

# The related factors for the recovery and maintenance time of sinus rhythm in hospitalized patients with cardiopulmonary resuscitation

## A single-center retrospective case–control study

Jun Hua Lv, MD, Dan Wang, MD, Meng Na Zhang, MD, Zheng Hai Bai, MD, Jiang-Li Sun, MD, Yu Shi, MD, Hong Hong Pei, PhD\*, Zheng-Liang Zhang, PhD, Hai Wang, MD\*

### Abstract

No matter in or outside hospital, the success rate of cardiopulmonary resuscitation (CPR) is very low. The sign of successful CPR is the recovery of spontaneous circulation. The premise of the recovery of spontaneous circulation is the recovery and maintenance of sinus rhythm, but there is still no related research.

We aim to study the factors for the recovery and maintenance time of sinus rhythm in patients with CPR.

A single-center retrospective case–control study.

Ethical review was obtained (ethical approval number: 20180031).

The second affiliated hospital of Xi'an Jiaotong University, Xi'an Shaanxi, China.

From January 2011 to December 2016, totally 344 cases met the inclusion and exclusion criteria, sinus rhythm recovered group (SR group) (n=130 cases), sinus rhythm unrecovered group (SUR group) (n=214 cases).

The multivariate logistic regression analysis showed that red blood cell counts (OR=1.30, 95% CI:1.04–1.63,  $P=.02$ ), rescue time (OR=0.95, 95% CI:0.94–0.97,  $P<.001$ ), the usage of norepinephrine (OR=2.14, 95% CI:1.06–4.35,  $P=.04$ ) were important factor for the recovery of sinus rhythm in patients with CPR. Multivariate linear regression analysis showed that the dosage of epinephrine, the usage of naloxone and diagnosis were important factors for maintenance time of sinus rhythm after resuscitation,  $P<.05$ . The rescue time had high accuracy to predict the recovery of sinus rhythm, the area under the receiver operator characteristic (ROC) curve (AUC) was 0.84 (0.80, 0.88), sensitivity and specificity are respectively 71.54% and 93.46%.

Red blood cell counts, the rescue time and the usage of norepinephrine might be important factors for the recovery of sinus rhythm, and the dosage of epinephrine, the usage of naloxone and the diagnosis might be important factors for the maintenance time of sinus rhythm in patients with CPR.

**Abbreviations:** CPR = cardiopulmonary resuscitation, EICU = emergency ICU, ICU = intensive care unit, SR group = sinus rhythm recovered group, SUR group = sinus rhythm unrecovered group.

**Keywords:** cardiopulmonary resuscitation, sinus rhythm, spontaneous circulation

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Emergency Department & EICU, The Second Affiliated Hospital of Xi'an Jiaotong University, Xi'an, Shaan Xi, Peoples' Republic of China.

\* Correspondence: Hong Hong Pei, Xi'an Jiaotong University, Xi'an 710004, Shaan Xi, Peoples' Republic of China (e-mail: peihhz@outlook.com); Hai Wang, Emergency Department, The Second Affiliated Hospital of Xi'an Jiaotong University, Xi'an 710004, Shaan Xi, Peoples' Republic of China (e-mail: kingseajz@163.com).

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## 1. Introduction

Sudden cardiac death (SCD) from cardiac arrest is a major international public health problem accounts for an estimated 15% to 20% of all deaths.<sup>[1]</sup> No matter in or outside hospital, the success rate of cardiopulmonary resuscitation (CPR) is very low.<sup>[2–4]</sup> Therefore, the recovery of sinus rhythm is a core indicator for the outcome of CPR.<sup>[5–7]</sup> Although there were a lot of researches about CPR, most researches were focused on the final outcome of CPR and the specific intervention, while only a few researches were about the risk of spontaneous circulation recovery and there are not researches about the recovery of sinus rhythm. In our study, we would like to study the related factors for the recovery of sinus rhythm and maintenance time of sinus rhythm in patients with CPR.

## 2. Objective

We aim to study the related factors for the recovery and maintenance time of sinus rhythm in patients with CPR.

### 3. Methods

#### 3.1. Ethical approval

We had got the ethical approval (The Second Affiliated Hospital of Xi'an Jiaotong University Approval documents of the medical ethics committee, the approval number: 20180031).

#### 3.2. Study design

A single-center retrospective case-control study.

#### 3.3. Inclusion criteria

From January 2011 to December 2016, the cases with CPR were collected in emergency department, emergency ICU (EICU), coronary care unit (CCU), and intensive care unit (ICU) in our hospital.

#### 3.4. Exclusion criteria

- 1) Age less than 18 years;
- 2) pregnancy;
- 3) the majority of medical records or the critical data was missing.

#### 3.5. Grouping

The patients were divided into 2 groups: sinus rhythm recovered group (SR group) (n=130 cases), sinus rhythm unrecovered group (SUR group) (n=214 cases).

#### 3.6. Participants

From January 2011 to December 2016, 414 cases with CPR in EICU, CCU, and ICU were collected, among which 344 cases met the inclusion and exclusion criteria, SR group (n=130 cases), SUR group (n=214 cases).

#### 3.7. Primary outcome measure and secondary outcome measure

Primary outcome measure was the factors associated with the recovery of the SR after ROSC and the secondary outcome measure was the factors associated with the maintenance of the SR.

#### 3.8. The collected variables

- 1) the general items: age, sex, past history (whether complicated with hypertension, diabetes, coronary heart disease, atrial fibrillation, aspirin taking history, beta blocker, smoking, and drinking history), diagnosis and admission condition (divided into general, seriously ill, urgent, and critically ill by admissions physicians according to their experience), awareness, and vital signs (blood pressure, heart rate, respiratory frequency, and body temperature) at admission;
- 2) the related laboratory tests: blood routine, liver function, kidney function, electrolyte, blood fat, coagulation indicators, BNP, and troponin;
- 3) the drug that was used during CPR, including the usage of epinephrine, atropine, norepinephrine, isoprenaline, dopamine, metaraminol bitartrate, dobutamine, vasopressin, naloxone, amiodarone, anticoagulant, antiplatelet drugs, hormones, sodium bicarbonate, and lidocaine;

- 4) the non-drug treatment during CPR, including endotracheal intubation, external pacing, and electrical defibrillation;
- 5) the outcome of resuscitation and other related indicators, including the recovery of sinus rhythm, the maintenance time of sinus rhythm, the recovery of spontaneous breathing, rescue time and vital signs after rescue and so on.

#### Control of bias risk:

- 1) data collection: a detailed case report form (CRF) was made before the data was collected, and at the same time, each index was strictly defined to ensure the authenticity and reliability of data as much as possible;
- 2) data management: a professional data management software (Epidata) was used to manage our data;
- 3) data analysis: before data analysis, the data is strictly checked and cleaned, and then the missing values were analyzed by the method that missing value analysis to reduce the influence of missing value as much as possible;
- 4) control of confounding factors: multi-factor analysis method was adopted to control possible confounding factors.

#### Statistical analysis:

- 1) data cleaning and interpolation: when cases with many missing values or key data were missing, we would check out the medical record again and supplement the missing value if it is possible. If the case's missing values was too much to be supplemented or the key data was still missing, it would be deleted. We only remained the cases with a few missing values and without lack of the key data, and then the missing values of the remained cases were interpolated by the regression method of SPSS missing value analysis.
- 2) statistical description: Mean  $\pm$  standard deviation ( $\bar{x} \pm s$ ) was used for continuous variables of baseline data in the 2 groups, and counts data were shown by numerical values and percentages.
- 3) univariate analysis: first, univariate analysis was carried out according to whether sinus rhythm was recovered, in which the continuous data met the normal distribution and homogeneity of variance, *t* test would be performed, if it did not meet the normal distribution or homogeneity of variance, rank sum test would be used. Four tables or row lists chi-square test was used for counts data; at the same time, subgroup analysis was carried out between cardiovascular disease and non-cardiovascular disease.
- 4) multifactor analysis: when the *P* value of factors were less than .1 in univariate analysis, they would be incorporated into logical model for multifactor analysis. At the same time, the factors that might affect the recovery of sinus rhythm from a clinical point of view, even though the *P* value was much than .1, these factors were also included for the multifactor analysis. At the same time, multifactor linear correlation was carried out for the maintenance time of sinus rhythm.
- 5) the factors obtained from multifactor analysis were further evaluated by receiver operator characteristic (ROC) curve to evaluate the predictive value of the recovery of sinus rhythm. All statistical analyses were performed by SPSS 22 software and graph pad prism 6.0 was used to draw related statistical charts. *P* < .05 was considered as a statistical difference

### 4. Results

1. General information of the included cases: Totally 344 cases met the inclusion and exclusion criteria, SR group (n=130

**Table 1****General information.**

	SR group (n=130)	SUR group (n=214)	P value
Age, yr	67.43 ± 15.27	68.95 ± 16.47	.77
Sex, male/female	79/51	132/82	.91
Admission condition			
General, %	102 (78.5%)	161 (75.2%)	
Severe, %	24 (18.5%)	43 (20.1%)	
Urgent, %	3 (2.3%)	7 (3.3%)	
Critically ill, %	1 (0.8%)	3 (1.4)	.86
Admission consciousness			
Conscious, %	74 (56.9%)	128 (60.1%)	
Somnolence, %	34 (26.2%)	49 (23%)	
Coma, %	22 (16.9%)	36 (16.9%)	.79
Smoking, %	38 (29.2%)	56 (26.2%)	.62
Drinking, %	19 (14.6%)	19 (8.9%)	.11
Diabetes, %	28 (21.5%)	54 (25.2%)	.51
Hypertension, %	53 (40.8%)	98 (45.8%)	.37
Coronary heart Disease, %	41 (31.5%)	93 (43.5%)	.03
Atrial fibrillation, %	15 (11.6%)	31 (14.5%)	.52
Cerebral infarction, %	29 (22.3%)	34 (15.9%)	.15
Aspirin taking history, %	11 (8.5%)	17 (7.9%)	1.00
Medical insurance payment, %	66 (50.8%)	112 (52.3%)	.82
Systolic pressure, mmHg	126.40 ± 37.43	117.47 ± 35.461	.55
Diastolic pressure, mmHg	73.85 ± 20.93	69.59 ± 20.48	.60
Heart rate, times/min	96.73 ± 27.98	96.11 ± 27.35	.50
Breathing times, times/min	22.70 ± 8.51	22.21 ± 8.43	.79
Body temperature, °C	36.40 ± 3.42	36.67 ± 0.86	.13
Diagnosis			
Malignancy, %	4 (3.1%)	6 (2.8%)	
Lung infection, %	14 (10.8%)	26 (12.1%)	
Coronary heart disease, %	28 (21.5%)	73 (34.1%)	
Chronic renal insufficiency, %	5 (3.8%)	4 (1.9%)	
Chronic bronchitis, %	6 (4.6%)	18 (8.4%)	
Cerebral Hemorrhage, %	8 (6.2%)	8 (3.7%)	
Cerebral infarction, %	11 (8.5%)	9 (4.2%)	
Sepsis, %	10 (7.7%)	8 (3.7%)	
Gastrointestinal bleeding, %	4 (3.1%)	3 (1.4%)	
Arrhythmia, %	3 (2.3%)	6 (2.8%)	
Heart failure, %	4 (3.1%)	3 (1.4%)	
Heart valve Disease, %	4 (3.1%)	5 (2.3%)	
Others, %	29 (22.3%)	45 (21%)	.20

**Table 2****Related laboratory tests within 24 hours before resuscitation.**

	SR group (n=130)	SUR group (n=214)	P value
Red blood cell counts, x10 <sup>12</sup> /L	3.92 ± 2.29	3.57 ± 1.21	.15
Hemoglobin concentration, g/L	109.61 ± 29.30	109.04 ± 27.44	.66
Hematocrit, %	34.19 ± 9.15	33.76 ± 9.30	.74
Neutrophil, 10 <sup>9</sup> /L	10.81 ± 9.59	10.50 ± 9.20	.60
White blood cell, 10 <sup>9</sup> /L	12.66 ± 10.26	13.15 ± 11.75	.47
Eosinophil, 10 <sup>9</sup> /L	0.48 ± 1.53	0.48 ± 1.45	.99
Basophil, 10 <sup>9</sup> /L	0.15 ± 0.44	0.14 ± 0.40	.87
Eosinophil/basophil count	4.90 ± 16.42	4.16 ± 20.92	.73
Platelet count, 10 <sup>9</sup> /L	136.38 ± 83.64	131.99 ± 90.96	.51
Total bilirubin, umol/L	22.47 ± 34.66	29.99 ± 57.89	.02
Direct bilirubin, umol/L	11.92 ± 19.42	17.38 ± 36.94	.003
Indirect bilirubin, umol/L	11.74 ± 16.80	12.76 ± 25.20	.26
ALT, IU/L	259.27 ± 707.39	250.25 ± 1188.86	.58
AST, IU/L	355.62 ± 1230.21	515.63 ± 2438.47	.29
Albumin, g/L	32.01 ± 8.57	33.17 ± 8.39	.60
Globulin, g/L	26.37 ± 6.45	26.58 ± 8.00	.80
Prealbumin, mg/L	124.46 ± 65.69	113.74 ± 65.25	.52
Cholinesterase, U/L	3972.6 ± 2207.57	3956.2 ± 2237.19	.86
Urea nitrogen, mmol/L	14.22 ± 11.08	14.34 ± 10.38	.51
Blood creatinine, umol/L	206.22 ± 176.80	163.77 ± 151.34	.04
Total cholesterol, mmol/L	3.36 ± 1.62	3.52 ± 1.71	.42
Triglyceride, mmol/L	1.43 ± 1.86	1.84 ± 2.79	.20
High-density lipoprotein, mmol/L	0.91 ± 0.49	0.83 ± 0.48	.77
Low-density lipoprotein, mmol/L	1.82 ± 1.07	1.76 ± 1.18	.08
Lactate dehydrogenase, IU/L	552.67 ± 902.57	854.54 ± 1295.70	.04
Lactate dehydrogenase isoenzyme, U/L	21.50 ± 978.06	655.59 ± 2398.65	.001
Creatine kinase, U/L	911.54 ± 1934.84	1007.48 ± 2133.26	.80
Troponin, ng/mL	16.42 ± 35.91	12.78 ± 32.70	.40
Na <sup>+</sup> , mmol/L	139.23 ± 8.12	139.58 ± 9.52	.26
K <sup>+</sup> , mmol/L	4.07 ± 1.81	4.75 ± 6.47	.17
Ca <sup>2+</sup> , mmol/L	1.93 ± 0.26	1.96 ± 0.29	.47
PT, s	16.04 ± 7.77	15.47 ± 7.54	.52
PTR	1.36 ± 0.62	1.30 ± 0.61	.40
INR	1.39 ± 0.72	1.32 ± 0.70	.53
PT%, %	67.55 ± 26.53	69.14 ± 25.46	.14
APTT, s	42.16 ± 18.17	42.76 ± 21.66	.47
FIB, mg/dL	320.82 ± 145.16	318.69 ± 172.37	.16
TT, s	29.57 ± 149.99	19.37 ± 41.74	.07
D-D, ug/L	8351.41 ± 14783.19	7986.3 ± 16923.02	.86
PFDP, mg/L	43.95 ± 77.52	34.44 ± 85.93	.66

cases), SUR group (n=214 cases). The cases of SR group complicated with coronary heart disease were less than those of SUR group,  $P < .05$ . (see Table 1)

2. Related laboratory tests within 24 hours before CPR: total bilirubin, direct bilirubin, lactate dehydrogenase, and lactate dehydrogenase isoenzyme in SR group were lower than those in SUR group,  $P < .05$ . (see Table 2)
3. Related indicators in the process of CPR: the heart rate and SPO<sub>2</sub> in SR group were higher than those in the SUR group, while the rescue time, previous rescue times, the usage and dosage of atropine, and the usage and dosage of adrenaline in SR group were lower than those in SUR group,  $P < .05$ . (see Table 3)
4. Subgroup analysis between cardiovascular disease and non-cardiovascular disease showed that red blood cell counts, direct bilirubin, lactate dehydrogenase isoenzyme, systolic blood pressure, platelet counts, prealbumin, the usage of sodium bicarbonate were important factors for the recovery of sinus rhythm in patients with cardiovascular disease during CPR,  $P < .05$ . But the usage and dosage of atropine, the usage,

and dosage of adrenaline, SPO<sub>2</sub> and the rescue time were important factors for the recovery of sinus rhythm in patients with non-cardiovascular diseases during CPR,  $P < .05$ . (see Table 4)

5. Multivariate logistic regression analysis for the recovery of sinus rhythm showed that red blood cell counts (OR = 1.30, 95% CI: 1.04–1.63,  $P = .02$ ), rescue time (OR = 0.95, 95% CI: 0.94–0.97,  $P < .001$ ), the usage of norepinephrine (OR = 2.14, 95% CI: 1.06–4.35,  $P = .04$ ) were important factor for the recovery of sinus rhythm in patients with CPR. (see Table 5)
6. Multivariate linear regression analysis for the maintenance time of sinus rhythm showed that the dosage of epinephrine, the usage of naloxone and diagnosis were important factors for maintenance time of sinus rhythm after CPR,  $P < .05$ . (see Table 6)
7. Receiver operating characteristic curve (ROC) analysis showed that rescue time had high accuracy to predict the recovery of sinus rhythm, the area under the ROC curve (AUC) was 0.84

**Table 3**

**Related indicators in the process of CPR.**

	SR group (n = 130)	SUR group (n = 214)	P value
Heart rate at rescue times/min	29.81 ± 32.63	23.89 ± 20.28	.04
Rescue systolic pressure, mmHg	15.79 ± 26.53	13.56 ± 28.72	.71
Rescue diastolic pressure, mmHg	8.36 ± 15.62	6.96 ± 15.40	.31
Rescue SPO2 (%)	21.40 ± 28.72	12.97 ± 26.13	.03
Rescue duration, min	20.84 ± 31.02	59.76 ± 41.59	<.001
Intubation, %	105 (80.8%)	172 (80.4%)	1.00
External pacing, %	4 (3.1%)	12 (5.6%)	.31
Defibrillation, %	40 (30.8%)	78 (36.4%)	.29
Lidocaine, %	20 (15.4%)	20 (9.3%)	.12
Hormone, %	30 (23.1%)	42 (19.6%)	.50
Antiplatelet therapy, %	32 (24.6%)	66 (30.8%)	.22
Anticoagulant therapy, %	29 (22.3%)	43 (20.1%)	.68
Amiodarone, %	19 (14.6%)	24 (11.2%)	.40
Respiratory stimulants, %	19 (14.6%)	44 (20.6%)	.20
Sodium Bicarbonate, %	78 (60%)	136 (63.6%)	.57
Naloxone, %	26 (20.0%)	33 (15.4%)	.30
Norepinephrine, %	38 (29.2%)	43 (20.1%)	.07
Isoprenaline, %	24 (18.5%)	42 (19.6%)	.89
Metaraminol bitartrate, %	26 (20%)	26 (12.1%)	.06
Dobutamine, %	7 (5.4%)	10 (4.7%)	.80
Dopamine, %	66 (50.8%)	89 (41.6%)	.12
Atropine use times, times	4.30 ± 3.95	5.25 ± 3.68	.03
Atropine use, mg	2.44 ± 2.24	3.00 ± 2.01	.02
Epinephrine use times, times	4.81 ± 4.40	6.66 ± 4.30	<.001
Epinephrine use, mg	4.94 ± 4.62	6.97 ± 4.79	<.001
Epinephrine dosage/atropine dosage	2.37 ± 2.37	2.87 ± 3.07	.11

(0.80, 0.88), sensitivity and specificity are respectively 71.54% and 93.46%, while red blood cell counts had a poor accuracy to predict the recovery of sinus rhythm the area under the ROC curve (AUC) was 0.56 (0.51, 0.61), sensitivity and specificity are respectively 56.15% and 58.41%. (see Fig. 1)

**Table 4**

**Subgroup Analysis between cardiovascular disease and non-cardiovascular disease.**

Cardiovascular Disease	SR group (n = 39)	SUR group (n = 87)	P value
Red blood cell count	4.11 ± 1.55	3.57 ± 1.18	.03
Direct bilirubin	7.46 ± 17.59	16.66 ± 27.10	.03
Lactate dehydrogenase isoenzyme	87.85 ± 713.11	1062.05 ± 4061.46	.03
Systolic blood pressure during rescue	16.76 ± 25.76	15.53 ± 31.34	.04
Platelet count	168.36 ± 77.06	163.84 ± 82.21	.006
Prealbumin	128.87 ± 65.34	132.49 ± 54.95	.01
Use sodium bicarbonate, %	25 (64.1%)	71 (81.6%)	.04
Rescue duration, min	34.94 ± 44.30	69.15 ± 41.44	<.001
Non-cardiovascular disease	SR group (n = 91)	SUR group (n = 127)	P value
Atropine use times	4.35 ± 3.58	5.55 ± 3.82	.020
Atropine use	2.39 ± 1.98	3.16 ± 2.06	.006
Total adrenaline use	4.81 ± 4.43	7.68 ± 4.59	.000
Epinephrine usage	4.64 ± 4.07	7.42 ± 4.12	.000
Rescue SPO2	21.73 ± 29.74	12.86 ± 28.22	.026
Creatinine	209.10 ± 195.85	159.05 ± 142.28	.039
Rescue duration, min	17.54 ± 19.34	53.65 ± 40.96	<.001

**Table 5**

**Multivariate logistic regression analysis for the recovery of sinus rhythm.**

	β	Standard error	P value	OR (95% CI)
Constant	1.168	0.232	<.001	3.214 (-)
Red blood cell	0.265	0.114	.019	1.304 (1.044~1.628)
Rescue time	-0.047	0.007	.000	0.954 (0.942~0.966)
Norepinephrine	0.762	0.361	.035	2.143 (1.056~4.347)

**5. Discussion**

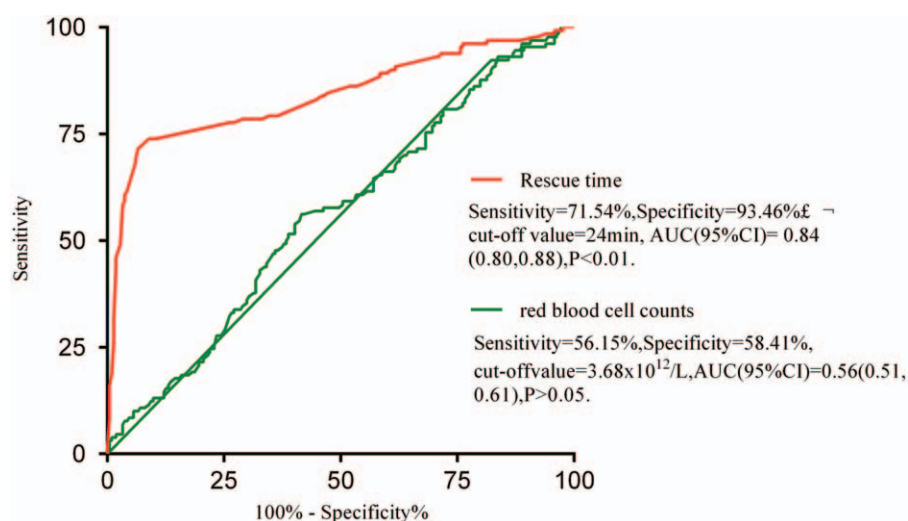
We found that the cases of SR group complicated with coronary heart disease were less than those of SUR group,  $P < .05$ . Total bilirubin, direct bilirubin, lactate dehydrogenase, and lactate dehydrogenase isoenzyme in SR group were lower than those in SUR group,  $P < .05$ . The heart rate and SPO2 in SR group were higher than those in the SUR group, while the rescue time, previous rescue times, the use times and dosage of atropine, and the use times and dosage of epinephrine in SR group were lower than those in SUR group,  $P < .05$ . Sub-group analysis showed the factors for the recovery of sinus rhythm were different between cardiovascular disease and non-cardiovascular disease. The multivariate analysis showed that red blood cell counts, the rescue time and the usage of norepinephrine were important factor for the recovery of sinus rhythm, while the dosage of epinephrine, the usage of naloxone and diagnosis were important factors for maintenance time of sinus rhythm in patients with CPR,  $P < .05$ . ROC analysis showed that the rescue time had highly accuracy to predict the recovery of sinus rhythm.

The recovery of spontaneous circulation in cardiac arrest is related to the perfusion of heart.<sup>[8]</sup> According to Poiseuille law, the smaller the vascular diameter, the greater the vascular resistance, and even small variation can lead to the sharp increase of vascular resistance.<sup>[9]</sup> Cardiac tissue perfusion is proportional to the pressure difference between the 2 ends of the blood vessel but inversely proportional to the vascular resistance.<sup>[10]</sup> For patients with coronary heart disease, atherosclerosis often leads to coronary artery stenosis and thrombosis.<sup>[11]</sup> Therefore, the patients with coronary heart disease will suffer from the increase of vascular resistance and the obvious decrease of perfusion pressure during CPR, which will lead to a significant decrease in the perfusion volume of cardiac tissue. The decrease of tissue perfusion will lead to ischemia and hypoxia of myocardial cells, a large number of ion pumps failure on myocardial cell membranes, the increase of membrane permeability, decrease of membrane fluidity and dysfunction of membrane receptors,<sup>[12]</sup> which will eventually lead to the dysfunction of myocardial cell excitability, conductivity, self-discipline and contractile,<sup>[9]</sup> and finally reduce the rate of the recovery of sinus rhythm and spontaneous circulation.

**Table 6**

**Multivariate linear regression analysis for the maintenance time of sinus rhythm.**

	Standardized β	Standard error	t value	P value
Constant		2554.845	2.711	.007
Epinephrine dose	-0.159	98.272	-2.996	.003
Naloxone use	-0.124	1266.251	-2.338	.02
Diagnosis	0.117	146.428	2.209	.03



**Figure 1.** ROC curves of rescue time and red blood cell counts for predicting the outcome of the recovery of sinus rhythm. ROC = receiver operator characteristic.

Fahhrettin oz's study found that bilirubin levels were correlated with coronary blood flow velocity, and the higher bilirubin, the lower flow of coronary blood.<sup>[13]</sup> In addition, hyperbilirubinemia will lead to increase the tension of vagus nerve,<sup>[14]</sup> which will reduce the generation and conduction of sinus rhythm, which is why hyperbilirubinemia with lower recovery of sinus rhythm in patients with CPR.

Myocardial ischemia and infarction are the most common causes of heart damage.<sup>[15]</sup> Compared with other indexes related to heart damage, lactate dehydrogenase and lactate dehydrogenase isoenzyme in SR group were lower than those in SUR group,  $P < .05$ , which was similar to previous studies.<sup>[16]</sup> However, troponin had no statistically significant difference between the 2 groups, the possible reason was that troponin was not used as a routine examination at admission, so that resulting in many missing values.

Before cardiac arrest happens, it is often accompanied with progressive deterioration of vital signs, such as obviously decline of heart rate and SPO<sub>2</sub>.<sup>[17]</sup> If we can identify them in time and start CPR as soon as possible, the success rate of CPR will be improved obviously. Heart rate can reflect the electrical activity of the heart and SPO<sub>2</sub> can reflect the perfusion of the recovered tissue.<sup>[18]</sup> The higher the heart rate and SPO<sub>2</sub> when starting CPR, it means that CPR more timely and better tissue perfusion, and the greater the possibility of the recovery of sinus rhythm and spontaneous circulation.

Although atropine was common used in CPR, the AHA's guidelines for CPR in 2015 had suggested that atropine should be only used when the heart rate was slow, especially when the heart rate was less than 50 times/min, because there was no evidence showed that atropine could increase the outcome of CPR.<sup>[18]</sup> Therefore, we infer that atropine is an important factor of the recovery of sinus rhythm especially when patients with low heart rate.

Epinephrine is a recommended drug for cardiac arrest by the guidelines, but its usage and dosage are still controversial.<sup>[19]</sup> Catecholamine substances (epinephrine and norepinephrine) in blood rapidly and dramatically increase about 50 times after cardiac arrest, and catecholamine receptors rapidly decrease in the early and gradual increase with time,<sup>[20]</sup> which is one of the theoretical bases for the use of epinephrine in CPR. However, in

some non-random study, although adrenaline can improve the success rate of spontaneous circulation, there is still great controversy about whether epinephrine can improve the final outcome of CPR.<sup>[21,22]</sup> But all the studies are observational studies, so the conclusions need to be further verified by randomized controlled trials.

Amiodarone and lidocaine are the most commonly used antiarrhythmic drugs, and amiodarone is more recommended in CPR.<sup>[23]</sup> Compared with lidocaine, amiodarone can improve the recovery of spontaneous circulation and hospital survival rate in treatment of ventricular fibrillation and pulseless ventricular tachycardia.<sup>[24]</sup> The latest guidelines recommend that sodium bicarbonate should not be used routinely except in patients with hyperkalemia or tricyclic antidepressant overdose,<sup>[18]</sup> because it may aggravate intracellular acidosis and reduce the success rate of CPR. Our study had the similar conclusions. Respiratory stimulants are not recommended for resuscitation of cardiac arrest. Because respiratory center is very sensitive to ischemia, when cardiac arrest, respiratory stimulant can not effectively stimulate the respiratory center, and re-use of respiratory stimulant may further worsen the disease.<sup>[18]</sup> In addition, there are many means of respiratory support for cardiac arrests, such as simple respirators and ventilators.

In the process of CPR, in addition to the drug therapy mentioned above, the treatments also include electrical defibrillation, cardiac pacing, endotracheal intubation, and so on. Ventricular fibrillation seldom spontaneously terminates, and electrical defibrillation is the only effective method to terminate ventricular fibrillation, especially early defibrillation can greatly increase the success rate of CPR.<sup>[18]</sup> As the importance of electrical defibrillation, all the clinician has fully realized the importance of electric defibrillation, and so electric defibrillation can be performed at the first time, and that is why there is no statistical difference between the 2 groups. However, the guidelines suggest that cardiac pacing should only be performed for patients with symptomatic bradycardia or high atrioventricular block.<sup>[18]</sup> In the early stage, simple respirator is more recommended to use for respiratory support, in order to reduce the interruption times of chest compressions as much as possible. Therefore, cardiac pacing and endotracheal intubation are not the key factors influencing the outcome of CPR.

Our study found that the higher the red blood cell counts, the higher recovery of sinus rhythm. The reason is that the higher red blood cell counts, the more higher ability to carry oxygen,<sup>[25]</sup> which is conducive to increasing the tissue oxygen supply, reducing the tissue ischemia and hypoxia. At present, related studies recommend the use of norepinephrine as a booster drug during CPR,<sup>[18]</sup> because it is more reliable and suitable to control. With the increase of rescue time, the recovery of sinus rhythm decreased significantly, this was consistent with previous studies. ROC curve analysis showed that rescue time had good predictive value for sinus rhythm recovery. The results of our study once again proved that the clinical rescue time should be at least more than 30 minutes.<sup>[26]</sup>

The recovery of Sinus rhythm is the prerequisite for the recovery of spontaneous circulation in patients with cardiac arrest. At the same time, the maintenance time of sinus rhythm is also an important prerequisite for keeping vital signs stable after CPR, and it is related to whether other resuscitation techniques have time to be implemented and the final outcome of CPR.<sup>[27]</sup> Therefore, we made a multi-factor linear regression analysis for the maintenance time of sinus rhythm. We found that the dosage of epinephrine, usage of naloxone and diagnosis were important factors influencing the maintenance time of sinus rhythm after CPR. The  $\beta$  coefficients of the dosage of epinephrine and usage of naloxone were  $-0.159$  and  $-0.124$  respectively, which indicated that with the increase of dosage of epinephrine and usage of naloxone, the maintenance time of sinus rhythm would decline, which might reduce the ultimate success rate of CPR. The possible reason is that the increased dosage of adrenaline would lead catecholamine increasing,<sup>[28]</sup> which would lead to an increase of ventricular arrhythmia and result in reducing maintenance time of sinus rhythm. The latest version of the guide suggests that naloxone should not be used as a routine drug for CPR, but only for patients with opioid poisoning.<sup>[18]</sup> Our study found that diagnosis also was an important factor for the maintenance time of sinus rhythm. Therefore, it is very important to treat the primary disease in patients with recovery of sinus rhythm after CPR.<sup>[29]</sup> These findings will make us evaluating the prognosis of patients with CPR more reliable and make the treatments of them more reasonable.

#### Limitations of this study:

- 1) some of the variables in our studies such as the average of SPO2 was about 20%, some studies had shown that SPO2 below 70% or 80% may not be accurate in almost all monitors, so we should be careful for the effect of SPO2 on the recovery of sinus rhythm and the maintenance time of sinus rhythm. At the same time, heart rate at rescue, rescue systolic pressure, and rescue diastolic pressure might be with the same risk.
- 2) this study is a retrospective study with some bias risks, and its research results should be carefully applied;
- 3) the sample size of this study is relatively small;
- 4) the cases included in this study are all in-hospital cases, which would limit their clinical application;
- 5) there are some missing values in the research data.

## 6. Conclusion

Red blood cell counts, the rescue time and the usage of norepinephrine might be important factors for the recovery of sinus rhythm, and the dosage of epinephrine, the usage of

naloxone and the diagnosis might be important factors for the maintenance time of sinus rhythm in patients with CPR.

Availability of data and material: please see the additional materials, <http://links.lww.com/MD/C786>.

## Author contributions

Authors' contributions: Jun Hua Lv wrote the manuscript, Dan Wang, Meng Na Zhang and Zheng Hai Bai collected relative data, Jiang-Li Sun, Yu Shi and Zheng Liang Zhang finished the statistical analysis, Hong-hong Pei and Hai Wang were responsible for research design, process guidance, and checking the data and correction.

**Conceptualization:** Zheng Hai Bai.

**Data curation:** Dan Wang, Meng Na Zhang.

**Formal analysis:** Jiang Li Sun, Yu Shi, Liang Zheng Zhang.

**Investigation:** Hai Wang.

**Methodology:** Hong Hong Pei, Hai Wang.

**Project administration:** Hong Hong Pei, Hai Wang.

**Supervision:** Hong Hong Pei.

**Validation:** Hai Wang.

**Writing – original draft:** Jun Hua Lv.

**Writing – review & editing:** Hai Wang.

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