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# Research article

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# Factors predicting the return of spontaneous circulation rate of cardiopulmonary resuscitation in China: Development and evaluation of predictive nomogram

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# ABSTRACT

*Background:* This study aimed to construct and internally validate a probability of the return of spontaneous circulation (ROSC) rate nomogram in a Chinese population of patients with cardiac arrest (CA).

*Methods*: Patients with CA receiving standard cardiopulmonary resuscitation (CPR) were studied retrospectively. The minor absolute shrinkage and selection operator (LASSO) regression analysis and multivariable logistic regression evaluated various demographic and clinicopathological characteristics. A predictive nomogram was constructed and evaluated for accuracy and reliability using C-index, the area under the receiver operating characteristic curve (AUC), calibration plot, and decision curve analysis (DCA).

*Results:* A cohort of 508 patients who had experienced CA and received standard CPR was randomly divided into training (70 %, n = 356) and validation groups (30 %, n = 152) for the study. LASSO regression analysis and multivariable logistic regression revealed that thirteen variables, such as age, CPR start time, Electric defibrillation, Epinephrine, Sodium bicarbonate (NaHCO<sub>3</sub>), CPR Compression duration, The postoperative prothrombin (PT) time, Lactate (Lac), Cardiac troponin (cTn), Potassium (K<sup>+</sup>), D-dimer, Hypertension (HBP), and Diabetes mellitus (DM), were found to be independent predictors of the ROSC rate of CPR. The nomogram model showed exceptional discrimination, with a C-index of 0.933 (95 % confidence interval: 0.882–0.984). Even in the internal validation, a remarkable C-index value of 0.926 (95 % confidence interval: 0.875–0.977) was still obtained. The accuracy and reliability of the model were also verified by the AUC of 0.923 in the training group and 0.926 in the validation group. The calibration curve showed the model agreed with the actual results. DCA suggested that the predictive nomogram had clinical utility.

*Conclusions:* A predictive nomogram model was successfully established and proved to identify the influencing factors of the ROSC rate in patients with CA. During cardiopulmonary resuscitation, adjusting the emergency treatment based on the influence factors on ROSC rate is suggested to improve the treatment rate of patients with CA.

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#### 1. Introduction

Cardiac arrest (CA) is a severe medical emergency characterized by the cessation of cardiac mechanical activity and the absence of circulation signs, it is one of the leading causes of adult deaths [1]. It is a significant public health concern, with a high incidence rate and low survival rate. Annually, Europe has an estimated 280,000 cases of out-of-hospital CA (OHCA), while in the United States, the number is 380,000. Additionally, in-hospital CA (IHCA) affects about 300,000 people each year worldwide [2]. In China, approximately 550,000 people die annually due to CA [3–5].

Cardiopulmonary resuscitation (CPR) is globally recognized as the most effective method for CA, and the return of spontaneous circulation (ROSC) indicates early successful resuscitation in patients with CA. In recent years, despite advances in CPR technology, the prospects for OHCA and IHCA patients are still not optimistic, with low ROSC and survival rates. The rate of discharged IHCA patients in the US and Europe who have achieved good function is 25.8 %, while for OHCA, it is only 8.2 % [6].

Since 2012, the survival rate of OHCA has not improved [7–11]. According to Hua's research, the survival rate of patients with CA in China after discharge is only 1.3 %, and the proportion of those with good neurological function is even lower at 1 % [12]. In Beijing, the survival rate after being discharged from IHCA is 9.1 %, and 1.3 % for OHCA [13,14].

Numerous studies have demonstrated that the success of resuscitation is reliant on the connections in the survival chain of CA and high-quality CPR. The success of ROSC in patients is closely linked to the rescuer's quality of CPR [15]. Additionally, it is strongly connected to the patient's physical condition [16]. The outcome depends on their physiological state, which is determined by the rescuer's efforts [17,18].

The 2020 American Heart Association (AHA) CPR guidelines [6] emphasize the significance of being able to recognize patients with high ROSC probability and reversible CA, especially with the emergence of advanced devices such as extracorporeal cardiopulmonary resuscitation (ECPR). Currently, in China and abroad, most research and attention is on how to do CPR of high quality. However, prognostic prediction in CPR also involves deciding when to end resuscitation. Unfortunately, no unified consensus exists on when and what indications to stop CPR in China or abroad. This study aims to create an efficient and straightforward predictive tool to estimate the ROSC rate in CA patients. Factors such as the start time of CPR, initial heart rhythm, defibrillation, various blood indicators during resuscitation, epinephrine, and sodium bicarbonate dosage will be evaluated to determine the resuscitation termination timing accurately. This tool can identify CA patients with therapeutic potential or those who may be eligible for ECPR and decide when to end resuscitation. This will help reduce futile rescue attempts, prevent complications due to excessive compression, and conserve medical resources, thus providing valuable guidance for clinical intervention of CA patients.

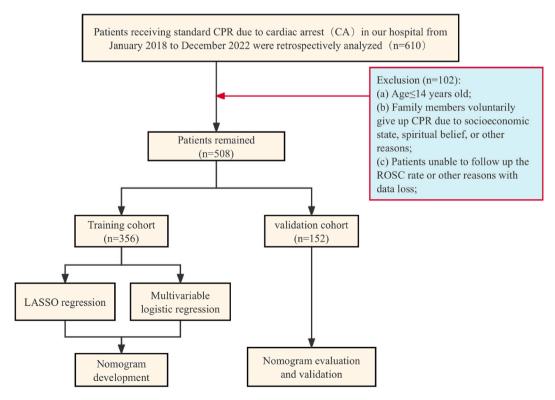


Fig. 1. Study flowchart.

#### 2.1. Patients

A retrospective analysis was conducted in the Second Affiliated Hospital & Yuying Children's Hospital of Wenzhou Medical University from January 2018 to December 2022, involving 508 patients who had undergone standard CPR due to CA and fulfilled the inclusion and exclusion criteria.

The inclusion criteria of this study were: (1) Patients aged>14 years old; (2) Patients undergoing standard high-quality CPR due to CA; (3) The duration of CPR is at least 30 min unless ROSC in 30 min; (4) Family members sign the informed consent form.

The exclusion criteria: Exclusion (n = 102): (1) Age $\leq$ 14 years old; (2) Family members voluntarily give up CPR due to socioeconomic state, spiritual belief, or other reasons; (3) Patients unable to follow up the ROSC rate or other reasons with data loss.

The study was approved by the Ethics Committee of the Second Affiliated Hospital & Yuying Children's Hospital of Wenzhou Medical University (Ethical approval number: 2023-K-182-01). This study followed the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis (TRIPOD) reporting guideline [19,20].

The selection procedure of study participants is summarized in Fig. 1.

#### 2.2. Demographic and clinicopathological variables

Demographic data of patients was collected and recorded retrospectively, including age, gender, CPR start time, electric defibrillation, respiratory assistance mode, injury, epinephrine, NaHCO<sub>3</sub>, CPR compression duration, the PT time, the postoperative activated partial thromboplastin (APTT) time, lac, hemoglobin, PH value, blood glucose, cTn, potassium, D-dimer, HBP, and DM. Patients who received standard high-quality CPR and returned to spontaneous circulation for more than 24 h were classified into the ROSC success group, while those who did not return to spontaneous circulation or returned for less than 24 h were classified into the ROSC failure group. All information was obtained from the medical record systems.

#### 2.3. Statistical analysis

R software was used to generate random numbers for all datasets. Random numbers were employed to assign 70 % (n = 356) of all enrolled patients to the training group and 30 % (n = 152) to the validation group. The LASSO method was utilized to identify the most effective predictive factors from the patients with CA receiving standard CPR.

A multivariable logistic regression model was developed to predict the ROSC rate in patients receiving CPR. Sociodemographic variables with a P-value of  $\leq 0.05$  and variables associated with clinical characteristics were included in the model to form a nomogram. The discrimination performance of the nomogram was evaluated using Harrell's C-index and the AUC in both the training and validation groups. Calibration accuracy was assessed using a calibration plot, and the clinical effectiveness was evaluated through DCA.

Statistical analysis was performed using SPSS version 26.0 and the R software (Version 3.4.1; https://www.R-project.org).

# 3. Results

#### 3.1. Patients' characteristics

Between January 2018 and December 2022, 508 patients who experienced CA underwent high-quality CPR in the Emergency Department of the Second Affiliated Hospital of Wenzhou Medical University. According to the definition of ROSC, the ROSC success group is (n = 147), and the ROSC failure group is (n = 361). Random numbers were used to assign 70 % (n = 356) of the enrolled patients to the training cohort and 30 % (n = 152) to the validation cohort. The demographic and clinical characteristics of the two groups were then statistically described, as shown in Table 1.

# 3.2. LASSO regression analysis and multivariate logistic regression analysis

A LASSO regression model was employed to select the 13 most relevant features from the 20 features in the training set. The results indicated that age, CPR start time, electric defibrillation, epinephrine, NaHCO<sub>3</sub>, CPR compression duration, PT time, lac, cTn, potassium, D-dimer, HBP, and DM were the most critical predictors with non-zero coefficients, as detailed in Fig. 2A, B. Following a multivariate logistic regression analysis, age (>60 years old), duration of CPR compression (>30 min), CPR start time (5 min after CA), no electric defibrillation, epinephrine (>10 mg), no NaHCO<sub>3</sub> injection, PT time (>40 s), lac (>2.2 mmol/L), cTn value (>0.034 ng/ml), potassium (K+ >5.5 mmol/L), and D-dimer (between 10 and 19.9  $\mu$ g/L) were identified as independent predictors of the occurrence of ROSC failure during CPR (Table 2).

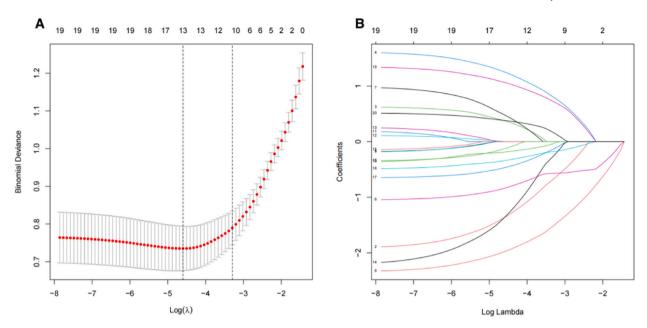
#### 3.3. Development of a nomogram model of the probability of successful CPR prediction

This study used thirteen variables to develop a nomogram model for predicting the probability of ROSC during CPR. As illustrated in Fig. 3, each independent predictor was assigned a value between 0 and 100, and the total score was obtained by adding these points.

#### Table 1

Different demographic and clinical characteristics between ROSC failure and success groups.

Characteristics	n (%)		
	ROSC failure group( $n = 361$ )	ROSC success group( $n = 147$ )	Total(n = 508)
Age (years)			
< 60	49(13.6 %)	55(37.4 %)	104(20.5 %)
≥60	312(86.4 %)	92(62.6 %)	404(79.5 %)
Gender			
Female	99(27.4 %)	49(33.3 %)	148(29.1 %)
Male	262(72.6 %)	98(66.7 %)	360(70.9 %)
CPR start time			
≤5mins	146(40.4 %)	47(32.0 %)	193(38.0 %)
> 5mins	215(59.6 %)	100(68.0 %)	315(62.0 %)
Electric defibrillation			
None	304(84.2 %)	83(56.5 %)	387(76.2 %)
Yes	57(15.8 %)	64(43.5 %)	121(23.8 %)
Respiratory assistance mode			
No ventilator support	115(31.9 %)	65(44.2 %)	180(35.4 %)
Ventilator support	246(68.1 %)	82(55.8 %)	328(64.6 %)
Epinephrine (mg)			
None	12(3.3 %)	36(24.5 %)	48(9.4 %)
1-10	134(37.1 %)	102(69.4 %)	236(46.5 %)
>10	215(59.6 %)	9(6.1 %)	224(44.1 %)
Sodium bicarbonate	213(33.0 %)	)(0.1 /0)	224(44.1 70)
None	117(32.4 %)	65(44.2 %)	182(35.8 %)
Yes	244(67.6 %)	82(55.8 %)	326(64.2 %)
CPR Compression duration	244(07.0 %)	82(33.8 %)	320(04.2 %)
-	100(05 5 0())	101(00.1.0/)	050(51.0.0/)
≤30mins	128(35.5 %)	131(89.1 %)	259(51.0 %)
> 30mins	233(64.5 %)	16(10.9 %)	249(49.0 %)
Injury			
None	247(68.4 %)	135(91.8 %)	382(75.2 %)
Yes	114(31.6 %)	12(8.2 %)	126(24.8 %)
The postoperative prothrombin tin			
< 20s	243(67.3 %)	131(89.1 %)	374(73.6 %)
20-40s	80(22.2 %)	12(8.2 %)	92(18.1 %)
> 40s	38(10.5 %)	4(2.7 %)	42(8.3 %)
The postoperative activated partial	l thromboplastin time (APTT)		
< 45s	131(36.3 %)	98(66.7 %)	229(45.1 %)
45–70s	125(34.6 %)	36(24.5 %)	161(31.7 %)
> 70s	105(29.1 %)	13(8.8 %)	118(23.2 %)
hemoglobin(g/L)			
< 60	26(7.2 %)	3(2.0 %)	29(5.7 %)
60-90	46(12.7 %)	16(10.9 %)	62(12.2 %)
> 90	289(80.1 %)	128(87.1 %)	417(82.1 %)
PH value			
< 7.0	157(43.5 %)	34(23.1 %)	191(37.6 %)
≥7.0	204(56.5 %)	113(76.9 %)	317(62.4 %)
Lactate(mmol/L)		110(701570)	017(021170)
≤2.2	12(3.3 %)	18(12.2 %)	30(5.9 %)
>2.2	349(96.7 %)	129(87.8 %)	478(94.1 %)
	349(90.7 %)	129(87.8 %)	470(94.1 %)
Blood glucose(mmol/L)	56(15.5 %)	10(6.8.%)	66(12.0.04)
< 6.1 6.1–25	. ,	10(6.8 %) 126(85.7 %)	66(13.0 %) 398(78.3 %)
	272(75.4 %)		
> 25 Cordiae tropopin(ng/ml)	33(9.1 %)	11(7.5 %)	44(8.7 %)
Cardiac troponin(ng/ml)			00/17 0 0/2
0-0.034	60(16.6 %)	28(19.0 %)	88(17.3 %)
>0.034	301(83.4 %)	119(81.0 %)	420(82.7 %)
Potassium(mmol/L)			
< 3.5	84(23.3 %)	55(37.4 %)	139(27.4 %)
3.5–5.5	204(56.5 %)	75(51.0 %)	279(54.9 %)
> 5.5	73(20.2 %)	17(11.6 %)	90(17.7 %)
D-dimer(µg/L)			
< 0.5	11(3.0 %)	31(21.1 %)	42(8.3 %)
0.5–9.9	141(39.1 %)	82(55.8 %)	223(43.9 %)
10–19.9	37(10.2 %)	9(6.1 %)	46(9.1 %)
$\geq 20$	172(47.7 %)	25(17.0 %)	197(38.7 %)
Hypertension			
None/unknown	314(87.0 %)	83(56.5 %)	397(78.1 %)
Yes	47(13.0 %)	64(43.5 %)	111(21.9 %)
Diabetes			
			400(05.0.0/)
None/unknown	326(90.3 %)	106(72.1 %)	432(85.0 %)



**Fig. 2.** Demographic and clinical feature selection using the LASSO binary logistic regression model. **(A)** Optimal parameter (lambda) selection in the LASSO model used fivefold cross-validation via minimum criteria.  $\lambda = 0.0101$ . The partial likelihood deviance (binomial deviance) curve was plotted versus log(lambda). Dotted vertical lines were drawn at the optimal values by using the minimum criteria and the 1 SE of the minimum criteria (the 1-SE criteria). **(B)** LASSO coefficient profiles of the 20 features. A coefficient profile plot was produced against the log(lambda) sequence. Abbreviations: LASSO, least absolute shrinkage and selection operator; SE, standard error.

The probability of successful CPR was then calculated based on the total score. The higher the total score, the higher the rate of successful CPR.

The self-verification of the nomogram model was conducted, revealing a C-index of 0.933 (95 % CI: 0.882–0.984) for the prediction nomogram in the training cohort. We then drew the ROC curve of the predicted probability, and the AUC value for the prediction of successful CPR was 0.923 (Fig. 4A), indicating that the nomogram prediction model has excellent discrimination. Additionally, the calibration curve of the nomogram in CA patients who underwent CPR also showed good agreement in this cohort.

# 3.4. Validation of the nomogram

Thirty percent (30 %) of cases progressed in the validation cohort, and the C-index was 0.926 (95 % CI: 0.875–0.977), demonstrating the prediction model's discriminability. The AUC was 0.926 in the validation cohort, indicating the model's accuracy (Fig. 4B). Furthermore, the Calibration curve in Fig. 5(A, B) illustrates the prediction model's consistency and fitting degree to be good.

## 3.5. Decision curve analysis of the prediction model

The DCA was utilized to assess the clinical utility of the nomogram, which is illustrated in Fig. 6. The results of the DCA showed that the nomogram had a high net benefit across a wide range of high-risk thresholds (ranging from 0.06 to 0.91).

# 4. Discussion

Verbeek et al. proposed the concept of "termination of resuscitation" in 2002 [21], highlighting the fact that CPR will eventually come to an end, either with the patient's ROSC or with clinical death. Nevertheless, there is still no consensus on when to stop the resuscitation process.

Previous research has demonstrated that the likelihood of ROSC succeeding after CPR lasting longer than 30 min is very low and can lead to irreversible brain damage. Consequently, it is recommended to use 30 min as a benchmark for ceasing resuscitation efforts [22,23]. The 2015 European CPR guidelines suggest that, despite advanced life support, CPR can be terminated when CA time is over 20 min [24]. The "2020 AHA Guidelines for CPR" suggest that for OHCA patients, if after 20 min of CPR, the partial pressure of end-tidal carbon dioxide ( $P_{ET}CO_2$ ) still does not exceed 10 mmHg (1 mmHg = 0.133 kPa) as a factor to consider when deciding whether to terminate resuscitation [6]. Nevertheless, with the advancement of technologies such as ECPR, and targeted temperature management (TTM), a few studies have reported successful cases of extended CPR [25,26]. However, the execution of ECPR necessitates a highly specialized team, special equipment, effective management protocols, and reasonable intervention for complicated complications, which are costly. Therefore, whether to stop CPR cannot solely rely on the duration of CPR. As personalized healthcare is

#### L. Yan et al.

#### Table 2

Multivariable logistic regression of predictors for the probability of successful CPR patients.

Intercept and variable	Prediction model			
	β	Odds ratio (95 % CI)	P-value	
Intercept	5.184	178.446	0.01	
Age				
< 60	Reference			
≥60	-1.96	0.141(0.055-3.442)	0.359	
CPR start time				
$\leq$ 5mins	Reference			
> 5mins	-0.733	0.480(0.224-1.031)	0.060	
Electric defibrillation				
None	Reference			
Yes	1.807	6.092(2.281-16.271)	0.000	
Epinephrine (mg)			0.001	
None	Reference			
1-10	0.258	1.294(0.359-4.665)	0.693	
>10	-2.598	0.074(0.011–0.499)	0.007	
Sodium bicarbonate				
None	Reference			
Yes	0.650	1.915(0.806-4.551)	0.141	
PR Compression duration	0.000	11910(01000 11001)	01111	
<30mins	Reference			
> 30mins	-1.503	0.223(0.064-0.772)	0.018	
The postoperative prothrombin time (PT)	-1.505	0.223(0.004-0.772)	0.532	
< 20s	Reference		0.332	
20–40s	-0.433	0.649(0.225-1.874)	0.424	
> 40s	-0.433	0.510(0.113–2.297)	0.424	
Lactate(mmol/L)	-0.072	0.310(0.113-2.297)	0.381	
	Deferrere			
≤2.2 > 2.2	Reference	0.105(0.014.0.701)	0.000	
>2.2	-2.252	0.105(0.014–0.781)	0.028	
Cardiac troponin(ng/ml)	<b>D</b> - (			
0-0.034	Reference	0 (00(0 000 1 (50)	0.400	
>0.034	-0.369	0.692(0.288–1.658)	0.408	
Potassium(mmol/L)			0.048	
< 3.5	Reference			
3.5–5.5	-0.095	0.373(0.162–0.860)	0.021	
> 5.5	-1.068	0.344(0.111–1.063)	0.064	
D-dimer(µg/L)			0.020	
< 0.5	Reference			
0.5–9.9	-0.875	0.417(0.076-2.293)	0.314	
10–19.9	-2.375	0.093(0.012-0.721)	0.023	
$\geq 20$	-1.749	0.174(0.030-1.019)	0.053	
Hypertension				
None/unknown	Reference			
Yes	1.380	3.974(1.692–9.330)	0.002	
Diabetes				
None/unknown	Reference			
Yes	0.489	1.631(0.653-4.072)	0.294	

Note:  $\beta$  is the regression coefficient.

Abbreviations: CI, confidence interval.

growing in popularity, personalized predictive models for ROSC are desperately needed.

Evaluating and forecasting the factors that can influence the success chance of ROSC is significant in order to stop "ineffective" or "futile" resuscitation, and to help sort out the patients with beneficial prospects for ECPR. Nomograms, based on user-friendly digital interfaces, are widely used as prognostic tools in oncology and medicine. These nomograms are more precise and simpler to understand, thus helping in better clinical decision-making. Our study was the first to apply such nomograms in patients with CA and CPR [27]. Our newly created prediction tool, which is based on 13 simple variables, including patient demographics, clinicopathological factors, therapeutic factors, and medicine-related factors, has been tested and validated to determine the likelihood of successful ROSC in CA patients. This nomogram enables individualized prediction of ROSC success probability.

In this study, approximately 29 % of CA patients achieved ROSC success. Factors that were associated with the probability of ROSC in CA patients receiving CPR included age, start time of CPR, electric defibrillation, epinephrine, NaHCO<sub>3</sub>, CPR compression duration, PT time, lac, cTn, potassium (K+), D-dimer, HBP, and DM. The nomogram showed that the main inhibiting factors for ROSC in CA patients included: 1) Age of over 60; 2) Long CPR compression duration (>30 min); 3) Late start of CPR (>5 min after CA); 4) No defibrillation; 5) Epinephrine usage >10 mg; 6) No NaHCO<sub>3</sub> injection; 7) Coagulation dysfunction (PT time >40 s); 8) Acidosis (Lac value > 2.2 mmol/L); 9) Myocardial damage (cTn abnormal, >0.034 ng/ml); 10) Hyperkalemia (K+ > 5.5 mmol/L); 11) D-dimer between 10 and 19.9  $\mu$ g/L; and 12) no HBP and DM.

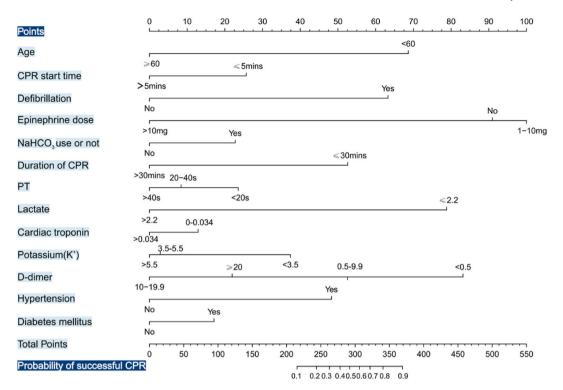


Fig. 3. Development of a nomogram model of probability of successful CPR prediction. An individual patient's value is located on each variable axis, and a line is drawn upward to determine the number of points received for each variable value. The sum of these numbers is located on the Total Points axis, and a line is drawn downward to the probability of successful CPR in patients with CA.

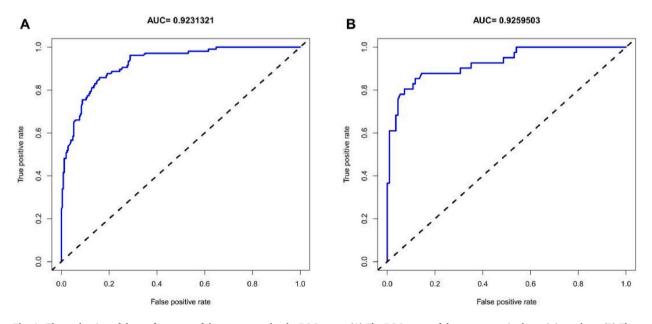


Fig. 4. The evaluation of the performance of the nomogram by the ROC curve. (A) The ROC curve of the nomogram in the training cohort. (B) The ROC curve of the nomogram in the validation cohort.

Studies have shown that age is a major factor in the success of CPR, especially for those over 60 years old, with a low success rate and discharge survival rate, and poor prognosis of neurological function [28,29]. Additionally, ECPR has been found to be more successful in those under 66 years old [30–33]. Therefore, when considering the prognosis of elderly patients and the high cost of ECPR, age should be taken into account when deciding to terminate CPR. However, other factors such as social culture, religious

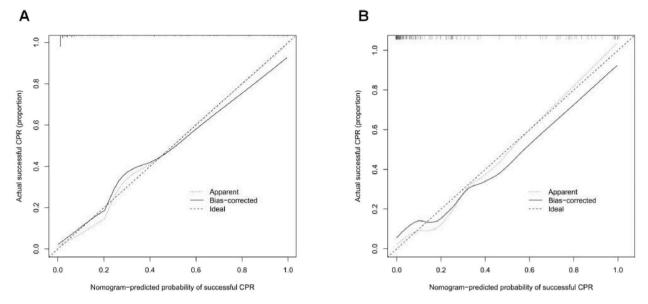


Fig. 5. The evaluation of the performance of the nomogram predicting the probability of successful CPR in patients with CA in the testing cohort(A) and validation cohort(B), illustrated the prediction model's consistency and fitting degree to be good.

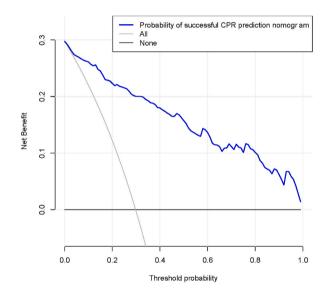


Fig. 6. Decision curve analysis for the validation set. A horizontal line indicates that all samples are negative and not treated, with a net benefit of zero. An oblique line indicates that all samples are positive. The net benefit has a negative slope.

beliefs, ethics, morals, economic status, and the family's willingness to treat should also be considered.

This research determined that patients with a CA starting time exceeding 5 min had a low rate of achieving ROSC. This conclusion agrees with other studies such as those conducted by Gomes et al., Xue et al., and Hajbaghery et al. Gomes et al. found that the chances of survival for those with a CPR start time  $\leq 5$  min were 2.53 times higher than those who had a CPR start time > 5 min (with a 95 % confidence interval) [29]. Xue et al. discovered that those with CPR start times  $\leq 5$  min had a higher ROSC success rate, discharge survival rate, and good neurological function rate [34]. Hajbaghery et al. found that most discharged survivors and short-term survivors had CPR start times between 1 and 6 min, with 81.8 % of discharged survivors beginning CPR within the first 3 min of the arrest [35]. Achieving ROSC as soon as possible is essential for reducing organ ischemic damage and improving the prognosis of CA. Thus, early identification of CA and swift initiation of CPR are paramount for improving outcomes from CA [6]. To maximize the benefits for CA patients, hospitals should construct and improve rapid response teams (RRTs), with a medical emergency team led by a critical care physician being particularly effective in reducing mortality in IHCA patients [36,37]. A retrospective cohort study in 2020 showed that RRTs significantly decreased overall mortality in the hospital [38].

This study found that patients with prolonged CPR compression (>30 min) have a low probability of ROSC success, which agrees with the findings of Xue et al., which showed that those with CPR duration  $\leq$ 15 min had a higher ROSC success rate, discharge survival rate, and good neurological function rate [34]. Experts believe that the duration of CPR reflects the severity of the illness, and the effectiveness of CPR, while the reduced survival chances may be due to the reduction of cerebral blood flow, increased ischemia, and hypoxia in different tissues, as the resuscitation continues [39,40]. Nonetheless, a differing opinion suggests that extending the resuscitation period is not always a lost cause [36]. Some research has indicated that resuscitation time is not an absolute factor in selecting ECPR, and ECPR can allow CPR time to last for 90 min [41,42]. Therefore, for CA patients with particular populations, potential reversible causes, and conditions for ECPR, the CPR time should be thoughtfully extended [25,26,43].

This research found that patients with electric defibrillation have a high chance of achieving ROSC. Many studies have demonstrated a link between early defibrillation and ROSC success, with the earlier the defibrillation, the higher the success rate [35,44–46], confirming our findings. If CPR is initiated too late (CA>5 min), the initial rhythm may have changed from a defibrillable rhythm (Ventricular fibrillation or Pulseless ventricular tachycardia) to a non-defibrillable rhythm (asystole or pulseless electrical activity). Additionally, as the CA time increases, defibrillation sensitivity decreases due to changes in myocardial energy metabolism, leading to a decrease in ROSC success rate. It is widely accepted that the initial defibrillate rhythm is always beneficial for CA patients, but optimizing defibrillation. Depending on the skill level of the rescuer, manual mode can be used when using defibrillation instruments to reduce the time for automatic mode rhythm analysis, and CPR should be resumed immediately after defibrillation. However, it does not support double sequential defibrillation (DSD) [6].

Epinephrine has been found to increase the chances of successful ROSC in CA patients, with the highest success rate being seen when doses of 1–10 mg are administered in this research. Studies of 8014 OHCA patients showed that epinephrine could improve ROSC and survival rates [47]. Gomes, Xue et al. also observed that lower doses of epinephrine ( $\leq$ 5 mg) were a positive factor for ROSC [29,34]. On the other hand, doses of epinephrine higher than 10 mg could be indicative of a prolonged CPR period (over 30 min) or a more serious condition requiring repeated use of epinephrine. Research has demonstrated that while epinephrine can increase global cerebral and coronary blood flow, it may reduce microcirculatory flow. Additionally, the premature administration of epinephrine in the first few minutes of CA can be detrimental, due to the increased myocardial oxygen demand caused by epinephrine. The excitability of epinephrine receptors in CA patients with severe disease is reduced, and CPR outcomes cannot be improved by increasing doses and frequency [48]. Studies have shown that administering epinephrine within 2 min of initial defibrillation may lead to a decrease in survival rate and a worse neurological outcome [49]. Thus, the long-term effects of epinephrine on patients remain uncertain. It is recommended to identify defibrillable rhythms quickly and delay the timing of epinephrine administration. If a patient has received more than 10 mg of epinephrine but still does not achieve ROSC, it may be time to terminate CPR.

This research found that acidosis is a hindrance to successful ROSC (lactate level >2.2 mmol/L). This is because when the heart stops suddenly, blood stasis occurs, and as CPR time increases, tissue ischemia and hypoxia become worse, leading to a decreased chance of survival [40,41]. Acidosis also affects the prognosis of patients, as it can cause hyperkalemia, which is another inhibitor of ROSC success. Additionally, acidosis can reduce the effectiveness of epinephrine [50]. A study on ECPR treatment showed that patients with severe acidosis should not be included in ECPR treatment [51]. A multicenter study in Japan involving 260 ECPR patients concluded that a pre-ECPR pH < 7.03 was associated with a worse prognosis [52]. Other studies have suggested that physiological assessment may be more important than set time or age limits for inclusion criteria [53]. The 2020 AHA Guidelines for CPR point out that acidosis and hyperkalemia are reversible indicators of CPR [6]. Therefore, to boost the ROSC rate and to meet the criteria for ECPR, active intervention and correction of acidosis should be taken. The important way to correct acidosis is through the use of NaHCO<sub>3</sub> is used during CPR, P<sub>ET</sub>CO<sub>2</sub> will temporarily increase [54], P<sub>ET</sub>CO<sub>2</sub> is linked to cardiac output and coronary perfusion pressure (CPP) during CPR, which can be used to monitor the quality of external chest compression [55], and to evaluate the prognosis of CPR patients. When P<sub>ET</sub>CO<sub>2</sub> <10 mmHg, the ROSC success rate will be reduced [56,57]. Nevertheless, the 2020 Guidelines do not recommend the routine use of NaHCO<sub>3</sub> in CPR. As CPR drug therapy progresses slowly at present, with the deepening of relevant research, more potential resuscitation drugs may be discovered [6].

This research indicates that hyperkalemia is a hindrance to the success of ROSC. This could be due to the strong relationship between the severity of hyperkalemia and the amount of cardiac damage [58]. A retrospective study by Einhorn et al., on 245808 adult American veterans revealed that when the potassium level was higher than 5.5 mmol/L, the 24-h mortality rate of patients increased [59]. Additionally, Goyal and Grodzinsky et al. found that out of 38689 patients with AMI, the higher the potassium level, the higher the mortality rate [60]. Therefore, it is essential to provide timely potassium-lowering treatment during the diagnosis and treatment process.

This research demonstrated that when PT time is over 40 s (abnormal coagulation function) and D-dimer is between 10 and 19.9  $\mu$ g/L (hypercoagulable state), it is a prohibiting factor for ROSC. This may be attributed to the extended duration of CPR, which leads to hypoperfusion and ischemia-reperfusion injury in significant organs, resulting in increased blood coagulation, increased blood density, and the formation of microthrombosis, exacerbating tissue hypoperfusion and cerebral hypoperfusion [61,62]. Studies also indicate that CPR is a process of ischemia-reperfusion that can provoke systemic inflammatory response syndrome (SIRS) [63], prompting coagulation dysfunction and further developing into multiple organ dysfunction syndrome (MODS), leading to a high mortality rate after resuscitation [62]. Gando et al.'s research also showed that the D-dimer in SIRS patients increased significantly due to the activation of plasmin and fibrin degradation [64], and D-dimer is seen as a sensitive and reputable molecular marker in the early diagnosis of disseminated intravascular coagulation (DIC). The higher the D-dimer level, the more serious the coagulation system dysfunction is, and the poorer the prognosis. Therefore, early treatment for coagulation disorders may improve the outcome of CA

# patients.

This study suggests that elevated cTn (myocardial damage) hinders successful resuscitation. Myocardial damage during CPR is caused by pre-existing conditions such as myocardial infarction or inadequate coronary perfusion due to CA. Chest compressions are only able to generate 10-20 % of average cardiac output, 5 % of normal coronary blood flow, and 15 % of normal cerebral blood flow. The level of cTn indicates the severity of myocardial damage [65–67]. This result agrees with other research findings that increased coronary perfusion pressure (CPP) helps improve myocardial perfusion and is linked to 24-h ROSC. Therefore, it is recommended to actively treat cardiogenic primary diseases during CPR and adhere to the standards of high-quality CPR. To evaluate and improve the effectiveness of CPR,  $P_{ET}CO_2$  or, if possible, invasive arterial pressure monitoring CPP can be used as the standard.

#### 5. Limitations

In our study, the history of HBP and DM beneficial affect the ROSC success rate in CPR, contrary to previous cognition. Possible reasons for this could be that medical staff may be too busy to take detailed medical histories, family members may not accurately recall or deny their past medical history due to emotional issues, or those who are aware of their past medical history may come to the hospital earlier and shorten the time for CPR to start. Additionally, hypotension may be an independent predictor of mortality after inhospital CPR, but further research is needed to verify the relationship between HBP, DM, and ROSC. Moreover, it is suggested that future studies should separate data from IHCA and OHCA patients, as the ROSC rate is significantly higher in IHCA compared to OHCA patients. Furthermore, the study was limited by its retrospective nature and the potential for patient selection biases. Additional research on external validation in various demographics and contexts is also necessary.

# 6. Conclusions

This study created and tested a probability of ROSC rate nomogram model for people with cardiac arrest, which can be used to help make decisions about when to stop resuscitation efforts for CA patients.

# Ethics approval and consent to participate

All experimental protocols were approved by the Ethics Committee of the Second Affiliated Hospital & Yuying Children's Hospital of Wenzhou Medical University (Ethical approval number: 2023-K-182-01). Informed consent was obtained from all subjects. All methods were carried out in accordance with relevant guidelines and regulations.

# Data availability statement

The data associated with our study haven't been deposited into a publicly available repository. However, we agree to share research data which can be obtained from the supplementary files.

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No.

#### **Consent for publication**

All authors have read and approved the final version of the manuscript and consented for publication.

# CRediT authorship contribution statement

Leilei Yan: Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis, Conceptualization. Lingling Wang: Writing – review & editing, Methodology, Investigation, Data curation. Liangliang Zhou: Validation, Methodology, Formal analysis, Data curation. Qianqian Jin: Writing – review & editing, Investigation, Formal analysis. Dejun Liao: Writing – review & editing, Investigation, Formal analysis. Hongxia Su: Supervision, Data curation. Guangrong Lu: Supervision, Data curation, Conceptualization.

# Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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#### Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e35903.

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