

A New Scoring System for Predicting Ventricular Arrhythmia Risk in Patients with Acute Myocardial Infarction

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Objective: In this study, a risk score for ventricular arrhythmias (VA) were evaluated for predicting the risk of ventricular arrhythmia (VA) of acute myocardial infarction (AMI) patients.

Methods: Patients with AMI were divided into two sets according to whether VA occurred during hospitalization. Another cohort was enrolled for external validation. The area under the curve (AUC) of receiver operating characteristic (ROC) was calculated to evaluate the accuracy of the model.

Results: A total of 1493 eligible patients with AMI were enrolled as the training set, of whom 70 (4.7%) developed VA during hospitalization. In-hospital mortality was significantly higher in the VA set than in the non-VA set (31.4% vs 2.7%, $P=0.001$). The independent predictors of VA in patients with AMI including Killip grade ≥ 3 , STEMI patients, LVEF $<50\%$, frequent premature ventricular beats, serum potassium <3.5 mmol/L, type 2 diabetes, and creatinine level. The AUC of the model for predicting VT/VF in the training set was 0.815 (95% CI: 0.763–0.866). A total of 1149 cases were enrolled from Xuzhou Center Hospital as the external validation set. The AUC of the model in the external validation set for predicting VT/VF was 0.755 (95% CI: 0.687–0.823). Calibration curves indicated a good consistency between the predicted and the observed probabilities of VA in both sets.

Conclusion: We have established a clinical prediction risk score for predicting the occurrence of VA in AMI patients. The prediction score is easy to use, performs well and can be used to guide clinical practice.

Keywords: ventricular tachycardia, ventricular flutter and fibrillation, risk stratification, scoring system, acute myocardial infarction

Introduction

Malignant ventricular arrhythmia (VA) is mainly manifested as persistent ventricular tachycardia (VT), ventricular flutter and fibrillation (VF) and other serious life-threatening arrhythmias originating from the ventricle.^{1,2} Malignant VA is one of the most common cause of death in patients with acute myocardial infarction (AMI).^{3,4} Early revascularization can significantly improve the prognosis of AMI patients.^{5,6} However, VA may still occur due to reperfusion myocardial injury or no-reflow.^{7–9} Thus, early assessment of VA risk in AMI patients can help clinicians to take active prevention and treatment measures, thus reducing the risk of in-hospital death and improving the prognosis.^{4,10–12} In this study, we aimed to explore independent predictors of VA in AMI patients during hospitalization, and use them to develop a clinical prediction model.

Methods

Study Population and Grouping

The study population was selected from Changzhou No.2 People's Hospital (Changzhou Acute Myocardial Infarction Registry dataset, <http://www.chictr.org.cn/searchproj.aspx>, ChiCTR1800014583). The validation set was selected from Xuzhou Center Hospital (Figure 1).

Patients diagnosed with AMI in the department of cardiology from two centers from December 2012 to January 2018 were selected and retrospectively analyzed. AMI was diagnosed according to the third edition of Global Definition Criteria for Acute Myocardial Infarction. Inclusion criteria: age >18 years and diagnosis of acute myocardial infarction at admission. Coronary angiography (CAG) was performed among all enrolled patients. Percutaneous coronary intervention (PCI) therapy was then performed following CAG in eligible patients. Patients who underwent coronary artery bypass graft (CABG) after coronary angiography were excluded.

The enrolled patients were divided into two sets according to whether VA occurred during hospitalization: VA set and non-VA set. Exclusion criteria included autoimmune diseases, recent infection, pregnancy, severe hepatic or renal dysfunction, myocarditis, and prior cardiac surgery.

Ethics Approval

All the enrolled patients had signed informed consent at the time of inclusion, and the project had been approved by the Ethics Committee of Changzhou No.2 People's Hospital (Ethics number: [2018]KY005-01) and Xuzhou Center Hospital (Ethics number: XZXY-LK-20211021-037). The study was performed in accordance with the Declaration of Helsinki.

Data Collection

The data about patients' basic characteristics and VA were collected by reviewing the electronic medical record system. The collected variables including the basic information such as age, gender, medical history, diagnosis, vital signs during

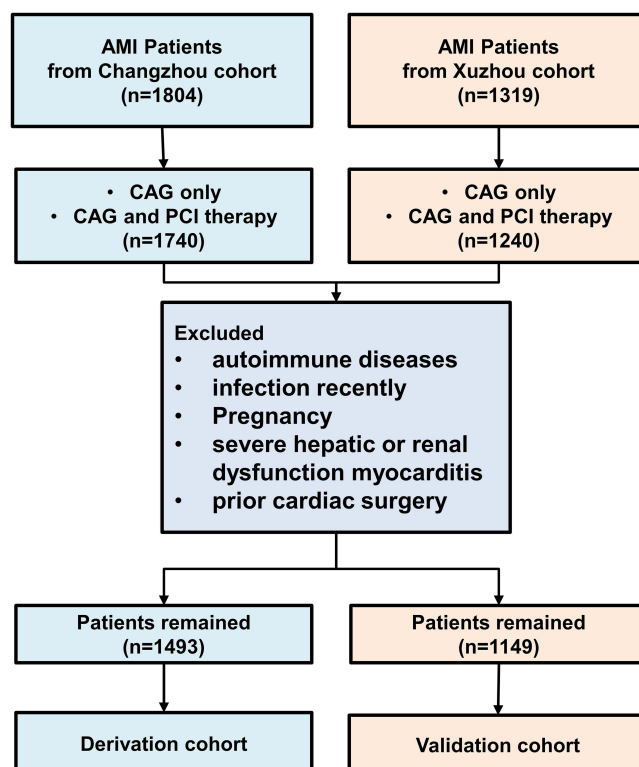


Figure 1 Workflow of the inclusion and exclusion of the study subjects.

Abbreviations: AMI, acute myocardial infarction; CAG, coronary angiography; PCI, percutaneous coronary intervention.

hospitalization, hospital electrocardiogram characteristics, laboratory parameters, interventional treatment related variables and medications. Echocardiography data during hospitalization were also collected.

Endpoint

The primary endpoint was the occurrence of malignant VA during hospitalization, including persistent ventricular tachycardia, ventricular flutter, and ventricular fibrillation, and the secondary endpoint was the all-cause mortality during hospitalization.

Statistical Analysis

Continuous variables were described using mean \pm standard deviation or median, and 25th and 75th percentiles. Categorical variables were expressed by absolute values (percentages, %). Comparisons between two sets were performed using Student's *t*-test for continuous variables and chi-square or Fisher exact test for categorical variables. A multivariate logistic regression analysis was performed to sift the independent predictors of VA. A clinical prediction model was constructed. The risk score was calculated by coefficients of the logistic regression model (β value \times 10). The area under the curve (AUC) of receiver operating characteristic (ROC) was used to evaluate the accuracy of the prediction model in the training and validation sets. A two-sided test was used. $P < 0.05$ was considered statistically. SPSS 22.0 was used for statistical analysis.

Results

Baseline Clinical Data

A total of 1493 eligible AMI patients from Changzhou No.2 People's Hospital were enrolled, of which 70 patients (4.69%) developed VA during hospitalization, and 61 patients (4.09%) died in the hospital. As shown in Table 1, the VA set contained a lower percentage of smokers, higher percentages of patients complicated with diabetes, with Killip grade ≥ 3 , with left ventricular ejection fraction (LVEF) $> 50\%$, and with ST-segment elevation myocardial infarction (STEMI). The mortality in VA set was also significantly higher in the VA set (Table 1).

Table 1 Baseline Characteristics of the Patients Included in the Study

Variable	VT/VF		<i>t</i> / χ^2 Value	P value
	No (n=1423)	Yes (n=70)		
Age, y	66.5 \pm 13.8	69.1 \pm 14.3	1.537	0.125
Male, sex	1017 (71.5)	46 (65.7)	1.077	0.299
SBP, mmHg	132.6 \pm 24.6	127.5 \pm 26.1	-1.701	0.089
DBP, mmHg	79.4 \pm 16.6	77.3 \pm 16.5	-1.013	0.314
Smoking	716 (50.3)	26 (37.1)	4.631	0.031 ^a
Alcohol drinking	172 (12.1)	8 (11.4)	0.027	0.869
Diabetes mellitus	367 (25.8)	33 (47.1)	15.509	<0.001 ^a
Hypertension	941 (66.1)	51 (72.9)	1.355	0.244
Killip class ≥ 3	133 (9.3)	23 (32.9)	39.413	<0.001 ^a
STEMI	889 (62.5)	53 (75.7)	5.023	0.025 ^a
LVEF $> 50\%$	981 (68.9)	28 (40.0)	25.503	<0.001 ^a
Hospital deaths	39 (2.7)	22 (31.4)	140.116	<0.001 ^a
Electrocardiogram feature				
Heart rate, beats/min	80.6 \pm 16.7	86.9 \pm 19.9	3.046	0.002 ^a
Sinus rhythm	1364 (95.9)	63 (90.0)	5.411	0.021 ^a
PVC	27 (1.9)	16 (22.9)	104.785	<0.001 ^a
QRS > 0.12 s	8 (0.6)	2 (2.9)	5.282	0.076

(Continued)

Table 1 (Continued).

Variable	VT/VF		t/ χ^2 Value	P value
	No (n=1423)	Yes (n=70)		
Baseline laboratory				
White blood cell ($\times 10^9/L$)	9.6 \pm 3.8	10 \pm 3.5	0.871	0.384
Neutrophil count (%)	75.5 \pm 10.8	77.5 \pm 10.9	1.516	0.130
Hemoglobin (g/L)	133.9 \pm 20.1	125.3 \pm 19.6	-3.584	0.001 ^a
Creatinine (μ mol/L)	85.8 \pm 35.6	110 \pm 60.8	5.326	<0.001 ^a
Glucose (mmol/L)	8.2 \pm 4.0	10.5 \pm 7.3	2.894	0.004 ^a
Albumin (g/L)	37.8 \pm 4.2	36.5 \pm 6.2	-1.560	0.119
Blood uric acid (μ mol/L)	344.7 \pm 108.9	371.3 \pm 129.6	1.240	0.215
Triglyceride (mmol/L)	1.6 \pm 1.3	1.6 \pm 1.5	0.086	0.931
Total cholesterol (mmol/L)	4.4 \pm 4.1	4.3 \pm 1.1	-0.210	0.834
High-density lipoprotein (mmol/L)	1.2 \pm 0.4	1.2 \pm 0.4	1.186	0.236
Low-density-lipoprotein (mmol/L)	2.4 \pm 0.8	2.5 \pm 0.8	0.285	0.776
Serum potassium < 3.5mmol/L	279 (19.6)	22 (31.4)	5.793	0.016 ^a

Notes: Values are expressed as mean \pm SD or n (%). ^aP value <0.05 was considered statistically significant.

Abbreviations: VT/VF, ventricular tachycardia/ventricular flutter and fibrillation; SBP, systolic blood pressure; DBP, diastolic blood pressure; STEMI, ST-segment elevation myocardial infarction; LVEF, left ventricular ejection fraction; PVC, frequent premature ventricular contractions.

The VA set showed a higher average heart rate, a lower percentage of patients with sinus rhythm, a higher percentage of patients with frequent premature ventricular contractions and QRS wave broadening on baseline electrocardiogram (Table 1). The VA set presented lower serum hemoglobin and potassium levels, but high creatinine and blood glucose levels at admission (Table 1).

Comparison of Treatment-Related Variables Between the Two Sets

Fewer patients in the VA set presented with the left circumflex artery (LCX) as the culprit vessel. A lower percentage of patients received ticagrelor, and a higher percentage of patients received oral or intravenous diuretics in the VA set (Table 2).

Table 2 Medications Treatments and Angiographic Characteristics

Variable	VT/VF		χ^2 Value	P value
	No (n=1423)	Yes (n=70)		
Angiographic Findings				
STENT	1352 (95.0)	67 (95.7)	0.070	1.000
LM	10 (0.7)	2 (2.9)	3.884	0.106
LAD	700 (49.2)	42 (60.0)	3.918	0.141
RCA	440 (30.9)	16 (22.9)	2.045	0.153
LCX	213 (15.0)	8 (11.4)	21.544	<0.001 ^a
Cardiovascular medications				
Angiotensin-converting enzyme inhibitor	848 (59.6)	34 (48.6)	3.352	0.067
Diuretics	266 (18.7)	21 (30.0)	5.493	0.019 ^a
Beta-blockers	848 (59.6)	42 (60.0)	0.005	0.946
Aspirin	1375 (96.6)	68 (97.1)	0.055	1.000
Ticagrelor	914 (64.2)	36 (51.4)	4.725	0.030 ^a
Clopidogrel	510 (35.8)	33 (47.1)	3.683	0.055
GP1Ib/IIIa receptor antagonist	689 (48.4)	37 (52.9)	0.526	0.468
Statin	1270 (89.2)	66 (94.3)	1.799	0.231
Low-molecular-weight heparin	1393 (97.7)	69 (98.6)	0.152	1.000

Notes: Values are expressed as n (%). ^aP value <0.05 was considered statistically significant.

Abbreviations: LM, left Main; LAD, left anterior descending; RCA, right coronary artery; LCX, left circumflex coronary artery;

Table 3 Multivariate Regression Analysis of Predictors of VT/VF Risk in Patients with AMI

Variable	β Value	OR Value	95% CI	P value	Rating Score
Diabetes mellitus	0.977	2.658	1.56–4.54	<0.001 ^a	10
KILLIP class ≥ 3	1.552	4.722	2.55–8.74	<0.001 ^a	16
STEMI	0.954	2.597	1.39–4.87	0.003 ^a	10
LVEF < 50%	0.886	2.425	1.42–4.13	0.001 ^a	9
PVC	2.834	17.014	7.79–37.15	<0.001 ^a	28
Serum potassium<3.5mmol/L	0.754	2.126	1.18–3.84	0.012 ^a	8
Creatinine $\leq 100\mu\text{mol/L}$				0.013 ^a	0
100 $\mu\text{mol/L}$ <Creatinine $\leq 200\mu\text{mol/L}$	0.339	1.404	0.77–2.56	0.269	3
200 $\mu\text{mol/L}$ <Creatinine $\leq 300\mu\text{mol/L}$	1.512	4.538	1.64–12.59	0.004 ^a	15

Note: ^aP value <0.05 was considered statistically significant.

Abbreviations: AMI, acute myocardial infarction; VT/VF, ventricular tachycardia/ventricular flutter and fibrillation; STEMI, ST-segment elevation myocardial infarction; LVEF, left ventricular ejection fraction; OR, odds ratio; CI, confidence interval; β multiply 10, rounding integers to the nearest whole score.

Predictors of Malignant VA

Both univariate and multivariate Logistic regression analyses were used to analyze predictors of malignant VA in patients with AMI. After adjustment, the independent predictors of VA included Killip grade ≥ 3 , STEMI patients, LVEF <50%, frequent premature ventricular beats, serum potassium <3.5 mmol/L, type 2 diabetes, and creatinine level. The risk of VA was scored according to the β value of each variable. The clinical prediction model was established according to the predictors in Table 3.

Internal Validation of the Model

Based on the factors in the regression analyses (Table 3), the clinical prediction model was constructed (Figure 2). Its AUC value for predicting VA in the training set was 0.815 (95% CI: 0.763–0.866), suggesting that the model could accurately predict the VA risk in AMI patients Figure 3A.

External Validation of the Model

We also validated the accuracy of the model in an external set of 1149 cases from Xuzhou Center Hospital. Baseline and clinical data of the validation set are shown in Table 4. The AUC of the model for predicting VA in the validation set was

VA risk prediction model

Variable	Rating score
Diabetes mellitus	10
Killip class ≥ 3	16
STEMI	10
LVEF < 50%	9
PVC	28
Serum potassium<3.5mmol/L	8
Creatinine $\leq 100\mu\text{mol/L}$	0
100 $\mu\text{mol/L}$ <Creatinine $\leq 200\mu\text{mol/L}$	3
200 $\mu\text{mol/L}$ <Creatinine $\leq 300\mu\text{mol/L}$	15

Figure 2 Risk prediction model of VA. The predictive variables were listed in the left column and the rating score was showed in the right column. The scores of each variable were added up to get the total score.

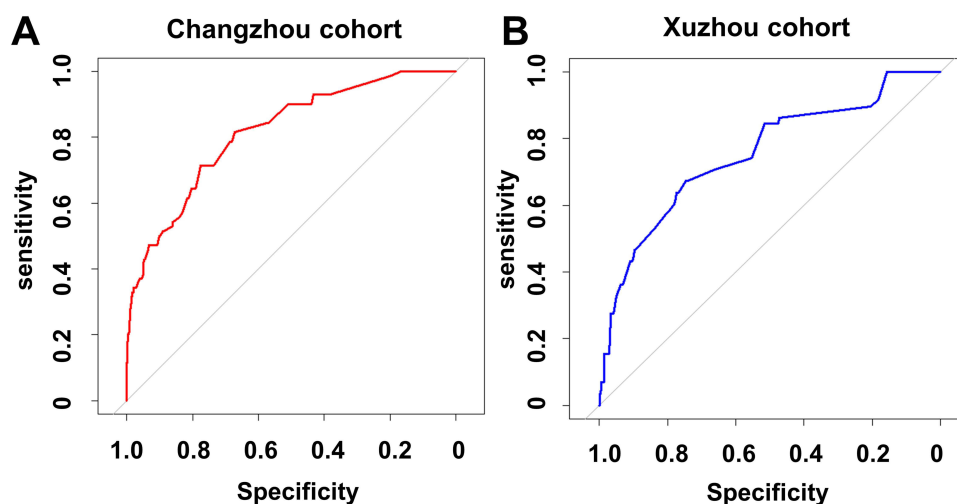


Figure 3 The ROC curve of the prediction model from two centers. **(A)** The ROC curve of the prediction model from Changzhou cohort. **(B)** The ROC curve of the prediction model from Xuzhou cohort.

0.755 (95% CI: 0.687–0.823) (Figure 3B). Finally, calibration curves indicated a good consistency between the predicted and observed probabilities of VA in both training and validation sets (Figure 4A and B).

Discussion

In the present study, we analyzed the risk factors associated with malignant VA during hospitalization in patients with AMI. The VA prediction model based on these factors showed a high accuracy in the training and validation sets. It is convenient for clinicians to early and quickly stratify AMI patients.^{4,10,13,14}

Table 4 Baseline Characteristics of the Patients in the Validation Group

Variable	VT/VF		P value
	No (n=1091)	Yes (n=58)	
Age, y	63.7±13.9	70.1±15.3	0.001 ⁺
Male, sex	824(75.5)	38(65.5)	0.086
SBP, mmHg	131.1±23.7	121.4±29.5	0.003 ⁺
DBP, mmHg	78.5±14.8	72.9±18.9	0.006 ⁺
Smoking	495(45.4)	17(29.3)	0.016 ⁺
Alcohol drinking	80(7.3)	5(8.6)	0.914
Diabetes mellitus	425(39.0)	22(37.9)	0.876
Hypertension	729(66.8)	45(77.6)	0.088
Killip class≥ 3	137(12.6)	26(44.8)	<0.001 ⁺
STEMI	623(57.1)	37(63.8)	0.315
Electrocardiogram feature			
Heart rate, beats/min	78.6±15.0	82.0±22.0	0.103
Baseline laboratory			
White blood cell (×10 ⁹ /L)	9.8±3.7	7.8±12.1	0.001 ⁺
Neutrophil count (%)	71.2±12.7	73.0±14.9	0.288
Hemoglobin (g/L)	140.7±20.7	130.0±22.3	<0.001 ⁺
Creatinine (μmol/L)	86.2±82.8	100.4±59.2	0.198
Glucose (mmol/L)	6.9±2.8	8.6±3.7	<0.001 ⁺
Albumin (g/L)	39.7±3.8	37.5±4.8	<0.001 ⁺
Blood uric acid (μmol/L)	352.0±113.0	363.5±168.9	0.462

(Continued)

Table 4 (Continued).

Variable	VT/VF		P value
	No (n=1091)	Yes (n=58)	
Triglyceride (mmol/L)	1.8±1.5	1.5±0.9	0.129
Total cholesterol (mmol/L)	4.2±1.2	3.1±2.1	<0.001 ^a
High-density lipoprotein (mmol/L)	1.0±0.3	1.1±0.3	0.053
Low-density-lipoprotein (mmol/L)	2.5±0.8	2.3±0.8	0.057
Glycosylated hemoglobin	6.5±1.9	5.4±3.6	<0.001 ^a

Notes: Values are expressed as mean + SD or n (%). ^aP value <0.05 was considered statistically significant.

Abbreviations: VT/VF, ventricular tachycardia/ventricular flutter and fibrillation; SBP, systolic blood pressure; DBP, diastolic blood pressure; STEMI, ST-segment elevation myocardial infarction.

Malignant VA is one common cause of deaths (more than half are sudden) after AMI.^{15–18} The Grace Global Registry in May 2007 suggests that the incidence of malignant VA is 11.7% in STEMI patients and 4.9% in NSTEMI patients. For those patients with malignant VA in AMI patients, the mortality increases significantly, which is consistent with the

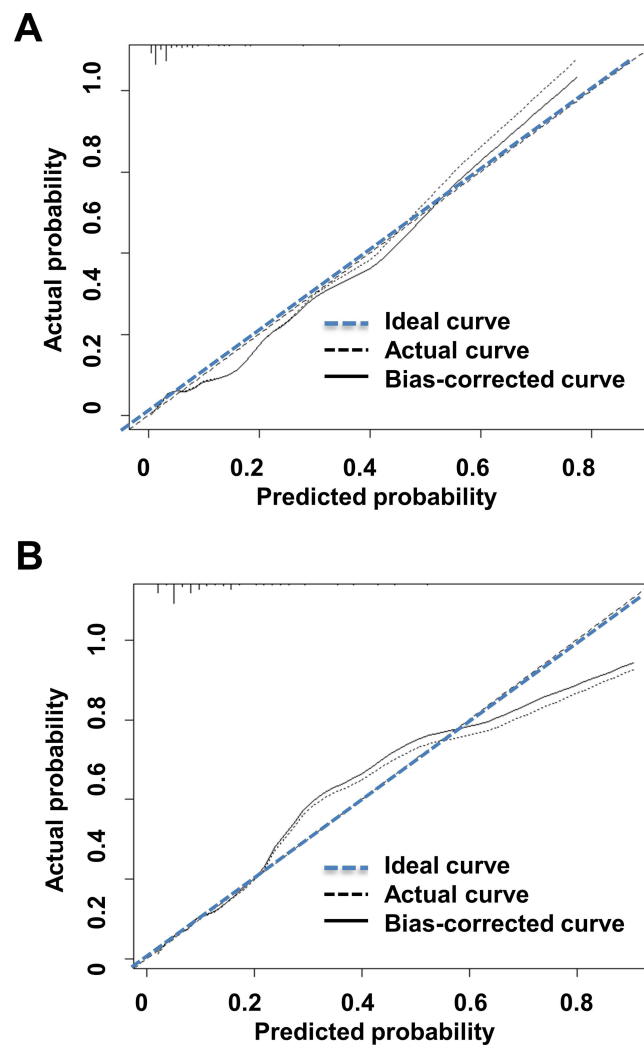


Figure 4 The calibration curve of the prediction model in the training (A) and the validation (B) set. X-axis: probability of VA as predicted by the new model; Y-axis: the actual probability of VA in the cohort. The dotted blue line represents the ideal curve where the predicted value is the same as the observed ones. The dotted black line represents the actual calibration curve in the training and the validation set. The black line represents the bias-corrected calibration curve.

results observed in our study. The incidence of malignant VA is still high in AMI patients, therefore resulting in a poor prognosis. So, our prediction model can help clinicians to take active preventive measures, individualize management and improve the prognosis of AMI patients.

In our prediction model, we found that Killip grade ≥ 3 at admission and LVEF $< 50\%$ were two strong predictors of VA risk, suggesting that cardiac function after myocardial injury is closely related to the risk of VA post AMI. Lee et al have also reported a similar conclusion in their cohort study. After AMI, the extensive death of cardiomyocytes leads to the formation of local scars in the myocardium, thus weakening cardiac systolic function and disrupting cardiac electrical activity. In addition, premature ventricular contraction is also an independent risk factor for malignant VA, suggesting that active measures should be taken to reduce the risk of VA and sudden death. For AMI patients with significantly worse cardiac functions or recurrent and persistent VA, early ICD implantation should be performed to reduce the risk of VA and death.¹⁹ Cardiac function may be improved significantly after revascularization therapy after AMI. In the present study, the patients who had undergone early ICD implantation were excluded. In a long follow-up, the value of ICD implantation for predicting the risk of VA should be fully considered, which may increase the accuracy of the present prediction model.

It is reported that electrolyte disorders are one main cause of cardiac electrical storms. We found that patients with hypokalemia are more likely to develop malignant VA, which suggests that electrolyte disorders, especially abnormal blood potassium and magnesium levels, should be intervened during the overall treatment of AMI.^{20–22} We also found that type-2 diabetes and baseline creatinine level were also strongly associated with the risk of VA in AMI patients.^{23–25} It has been reported that type 2 diabetes predicts a poor prognosis of AMI.^{26–28} Renal impairment in the early stage of AMI was also closely associated with an adverse prognosis in a short term.^{29–31} A recent study has reported that acute kidney injury in AMI patients is associated with a high mortality in a long term.³² Early identification of patients at a high risk of acute kidney injury is important, and an artificial intelligence model for predicting acute kidney injury risk has been developed.³³ In another study, age, creatinine and ejection fraction scores showed a high predictive value for in-hospital mortality in cardiogenic shock patients.³⁴ Cardiogenic shock increases the mortality in AMI patients. Early use of IABP can improve the prognosis of these patients.³⁵ In our previous studies, we have also found that a lower systolic blood pressure level at admission and a low level of free triiodothyronine are independently associated with the short-term outcomes in patients with AMI.^{36–38} In the current study, hypotension and free triiodothyronine were not associated with the risk of VA. Therefore, more attention should be paid to blood glucose and renal function in patients with AMI.

There are also some limitations in the present study. First, the sample size is relatively small. The accuracy of the prediction model should be validated in a larger cohort. Second, this study is a retrospective study of patients from two centers. A prospective study based on more centers is needed to evaluate the accuracy of the model. Third, we only observed the occurrence of malignant VA in AMI patients in a short term. A long-term follow-up is still needed in the future study.

Conclusion

We have established a clinical prediction risk score for predicting the occurrence of VA in AMI patients. The prediction score is easy to use, performs well and can be used to guide clinical practice.

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Disclosure

The authors report no conflicts of interest in this work.

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