardiologists were more likely to assess alternatives in the refusal group (*P* = 0.001). Of all the discussions, only 13 (11.3%) contained all seven elements, which indicating that assessment for decision making was incomplete in most

patients. Signers in the consent group more realized the importance of timely reperfusion and the benefits of primary PCI (*P* < 0.001 and *P* = 0.015, respectively).

## Discussion

During the clinical practice, a lot of STEMI patients presented to hospitals with capability to provide cardiac catheterization 24 h/day chose to receive thrombolytic therapy or conservative medical treatment, but little is known about



**Fig. 1** The CART prediction model for refusal of percutaneous coronary intervention for acute myocardial infarction. A point of VAS  $\geq 7$  was considered the self-rated severe symptoms. Renal insufficiency was defined as glomerular filtration rate  $< 60$  ml/min/1.73 m<sup>2</sup>. TN, terminal node

**Table 2** Performance of the model for refusal of PCI

| Characteristics              | Derivation cohort (n=288) | Validation cohort (n=115) |
|------------------------------|---------------------------|---------------------------|
| Prevalence of refusal of PCI | 18.1%                     | 15.7%                     |
| Low-risk group               | n=159                     | n=76                      |
| Terminal node 4              | 6/159 (4%)                | 5/76 (7%)                 |
| Intermediate-risk group      | n=44                      | n=13                      |
| Terminal node 3              | 8/44 (18%)                | 3/13 (23%)                |
| High-risk group              | n=85                      | n=26                      |
| Terminal node 1              | 27/60 (45%)               | 8/22 (36%)                |
| Terminal node 2              | 11/25 (44%)               | 2/4 (50%)                 |
| Sensitivity                  | 88%                       | 72%                       |
| Specificity                  | 64%                       | 73%                       |
| Positive predictive value    | 35%                       | 33%                       |
| Negative predictive value    | 96%                       | 93%                       |

PCI percutaneous coronary intervention

factors associated with the choice of PCI at these facilities [19, 20]. Similar to previous studies, we found that a substantial number of STEMI patients presented to our hospital within 12 h from the onset of symptoms actually refused or did not undergo PCI. We identified several key clinical factors, such as self-rated mild symptom, renal insufficiency and older age, which were associated with refusal of primary

**Table 3** Multivariable regression analysis of factors related to refusal of PCI

| Variables                   | Wald | Adjusted OR (95% CI) | P      |
|-----------------------------|------|----------------------|--------|
| Self-rated severe symptoms  | 28.8 | 0.13 (0.05–0.33)     | <0.001 |
| Renal insufficiency*        | 16.7 | 8.97 (3.15–25.5)     | <0.001 |
| Age $\geq 75$ years         | 10.6 | 5.03 (1.65–15.30)    | 0.004  |
| Prior myocardial infarction | 4.3  | 3.15 (1.09–9.05)     | 0.034  |
| Outlander                   | 5.5  | 4.41 (1.10–17.65)    | 0.036  |

After adjustment of on the job, medical insurance, diabetes mellitus, current smoking ischemic stroke and positive troponin on admission PCI percutaneous coronary intervention

\*Renal insufficiency, glomerular filtration rate  $< 60$  ml/min/1.73m<sup>2</sup>

PCI. Moreover, the patients’ willingness of not choosing PCI could be recognized by our predictive tool using clinical available variants. Overall, the prevalence of refusal of PCI was 18.1% and 15.7% among derivation cohort and validation cohort. As a result, the risk predicted by this model varied more than tenfold (from 4 to 50%) and thus patients could be divided into various risk groups to receive suitable therapy rapidly.

Lower rates of primary PCI (16.3% ~ 65.5%) reported in previous studies reflect the real-world practice on a nationwide scale of China [20, 21]. In the present study, 78.4% of patients with STEMI received primary PCI. This represents a relative high rate of primary PCI, since our population included patients with a pre-hospital delay  $< 12$  h and we also did not exclude patients with contraindications to thrombolytic therapy, and patients were served by a 24/7 (24 h service 7 days a week) service primary PCI center. However, the rate of PCI observed in the present study was still lower than those reported in United States and European countries [22, 23]. In the NCDR AR-G registry, 93.8% of patients with STEMI received reperfusion therapy, and 83.0% received primary PCI [23]. In a contemporary Euro Heart Survey, 81.3% of STEMI patients admitted within the first 12 h received reperfusion therapy, and 64.0% received primary PCI [22].

Early reperfusion therapy, especially primary PCI, in patients with STEMI significantly reduces mortality [24–26]. Clinical factors, such as age and comorbidities that influence the choice of reperfusion therapies in patients with STEMI have been reported in several previous studies<sup>+</sup>. The GRACE investigators found that patients at an older age ( $\geq 75$  years) were less likely to receive reperfusion therapies [27], and coronary angiography and PCI rates decreased significantly with age [28]. The CRUSADE study also showed that increasing age was the strongest factor associated with lack of reperfusion therapies usage among eligible STEMI patients [29]. However, it was difficult to find

**Table 4** Baseline characteristics of validation cohort by consent to PCI

| Patient characteristics            | Consent to PCI   |                 |                | P      |
|------------------------------------|------------------|-----------------|----------------|--------|
|                                    | All<br>(n = 115) | Yes<br>(n = 97) | No<br>(n = 18) |        |
| <b>Demographic characteristics</b> |                  |                 |                |        |
| Age, years                         | 60.8 ± 13.4      | 60.5 ± 12.9     | 62.7 ± 16.1    | 0.421  |
| Male                               | 80 (69.6)        | 66 (68.0)       | 14 (77.8)      | 0.410  |
| Living with mate                   | 96 (83.5)        | 80 (82.5)       | 16 (88.9)      | 0.501  |
| On the job                         | 42 (26.5)        | 37 (38.1)       | 5 (27.8)       | 0.698  |
| Outlander                          | 36 (12.5)        | 9 (9.3)         | 8 (44.4)       | 0.011  |
| Medical insurance                  | 104 (90.4)       | 91 (93.8)       | 13 (72.2)      | 0.030  |
| <b>Medical history</b>             |                  |                 |                |        |
| Hyperlipemia                       | 32 (37.8)        | 29 (31.4)       | 3 (25.0)       | 0.388  |
| Hypertension                       | 64 (55.7)        | 54 (55.7)       | 10 (55.6)      | 0.993  |
| Diabetes mellitus                  | 31 (27.0)        | 25 (25.8)       | 6 (33.3)       | 0.507  |
| Current smoking                    | 52 (45.2)        | 47 (48.5)       | 5 (27.8)       | 0.106  |
| Renal insufficiency*               | 9 (7.8)          | 5 (5.2)         | 4 (22.2)       | 0.046  |
| Ischemic stroke                    | 14 (12.2)        | 8 (8.2)         | 6 (33.3)       | 0.003  |
| Family history of CAD              | 35 (30.4)        | 30 (30.9)       | 5 (27.8)       | 0.790  |
| <b>History of CAD</b>              |                  |                 |                |        |
| Prior CAD                          | 29 (25.2)        | 20 (20.6)       | 9 (50.0)       | 0.008  |
| Prior MI                           | 21 (18.3)        | 13 (13.4)       | 8 (44.4)       | 0.002  |
| Prior PCI                          | 19 (16.5)        | 14 (14.4)       | 5 (27.8)       | 0.161  |
| Prior CABG                         | 1 (0.9)          | 0 (0)           | 1 (5.6)        | 0.053  |
| <b>Situation on admission</b>      |                  |                 |                |        |
| Heart rate, beats/min              | 75.4 ± 18.6      | 75.1 ± 18.9     | 76.5 ± 17.6    | 0.914  |
| SBP, mmHg                          | 130.4 ± 29.7     | 131.1 ± 29.2    | 126.3 ± 33.1   | 0.692  |
| DBP, mmHg                          | 77.9 ± 19.9      | 78.4 ± 19.9     | 75.6 ± 20.6    | 0.508  |
| Cardiogenic shock                  | 7 (6.1)          | 6 (6.2)         | 1 (5.6)        | 0.919  |
| Killip > 2                         | 30 (26.1)        | 26 (26.8)       | 4 (22.2)       | 0.909  |
| Self-rated severe symptoms         | 89 (77.4)        | 81 (83.5)       | 8 (44.4)       | <0.001 |
| ST elevation of first ECG          | 97 (84.3)        | 84 (86.6)       | 13 (72.2)      | 0.123  |
| Positive troponin on admission     | 69 (60.0)        | 57 (58.8)       | 12 (66.7)      | 0.530  |
| EMS transportation                 | 31 (27.0)        | 26 (26.8)       | 5 (27.8)       | 0.932  |
| Pre-hospital delay > 4 h           | 40 (34.8)        | 33 (34.0)       | 7 (38.9)       | 0.690  |
| Off-hours arrival                  | 66 (57.4)        | 56 (57.7)       | 10 (55.6)      | 0.864  |

Data are presented as mean ± SD or n (%)

CAD coronary artery disease, MI myocardial infarction, PCI percutaneous coronary intervention, CABG coronary artery bypass graft, SBP systolic blood pressure, DBP diastolic blood pressure, EMS emergency medical service

\*Renal insufficiency, glomerular filtration rate < 60 ml/min/1.73m<sup>2</sup>

which reperfusion therapies in these studies. Besides, it was unclear whether the failure to perform reperfusion therapies was due to the patient-centered decision making. Emerging evidences evoked the relationship between age and decision to undergo primary PCI. Registry data from UK showed that primary PCI rate was lower in patients with age > 80 years [30]. Our study included STEMI patients at all age stages, and also found association between older age and refusal of primary PCI.

In China, a prospective study was performed in elderly patients with a first STEMI to identify factors influencing

the use of primary PCI, indicating that self-rate mild symptoms was associated with refusal of primary PCI [9]. In our study, self-rate mild symptoms are the best discriminator identified both by CART analysis and logistic regression. We also used VAS scale to estimate the pain to avoid subjective inconsistency and divide patients into severe and mild symptom group [16]. The model we developed used three variants including self-rate mild symptoms, older age and renal insufficiency and it was validated in an independent cohort. The sensitivity and specificity of the prediction tool were 88% and 64% in the derivation cohort and 72% and

73% in the validation cohort, indicating that the accuracy of the model is moderate. The NPV of the CART tool in the derivation and validation cohort were 96% and 93%, suggesting that the model is more suitable to safely rule out the patients choosing PCI.

The model produced three groups by four TNs. The high-risk group included: self-rated mild symptom (TN 1); self-rated severe symptom, glomerular filtration rate < 60 ml/min/1.73m<sup>2</sup> (TN 2). The intermediate-risk group: self-rated severe symptom, glomerular filtration rate < 60 ml/min/1.73m<sup>2</sup> and age ≥ 75 years (TN 3). The low-risk group: self-rated severe symptom, glomerular filtration rate < 60 ml/min/1.73m<sup>2</sup> and age < 75 years (TN 4). Patients judged to be at high risks may receive intensive attention and conserved therapy, while patients predicted to be at low risks may accept PCI immediately without hesitation and worry.

In contrast to previously reported results [27–30], which were conducted primarily in western countries, the present study did not find associations between sex, health insurance type, or cardiogenic shock and refusal of PCI. It was difficult to interpret but might be partly explained by the low operating costs, high medical insurance coverage and the tense doctor-patient relationship in modern Chinese society [31]. Patients with cardiogenic shock should be more likely to choose primary PCI due to the obvious survival benefit in this setting [32], but these subgroups of patients tend to be at higher risk of death during or after the procedure at the same time. In China, many patients blame the doctors directly for the deterioration of their health, claiming that doctors lack devotion and skills. Failing to find the relationship between cardiogenic shock and PCI use might be associated with fear of disputes with patients and negative publicity for doctors and hospitals and possible consequences of litigation.

There were some limitations in this study. First, it was a single-centered study, and the sample size was relatively small. Therefore, the model needs to be validated in large population. Second, the risk for refusal of PCI may be influenced by many potential factors not considered in this model, thus the model could be modified in the future research. Third, this model must be applied with complete medical data of patients and it could not replace the physicians experience and clinical judge.

## Conclusion

Almost 20% of eligible Chinese patients with STEMI refused or did not to undergo primary PCI. Patients at lower and higher risks can be easily identified for refusal of PCI by the predictive model using common clinical data. The predictive model might provide useful information for rapid recognition and early response for this population.

**Acknowledgements** This study was supported by National Natural Science Foundation of China (81770356).

**Conflict of interest** There were no potential conflicts of interest in this study, including related consultancies, shareholdings and grant funding.

**Statement of human and animal rights** Our study has been approved by the institutional research ethics committee of our hospital (2014PHB125-01) and has been performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki.

**Informed consent** Informed consent was obtained from each patient.

## References

1. GBD (2017) Causes of Death Collaborators (2018) Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 392:1736–1788
2. Benjamin EJ, Muntner P, Alonso A et al (2019) Heart Disease and Stroke Statistics-2019 Update: A Report From the American Heart Association. *Circulation* 139:e56–e66
3. Nguyen AV, Thanh LV, Kamel MG et al (2017) Optimal percutaneous coronary intervention in patients with ST-elevation myocardial infarction and multivessel disease: An updated, large-scale systematic review and meta-analysis. *Int J Cardiol* 244:67–76
4. O’Gara PT, Kushner FG, Ascheim DD et al (2013) 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* 127:529–555
5. Ibanez B, James S, Agewall S et al (2017) 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J* 39:119–177
6. Windecker S, Kolh P, Alfonso F et al (2015) 2014 ESC/EACTS guidelines on myocardial revascularization. *Euro Intervention* 10:1024–1094
7. Li J, Li X, Wang Q et al (2015) ST-segment elevation myocardial infarction in China from 2001 to 2011 (the China PEACE-Retrospective Acute Myocardial Infarction Study): a retrospective analysis of hospital data. *Lancet* 385:441–451
8. Xun YW, Yang JG, Song L et al (2010) In-hospital delay to primary angioplasty for patients with ST-elevated myocardial infarction between cardiac specialized hospitals and non-specialized hospitals in Beijing, China. *Chin Med J (Engl)* 123:800–805
9. Zhou S, Chen J, Xu RY et al (2014) Factors associated with the use of percutaneous coronary intervention in elderly Chinese patients with a first ST elevated acute myocardial infarction. *Patient Prefer Adherence* 8:257–262
10. Altamirano J, Lopez-Pelayo H, Michelena J et al (2017) Alcohol abstinence in patients surviving an episode of alcoholic hepatitis: Prediction and impact on long-term survival. *Hepatology* 66:1842–1853
11. Odaka Y, Takahashi J, Tsuburaya R et al (2017) Plasma concentration of serotonin is a novel biomarker for coronary microvascular dysfunction in patients with suspected angina and unobstructive coronary arteries. *Eur Heart J* 38:489–496

12. Kattan MW (2010) Classification and regression trees versus nomograms: a bone scan positivity example. *Eur Urol* 57:559–561
13. Lehmann G, Schmitt C, Kehl V et al (2003) Electrocardiographic algorithm for assignment of occluded vessel in acute myocardial infarction. *Int J Cardiol* 89:79–85
14. Hochholzer W, Trenk D, Fromm MF et al (2010) Impact of cytochrome P450 2C19 loss-of-function polymorphism and of major demographic characteristics on residual platelet function after loading and maintenance treatment with clopidogrel in patients undergoing elective coronary stent placement. *J Am Coll Cardiol* 55:2427–2434
15. Thygesen K, Alpert JS, Jaffe AS et al (2012) Third universal definition of myocardial infarction. *Circulation* 126:2020–2035
16. Bahreini M, Jalili M, Moradi-Lakeh M (2015) A comparison of three self-report pain scales in adults with acute pain. *J Emerg Med* 48:10–18
17. Rothberg MB, Sivalingam SK, Kleppel R et al (2015) Informed Decision Making for Percutaneous Coronary Intervention for Stable Coronary Disease. *JAMA Intern Med* 175:1199–1206
18. Song JX, Zhu L, Lee CY, Ren H et al (2016) Total ischemic time and outcomes for patients with ST-elevation myocardial infarction: does time of admission make a difference? *J Geriatr Cardiol* 13:658–664
19. Fazel R, Krumholz HM, Bates ER et al (2009) Choice of reperfusion strategy at hospitals with primary percutaneous coronary intervention: a National Registry of Myocardial Infarction analysis. *Circulation* 120:2455–2461
20. Zhang SY, Hu DY, Sun YH et al (2008) Current management of patients with ST elevation myocardial infarction in Metropolitan Beijing, China. *Clin Invest Med* 31:E189–E197
21. Gao R, Patel A, Gao W et al (2008) Prospective observational study of acute coronary syndromes in China: practice patterns and outcomes. *Heart* 94:554–560
22. Schiele F, Hochadel M, Tubaro M et al (2010) Reperfusion strategy in Europe: temporal trends in performance measures for reperfusion therapy in ST-elevation myocardial infarction. *Eur Heart J* 31:2614–2624
23. de Boer SP, Barnes EH, Westerhout CM et al (2011) High-risk patients with ST-elevation myocardial infarction derive greatest absolute benefit from primary percutaneous coronary intervention: results from the Primary Coronary Angioplasty Trialist versus thrombolysis (PCAT)-2 collaboration. *Am Heart J* 161:500–507
24. Keeley EC, Boura JA, Grines CL (2003) Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. *Lancet* 361:13–20
25. Stone GW (2008) Angioplasty strategies in ST-segment-elevation myocardial infarction: part I: primary percutaneous coronary intervention. *Circulation* 118:538–551
26. Dong S, Chu Y, Zhang H et al (2014) Reperfusion times of ST-Segment elevation myocardial infarction in hospitals. *Pak J Med Sci* 30:1367–1371
27. Eagle KA, Goodman SG, Avezum A et al (2002) Practice variation and missed opportunities for reperfusion in ST-segment-elevation myocardial infarction: findings from the Global Registry of Acute Coronary Events (GRACE). *Lancet* 359:373–377
28. Avezum A, Makdisse M, Spencer F et al (2005) Impact of age on management and outcome of acute coronary syndrome: observations from the Global Registry of Acute Coronary Events (GRACE). *Am Heart J* 149:67–73
29. Gharacholou SM, Alexander KP, Chen AY et al (2010) Implications and reasons for the lack of use of reperfusion therapy in patients with ST-segment elevation myocardial infarction: findings from the CRUSADE initiative. *Am Heart J* 159:757–763
30. Hall M, Laut K, Dondo TB et al (2014) Patient and hospital determinants of primary percutaneous coronary intervention in England, 2003–2013. *Heart* 102:313–319
31. Ranasinghe I, Rong Y, Du X et al (2014) System barriers to the evidence-based care of acute coronary syndrome patients in China: qualitative analysis. *Circ Cardiovasc Qual Outcomes* 7:209–216
32. Hochman JS, Sleeper LA, White HD et al (2001) One-year survival following early revascularization for cardiogenic shock. *JAMA* 285:190–192

**Publisher's Note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.