

ORIGINAL RESEARCH

Sustained Return of Spontaneous Circulation Following Out-of-Hospital Cardiac Arrest; Developing a Predictive Model Based on Multivariate Analysis

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Abstract: **Introduction:** Identifying the predictive factors of sustained return of spontaneous circulation (ROSC) following out-of-hospital cardiac arrest (OHCA) will be helpful in management of these patients. This study aimed to develop a predictive model in this regard. **Methods:** In a retrospective observational study, data of adult patients with OHCA, were collected from Vajira emergency medical services patient care report. Multiple logistic regression analysis with a regression coefficient was used to develop a predictive score for a sustained ROSC at the scene. Area under the receiver operating characteristic (ROC) curve (AUC) was used to validate the accuracy of the predictive score for a sustained ROSC. **Results:** Independent factors associated with a sustained ROSC included cardiopulmonary resuscitation (CPR) duration < 30 min (adjusted odds ratio (AOR)= 5.05, 95% confidence interval (CI): 3.34–7.65; $p < 0.001$); advanced airway management with an endotracheal tube (AOR= 3.06, 95% CI: 1.77–5.31; $p < 0.001$); advanced airway management with laryngeal mask airway (AOR= 3.42, 95% CI: 1.02–11.46; $p = 0.046$); defibrillation (AOR = 2.05, 95% CI: 1.31–3.2; $p = 0.002$); Capillary blood glucose (CBG) level < 150 mg% (AOR= 1.95, 95% CI: 1.05–3.65; $p = 0.035$); CBG at least 150 mg% (AOR= 2.87, 95% CI: 1.56–5.29; $p = 0.001$); pupil reflex (AOR = 2.96, 95% CI: 1.1–7.96; $p = 0.032$); and response time at most 8 min (AOR= 1.66, 95% CI: 1.07–2.57; $p = 0.023$). These were developed into the pupil reflex, response time, advanced airway management, defibrillation, CBG, and CPR duration (PRAD-CCPR) score. The most accurate cutoff point of score using Youden's index was ≥ 6 with AUC of 0.759 (95% CI: 0.715–0.802; $p < 0.001$), sensitivity of 62.0% (95% CI: 51.2–71.9%), specificity of 75.7% (95% CI: 69.4–81.2%), positive predictive value of 51.8% (95% CI: 40.9–62.3%), and negative predictive value of 79.5% (95% CI: 73.5–84.6%). **Conclusion:** An optimal PRAD-CCPR score of ≥ 6 provides an acceptable accuracy of 0.759 with sensitivity of 62.0% and specificity of 75.7% in prediction of sustained ROSC following OHCA. This predictive score might help CPR commanders to prognosticate the outcome of patients with OHCA at the scene.

Keywords: Emergency Medical Services; Out-of-Hospital Cardiac Arrest; Heart Arrest; Return of Spontaneous Circulation

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1. Introduction

Out-of-hospital cardiac arrest (OHCA) is a medical emergency condition requiring immediate management to save lives and an important global cause of death, especially in middle-income or developing countries. The reported number of the deceased due to cardiac arrest was a million per year (1). The worldwide prevalence was 50–60 per 100,000 populations (2). In the USA, the incidence in adults was more

than 350,000 per year, the survival rate was 10.8%, and only 9% had favorable neurological outcomes (3). The prevalence rates of 17–128 and 21–29 per 100,000 population in central America and Asia, respectively, were reported in a previous study (4). In Thailand, the survival rate of patients with OHCA at the scene, resuscitated by emergency medical services (EMS), was 25.6% (5).

According to the report of The Pan Asian Resuscitation Outcomes Study (PAROS) in Thailand, the survival rate was 4.0% (6), indicating that patients with OHCA have different outcomes based on each context of each country, such as differences in the study design, sample size, and demographic data, especially hospital data including prehospital management by EMS and management in the hospital (7).

A systematic review and meta-analysis showed that patients having OHCA with shockable rhythm had better survival outcomes than those with non-shockable rhythm (8). Bystander cardiopulmonary resuscitation (bystander CPR) and bystander automated external defibrillator (AED) significantly improved the survival outcomes of patients with OHCA (9). Previous studies have demonstrated that predictive factors for a sustained return of spontaneous circulation (sustained ROSC) included trauma cause (5, 10), response time (5, 11), bystander CPR (11), time to first chest compression (7), younger age (12), arrest in a public area (12), witnessed arrest (12), and shockable rhythm (12).

To the authors' knowledge, three studies have developed predictive scores for a sustained ROSC, namely, WATCH-CPR score (7), RACA score (13), NULL-PLEASE score (14), and P-ROSC (15). All previous studies have developed predictive scores in the context of management in the hospital or emergency department, which was difficult to apply in prehospital practice and lacked data on the time and treatment of patients at the scene, which are important in the prehospital context. Some studies have used laboratory data, which could not be applied in the prehospital context. However, a modeling study for the prediction of sustained ROSC of patients with OHCA at the scene would help paramedics and emergency nurse practitioners manage patients with OHCA, ethically.

Thailand is a middle-income country, and no emergency physicians are working with ambulances at the scene in many areas (10).

Resources are substantially limited in the prehospital context compared with the management at the emergency department. An important issue is how to efficiently resuscitate with the best outcome and lowest cost. Therefore, this study aimed to develop and validate a predictive model for a sustained ROSC of patients with OHCA at the scene.

2. Methods

2.1. Study design and settings

This retrospective observational study was conducted in Vajira Emergency Medical Service (V-EMS), Vajira Hospital, Faculty of Medicine, Navamindradhiraj University, Bangkok, Thailand, between January 1, 2019, and July 31, 2022. V-EMS was a leader of EMS unit zone area 1 from a total of nine area divisions of EMS in Bangkok, dispatched from Erawan Center, Bangkok, networking with public and private hospitals, a total of six hospitals, in an area of 50 km² with 500,000 population (5, 10).

During a response operation for patients with OHCA, the EMS team sent by V-EMS included at least three personnel (a paramedic or emergency nurse practitioner (ENPs) as operation team leader, and two emergency medical technicians. In each response operation, paramedics or ENPs would operate under offline and online medical protocols under the orders of emergency physicians (EPs). In patients with cardiac arrest, the American Heart Association guidelines of 2020 were applied. All team members had passed advanced cardiovascular life-support training.

The Standards for the Reporting of Observation Studies in Epidemiology (STROBE) statement were applied (16).

2.2. Participants

Data of adult patients (aged > 18 years) with OHCA were collected from EMS patient care report, coded with the Thailand emergency medical triage protocol and criteria-based dispatch (CBD) symptom group 6, which is cardiac arrest, managed by the V-EMS unit, Vajira Hospital, Faculty of Medicine, Navamindradhiraj University, Bangkok, Thailand, between January 1, 2019, and July 31, 2022.

The patients were managed in accordance with advanced cardiovascular life support (ACLS) based on CPR guidelines (17, 18).

Patients with incomplete or missing data, signs of irreversible death so that based on the judgement of the team leader no resuscitation was performed, do-not-resuscitate orders, cardiac arrest outside the scene, OHCA during transfer, i.e., patients with OHCA receiving CPR starting at the scene and continuing during hospital transfer, and termination of resuscitation at the scene were excluded.

2.3. Data collection

Data of patients with OHCA were collected from the EMS patient care report, which was a record of advanced EMS operation, Bangkok EMS (Erawan Center), and the standard form and unit in the Bangkok advanced emergency operation unit. This form contained data of EMS operation units, patients, and all treatments by EMS teams, recorded by dispatchers and paramedics or ENPs operating at the scene. These data

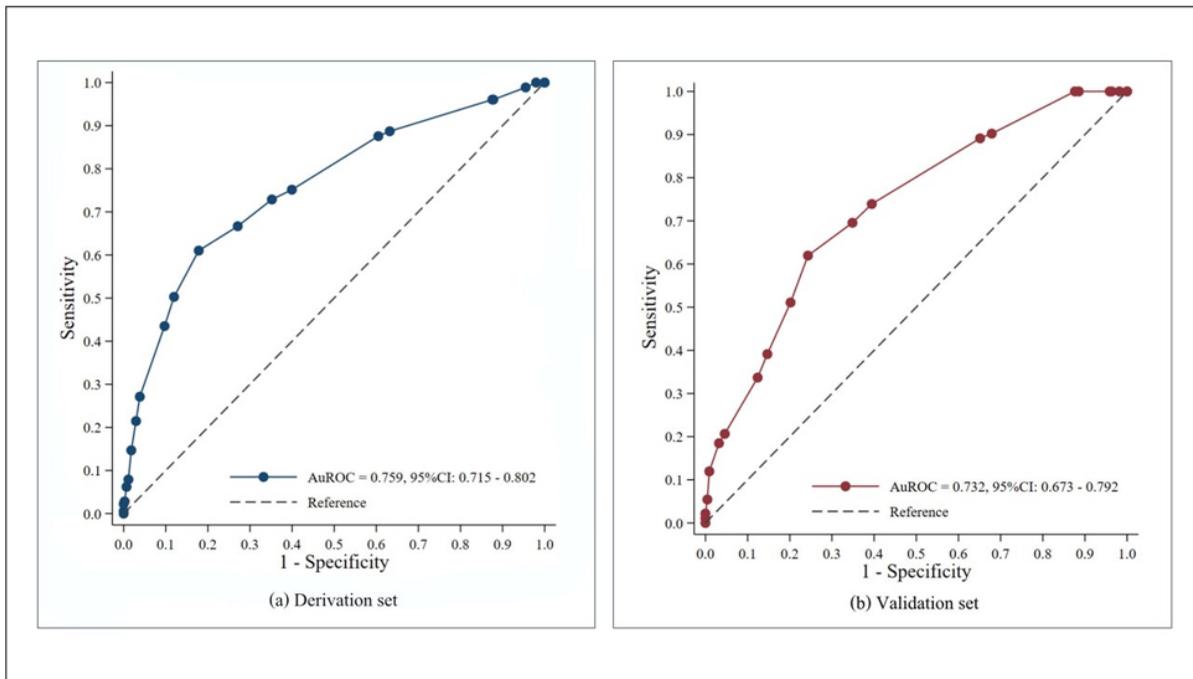


Figure 1: Receiver operating characteristic (ROC) curves for the predictive model of sustained return of spontaneous circulation among patients with out-of-hospital cardiac arrest at the scene: (a) derivation set and (b) validation set. AuROC: area under the ROC curve.

were a part of the remuneration for EMS operation units. All data were filled in and recorded in Microsoft Excel by a principal investigator. Data comprised general characteristics of patients with OHCA including sex, age, comorbidities, location type, witnessed arrest, bystander CPR, arrest type, type of traumatic arrest, type of non-traumatic arrest, time from arrest to chest compression, CPR duration, advanced airway management, defibrillation, fluid resuscitation, medication during CPR, Capillary blood glucose (CBG), pupil reflex, response time, and sustained ROSC at the scene.

2.4. Definitions

- The sustained ROSC was determined when chest compressions were not required for 20 minutes, and signs of circulation persisted for at least 20 minutes (7).
- Symptom group 6 was defined as OHCA according to the emergency level screening system of Thailand, classified according to CBD 6, severity level–critical (red) 6 critical 1 or 6 red 1, defined as cardiac arrest including unconsciousness, apnea, or pulselessness (5).
- Response time was defined as the duration from the emergency call to ambulance arrival at the scene (5).
- The time from arrest to chest compression was defined as the interval between sudden cardiac collapse to chest compression by a bystander.
- CPR duration was defined as the duration from the first medical contract (FMC) to the end of CPR based on the EMS

patient care report.

- The derivation set was defined as a new dataset used by the authors to develop the predictive score for a sustained ROSC of patients with OHCA at the scene.
- The validation set was defined as the dataset used to validate the accuracy of the predictive score for a sustained ROSC of patients with OHCA at the scene.

2.5. Sample size determination

The main objective of this study was to develop a predictive score for a sustained ROSC in patients with OHCA at the scene using multiple logistic regression analysis. Sample size estimation relied on multiple logistic regression analysis using the number of events per variable in a logistic regression analysis (19). The analysis required Enough samples to include at least 10 interesting events for each independent variable. At most, 15 variables in the development of the predictive score for a sustained ROSC were expected. The number of samples with interesting events, which was sustained ROSC, of 150 events/samples was required. The rate/incidence of sustained ROSC was 25.6%. Therefore, the total sample size for analysis was at least 586 ((150*100)/25.6 = 586). After 5% of the sample size was added using the formula (nnew = 586/[1 - 0.05]), the required sample size was calculated to be at least 617. Thus, the sample size for the development of the predictive score for a sustained ROSC was 620.

For the sample size estimation to validate the accuracy of the predictive score (validation set), the ratio of the sample size to the sample size during the development of the score (derivation set) was 1:2. Thus, sample sizes for the derivation and validation sets were 620 and the 310, respectively. Hence, the final sample size in the present study was 930, and simple random sampling was used.

2.6. Statistical analysis

A descriptive analysis was performed to examine the variable distribution. Continuous variables are presented as mean \pm standard deviation (SD) or median and interquartile range (IQR), and categorical variables are presented as frequencies and proportions. When comparing the two groups, differences were evaluated using independent t-test or Mann–Whitney U test for numeric variables and chi-square test or Fisher's exact test for categorical variables.

In the development of the predictive score, multivariable analysis with multiple logistic regression analysis and a backward stepwise selection method were used. All statistical tests were considered statistically significant at $p < 0.05$. Significant factors associated with a sustained ROSC were obtained from the univariable analysis. Regression coefficient, odds ratio (OR), and 95% confidence intervals (CI) were reported. The predictive score was developed using the regression coefficient.

The accuracy of the predictive score was validated using receiver operating characteristic (ROC) curve and area under the curve (AUC), using Youden's index to determine the best cutoff point. Sensitivity, specificity, accuracy, positive predictive value (PPV), negative predictive value (NPV), and area under the ROC curve were reported with 95% CI.

IBM SPSS Statistics for Windows, version 28.0 (IBM Corp., Armonk, NY, USA) and Stata version 13.0 (StataCorp, College Station, TX, USA) were used. All statistical tests were considered statistically significant at $p < 0.05$.

2.7. Ethical statement

This study was conducted in accordance with the tenets of the Declaration of Helsinki 1975 and its revisions in 2000. It was approved by the Institutional Review Board of the Faculty of Medicine Vajira Hospital, Navamindradhiraj University (COA no. 217/2565). Informed consent requirement was waived because of the retrospective nature and anonymity of all patient data.

3. Results

3.1. characteristics of patients in derivation set

620 cases were studied (66.0% male). Table 1 compares the baseline characteristics of patients between cases with and without sustained ROSC. The two groups had significant dif-

ferences regarding CPR duration ($p < 0.001$), Advanced airway management ($p = 0.001$), defibrillation ($p < 0.001$), the median concentrations of CBG ($p < 0.001$), Pupil reflex ($p < 0.001$), and response time ($p = 0.030$).

3.2. Developing the predictive model

Based on multivariate analysis using multiple logistic regression analysis and backward stepwise selection method, independent associated factors of sustained ROSC of patients with OHCA at the scene were: CPR duration < 30 min (AOR = 5.05, 95% CI: 3.34–7.65; $p < 0.001$); airway management at the scene with endotracheal tube (ETT) (AOR = 3.06, 95% CI: 1.77–5.31; $p < 0.001$) or laryngeal mask airway (LMA) (AOR = 3.42, 95% CI: 1.02–11.46; $p = 0.046$); defibrillation (AOR = 2.05, 95% CI: 1.31–3.2; $p = 0.002$); CBG level < 150 mg% (AOR = 1.95, 95% CI: 1.05–3.65; $p = 0.035$); CBG at least 150 mg% (AOR = 2.87, 95% CI: 1.56–5.29; $p = 0.001$); had pupil reflex (AOR = 2.96, 95% CI: 1.1–7.96; $p = 0.032$); had response time at most 8 min (AOR = 1.66, 95% CI: 1.07–2.57; $p = 0.023$) (Table 2).

The analyzed results of the predictive formula for a sustained ROSC of patients with OHCA at the scene in the form of logit transformation were used to develop the predictive score using a regression coefficient. CPR duration < 30 min was assigned 3 points; advanced airway management with ETT, 2 points; advanced airway management with LMA, 2.5 points; defibrillation, 1.5 points; CBG < 150 mg%, 1 point; CBG ≥ 150 mg%, 2 points; pupil reflex, 2 points; and response time ≤ 8 min, 1 point. The total score ranged from 0 to 15 points. The predictive score could predict sustained ROSC of patients with OHCA at the scene significantly with AUC of 0.759 (95% CI 0.715–0.802; $p < 0.001$).

3.3. Validation of model

310 cases were studied (65.8% male). Table 1 compares the baseline characteristics of patients between patients with and without sustained ROSC in the validation set.

Using the validation dataset with 310 patients, the predictive score could significantly predict sustained ROSC of patients with OHCA at the scene, with AUC of 0.732 (95% CI 0.673–0.792, $p < 0.001$). The predictive score of at least 6 had the highest Youden's index (0.377), which was the most suitable point in the prediction of sustained ROSC among patients with OHCA at the scene, with sensitivity of 62.0% (95% CI: 51.2–71.9), specificity of 75.7% (95% CI: 69.4–81.2), PPV of 51.8% (95% CI: 40.9–62.3), and NPV of 79.5% (95% CI: 73.5–84.6) (Table 3 and Figure 1).

4. Discussion

First, in this study, the incidence of sustained ROSC at the scene was 42.5% in patients with OHCA resuscitated by EMS in Thailand, which is a middle-income country, like the pre-

Table 1: Characteristics of patients with out-of-hospital cardiac arrest with and without sustained return of spontaneous circulation (ROSC) in derivation and validation sets

| Characteristics | Derivation set (n = 620) | | | | | | p-value | Validation set (n = 310) | | | | | | p-value |
|---|--------------------------|--------|--------------------------|---------|-----------------|--------|---------|--------------------------|---------|--------------------------|---------|----------------|---------|---------|
| | Total (n = 620) | | Sustained ROSC (n = 177) | | Death (n = 443) | | | Total (n = 310) | | Sustained ROSC (n = 218) | | Death (n = 92) | | |
| Sex | | | | | | | | | | | | | | |
| Male | 409 | (66.0) | 112 | (63.3) | 297 | (67.0) | 0.371 | 204 | (65.8) | 60 | (65.2) | 144 | (66.1) | 0.887 |
| Female | 211 | (34.0) | 65 | (36.7) | 146 | (33.0) | | 106 | (34.2) | 32 | (34.8) | 74 | (33.9) | |
| Age (year) | | | | | | | | | | | | | | |
| Mean ±SD | 63.86 ± 18.26 | | 62.37 ± 18.08 | | 64.46 ± 18.32 | | 0.197 | 63.14 ± 18.99 | | 62.77 ± 19.11 | | 63.29 ± 18.99 | | 0.827 |
| Comorbidities | | | | | | | | | | | | | | |
| Hypertension | 153 | (24.7) | 44 | (24.9) | 109 | (24.6) | 0.947 | 73 | (23.5) | 21 | (22.8) | 52 | (23.9) | 0.846 |
| Diabetes mellitus | 130 | (21.0) | 38 | (21.5) | 92 | (20.8) | 0.846 | 55 | (17.7) | 19 | (20.7) | 36 | (16.5) | 0.384 |
| Heart disease | 116 | (18.7) | 42 | (23.7) | 74 | (16.7) | 0.043 | 56 | (18.1) | 20 | (21.7) | 36 | (16.5) | 0.275 |
| Dyslipidemia | 29 | (4.7) | 7 | (4.0) | 22 | (5.0) | 0.590 | 11 | (3.5) | 1 | (1.1) | 10 | (4.6) | 0.184 |
| Respiratory disease | 87 | (14.0) | 10 | (5.6) | 77 | (17.4) | <0.001 | 53 | (17.1) | 7 | (7.6) | 46 | (21.1) | 0.004 |
| Stroke | 7 | (1.1) | 4 | (2.3) | 3 | (0.7) | 0.107 | 6 | (1.9) | 2 | (2.2) | 4 | (1.8) | 1.000 |
| Renal diseases | 29 | (4.7) | 9 | (5.1) | 20 | (4.5) | 0.761 | 17 | (5.5) | 7 | (7.6) | 10 | (4.6) | 0.286 |
| Cancer | 12 | (1.9) | 6 | (3.4) | 6 | (1.4) | 0.111 | 8 | (2.6) | 4 | (4.3) | 4 | (1.8) | 0.243 |
| Other | 19 | (3.1) | 7 | (4.0) | 12 | (2.7) | 0.416 | 12 | (3.9) | 6 | (6.5) | 6 | (2.8) | 0.193 |
| Location type | | | | | | | | | | | | | | |
| Non-public | 509 | (82.1) | 146 | (82.5) | 363 | (81.9) | 0.873 | 242 | (78.1) | 69 | (75.0) | 173 | (79.4) | 0.397 |
| Public | 111 | (17.9) | 31 | (17.5) | 80 | (18.1) | | 68 | (21.9) | 23 | (25.0) | 45 | (20.6) | |
| Witnessed arrest | | | | | | | | | | | | | | |
| No | 310 | (50.0) | 96 | (54.2) | 214 | (48.3) | 0.182 | 131 | (42.3) | 38 | (41.3) | 93 | (42.7) | 0.825 |
| Yes | 310 | (50.0) | 81 | (45.8) | 229 | (51.7) | | 179 | (57.7) | 54 | (58.7) | 125 | (57.3) | |
| Bystander CPR | | | | | | | | | | | | | | |
| No | 315 | (50.8) | 99 | (55.9) | 216 | (48.8) | 0.107 | 144 | (46.5) | 47 | (51.1) | 97 | (44.5) | 0.288 |
| Yes | 305 | (49.2) | 78 | (44.1) | 227 | (51.2) | | 166 | (53.5) | 45 | (48.9) | 121 | (55.5) | |
| Type of arrest | | | | | | | | | | | | | | |
| Non-trauma | 587 | (94.7) | 168 | (94.9) | 419 | (94.6) | 0.868 | 293 | (94.5) | 87 | (94.6) | 206 | (94.5) | 0.980 |
| Trauma | 33 | (5.3) | 9 | (5.1) | 24 | (5.4) | | 17 | (5.5) | 5 | (5.4) | 12 | (5.5) | |
| Type of traumatic arrest (n = 50) | | | | | | | | | | | | | | |
| Blunt | 28 | (84.8) | 8 | (88.9) | 20 | (83.3) | 1.000 | 15 | (88.2) | 3 | (60.0) | 12 | (100.0) | 0.074 |
| Penetrating | 5 | (15.2) | 1 | (11.1) | 4 | (16.7) | | 2 | (11.8) | 2 | (40.0) | 0 | (0.0) | |
| Type of non-traumatic arrest (n = 880) | | | | | | | | | | | | | | |
| Non-cardiogenic | 312 | (53.2) | 62 | (36.9) | 250 | (59.7) | <0.001 | 159 | (54.3) | 28 | (32.2) | 131 | (63.6) | <0.001 |
| Cardiogenic | 275 | (46.8) | 106 | (63.1) | 169 | (40.3) | | 134 | (45.7) | 59 | (67.8) | 75 | (36.4) | |
| Time from arrest to chest compression | | | | | | | | | | | | | | |
| < 15 min | 476 | (76.8) | 139 | (78.5) | 337 | (76.1) | 0.513 | 240 | (77.4) | 73 | (79.3) | 167 | (76.6) | 0.598 |
| ≥ 15 min | 144 | (23.2) | 38 | (21.5) | 106 | (23.9) | | 70 | (22.6) | 19 | (20.7) | 51 | (23.4) | |
| CPR duration | | | | | | | | | | | | | | |
| < 30 min | 263 | (42.4) | 112 | (63.3) | 151 | (34.1) | <0.001 | 126 | (40.6) | 50 | (54.3) | 76 | (34.9) | 0.001 |
| ≥ 30 min | 357 | (57.6) | 65 | (36.7) | 292 | (65.9) | | 184 | (59.4) | 42 | (45.7) | 142 | (65.1) | |
| Airway management | | | | | | | | | | | | | | |
| ETT | 456 | (73.5) | 147 | (83.1) | 309 | (69.7) | 0.001 | 245 | (79.0) | 81 | (88.0) | 164 | (75.2) | 0.016 |
| BVM | 148 | (23.9) | 24 | (13.6) | 124 | (28.0) | | 57 | (18.4) | 8 | (8.7) | 49 | (22.5) | |
| LMA | 16 | (2.6) | 6 | (3.4) | 10 | (2.3) | | 8 | (2.6) | 3 | (3.3) | 5 | (2.3) | |
| Defibrillation | | | | | | | | | | | | | | |
| No | 472 | (76.1) | 117 | (66.1) | 355 | (80.1) | <0.001 | 240 | (77.4) | 61 | (66.3) | 179 | (82.1) | 0.002 |
| Yes | 148 | (23.9) | 60 | (33.9) | 88 | (19.9) | | 70 | (22.6) | 31 | (33.7) | 39 | (17.9) | |
| Fluid resuscitation | | | | | | | | | | | | | | |
| No | 17 | (2.7) | 2 | (1.1) | 15 | (3.4) | 0.295 | 6 | (1.9) | 1 | (1.1) | 5 | (2.3) | 0.602 |
| 0.9% NaCl | 574 | (92.6) | 167 | (94.4) | 407 | (91.9) | | 295 | (95.2) | 87 | (94.6) | 208 | (95.4) | |
| Lactate ringer | 29 | (4.7) | 8 | (4.5) | 21 | (4.7) | | 9 | (2.9) | 4 | (4.3) | 5 | (2.3) | |
| Medication during CPR | | | | | | | | | | | | | | |
| Adrenaline | 618 | (99.7) | 177 | (100.0) | 441 | (99.5) | 1.000 | 310 | (100.0) | 92 | (100.0) | 218 | (100.0) | NA |
| 7.5% SB | 247 | (39.8) | 62 | (35.0) | 185 | (41.8) | 0.122 | 128 | (41.3) | 36 | (39.1) | 92 | (42.2) | 0.616 |

Table 1: Characteristics of patients with out-of-hospital cardiac arrest with and without sustained return of spontaneous circulation (ROSC) in derivation and validation sets

| Characteristics | Derivation set (n = 620) | | | | | | p-value | Validation set (n = 310) | | | | | | p-value |
|----------------------|--------------------------|----------|--------------------------|--------|-----------------|---------|---------|--------------------------|--------|--------------------------|--------|----------------|--------|---------|
| | Total (n = 620) | | Sustained ROSC (n = 177) | | Death (n = 443) | | | Total (n = 310) | | Sustained ROSC (n = 218) | | Death (n = 92) | | |
| Amiodarone | 56 | (9.0) | 17 | (9.6) | 39 | (8.8) | 0.753 | 27 | (8.7) | 6 | (6.5) | 21 | (9.6) | 0.375 |
| 50% glucose | 49 | (7.9) | 8 | (4.5) | 41 | (9.3) | 0.048 | 29 | (9.4) | 9 | (9.8) | 20 | (9.2) | 0.867 |
| 10% CG | 100 | (16.1) | 25 | (14.1) | 75 | (16.9) | 0.391 | 56 | (18.1) | 17 | (18.5) | 39 | (17.9) | 0.902 |
| CBG | | | | | | | | | | | | | | |
| Median (IQR) | 136.5 | 52.5–211 | 124 | 22–200 | 158 | 101–236 | <0.001 | 129.5 | 24–208 | 118 | 1–198 | 153 | 95–252 | <0.001 |
| Pupil reflex | | | | | | | | | | | | | | |
| Non-response | 598 | (96.5) | 162 | (91.5) | 436 | (98.4) | <0.001 | 298 | (96.1) | 84 | (91.3) | 214 | (98.2) | 0.008 |
| Response | 22 | (3.5) | 15 | (8.5) | 7 | (1.6) | | 12 | (3.9) | 8 | (8.7) | 4 | (1.8) | |
| Response time | | | | | | | | | | | | | | |
| ≤ 8 min | 162 | (26.1) | 57 | (32.2) | 105 | (23.7) | 0.030 | 81 | (26.1) | 25 | (27.2) | 56 | (25.7) | 0.786 |
| > 8 min | 458 | (73.9) | 120 | (67.8) | 338 | (76.3) | | 229 | (73.9) | 67 | (72.8) | 162 | (74.3) | |

Data are presented as mean ± standard deviation (SD); median (interquartile range; IQR), or frequency (%). Abbreviations:

BVM: bag valve mask; CPR: cardiopulmonary resuscitation; ETT: endotracheal tube; LMA: laryngeal mask airway; NA, data not applicable;

CBG: capillary blood glucose; SB: sodium bicarbonate; CG: calcium gluconate. P-value corresponds to ^fIndependent samples t-test,

^mMann–Whitney U test, ^cChi-square test, or ^fFisher's exact test.

Table 2: Multivariate logistic regression analyses to identify the independent factors associated with a sustained return of spontaneous circulation at the scene

| Factors | B | OR | 95% CI | p-value | Score |
|--------------------------------------|-------|------|--------------|---------|-------|
| CPR duration | | | | | |
| < 30 min | 1.620 | 5.05 | (3.34–7.65) | <0.001 | 3 |
| ≥ 30 min | | 1.00 | Reference | | |
| Advanced airway management | | | | | |
| Bag valve mask | | 1.00 | Reference | | |
| Endotracheal tube | 1.119 | 3.06 | (1.77–5.31) | <0.001 | 2 |
| Laryngeal mask airway | 1.230 | 3.42 | (1.02–11.46) | 0.046 | 2.5 |
| Defibrillation | | | | | |
| No | | 1.00 | Reference | | |
| Yes | 0.717 | 2.05 | (1.31–3.2) | 0.002 | 1.5 |
| Capillary blood glucose (mg%) | | | | | |
| (1) | | 1.00 | Reference | | |
| < 150 | 0.670 | 1.95 | (1.05–3.65) | 0.035 | 1 |
| ≥ 150 | 1.056 | 2.87 | (1.56–5.29) | 0.001 | 2 |
| Pupil reflex | | | | | |
| No response | | 1.00 | Reference | | |
| Response | 1.084 | 2.96 | (1.1–7.96) | 0.032 | 2 |
| Response time | | | | | |
| ≤ 8 min | 0.506 | 1.66 | (1.07–2.57) | 0.023 | 1 |
| > 8 min | | 1.00 | Reference | | |

Data are presented with 95% confidence interval (CI). OR: Adjusted odds ratio estimated by multiple logistic regression;

CPR: cardiopulmonary resuscitation. Variables included in the multivariable model had $p < 0.050$ in the univariate analysis.

Model summary: $-2 \text{ Log likelihood} = 623.963$, Cox & Snell R Square = 0.173, Nagelkerke R Square = 0.248.

Hosmer and Lemeshow test: Chi-square = 8.418, $df = 8$, $p\text{-value} = 0.394$. Constant: -3.704 .

vious study in a province in central Thailand, reporting an incidence of 39.0% for sustained ROSC (7). The present study demonstrated that ROSC achieved in Thailand was higher than that in a low-income country with an incidence of only 27.35% for ROSC in the emergency department (20). Previ-

ous empirical evidence showed that countries with high economic and social status had a low incidence of OHCA and significantly high rate of favorable outcomes for ROSC (21) (22). Second, six predictors were associated with a sustained ROSC at the scene, including CPR duration < 30 min, advanced air-

way management with endotracheal tube (ETT) and laryngeal mask airway (LMA), defibrillation, pupillary light reflex, and response time ≤ 8 min. The possible explanation regarding patients with OHCA having CPR duration < 30 min, specified as the duration from the FMC to the end of CPR, was that patients with OHCA having CPR duration < 30 min had a chance of sustained ROSC, consistent with a nationwide multicenter observational study in Japan reporting that patients with OHCA receiving CPR < 30 min would have an increased chance of ROSC at the scene and 1-month survival and favorable neurological outcome defined by cerebral performance category scores 1 or 2, compared with patients with OHCA having CPR duration > 30 min. However, the authors explained that the outcomes were due to factors such as shockable rhythm, witnessed arrest, and bystander CPR (23) and comparable with those of a previous study finding that the most optimal cutoff for prehospital CPR duration in the non-traumatic group of patients with OHCA for obtaining ROSC and favorable neurological outcome at hospital discharge was 12 min, independent of cardiac rhythm. A longer CPR duration did not increase the rate of achieving ROSC (24). Therefore, CPR duration could help emergency medical personnel working prehospitally properly decide whether to terminate CPR in patients requiring prolonged CPR. The explanation regarding patients with OHCA obtaining prehospital advanced airway management with ETT and LMA as factors that helped increase sustained ROSC at the scene compared with bag valve masks (BVMs) was consistent with our previous study from the national EMS database of Thailand, reporting that patients with OHCA who received advanced airway management with ETT had 3.88 times higher chance of ROSC at the scene compared with those with BVMs (10). Additionally, they were similar to results of several studies reporting that prehospital advanced airway with ETT and LMA by paramedics in patients with OHCA were associated with increased rate of ROSC at the scene, compared with patients with OHCA using BVMs (25-27), which was in contrast to a previous study finding that airway management with ETT during CPR in emergency department was associated with worsened outcome of ROSC and decreased survival until discharge at 28 days, compared with the non-ETT group with BVMs (28), and ETT and LMA applications during CPR for patients with in-hospital cardiac arrest were associated with increase of no-flow interval, compared with BVMs application. A high no-flow interval is associated with worsened neurological outcome, and helps emergency medical personnel in deciding for CPR initiation or termination in patients with OHCA (29).

ETT insertion is the gold standard definitive airway management, but it has numerous limitations, such as local protocol; in some areas or countries, paramedics or Emergency nurse practitioners (ENPs) are not allowed to insert ETT, except

when a physician is available and an ambulance is present at the scene. However, for the study area, paramedics and ENPs were allowed to insert ETT and administer medication in patients with OHCA under offline protocol (5). Defibrillation was associated with a sustained ROSC at the scene, which was similar to a previous systematic review and meta-analysis reporting that patients with OHCA who received prehospital defibrillation had increased 1-month favorable neurological outcomes, and the rate was higher in patients presenting with initial shockable heart rhythms including ventricular fibrillation (VF) and pulseless ventricular tachycardia (VT) compared with patients without defibrillation and presenting with non-shockable rhythms (8). In this study, prehospital CBG was associated with a sustained ROSC. Even if hypoglycemia was one of the reversible causes of cardiac arrest in 2005 guidelines (30) and removed in ACLS 2010 (31), 2015 (32), and 2020 (33), recently the observational study in the emergency department in Thailand found that patients with OHCA who had intra-arrest blood glucose level < 100 mg/dL had decreased rate of sustained ROSC (34), which was consistent with the results of a large study retrospectively collecting data of patients with in-hospital cardiac arrest for 10 years in Taiwan. It reported that patients who had intra-arrest blood glucose level < 150 mg/dL had worse neurological outcomes and decreased rate of ROSC (35). For the study area, prehospital CBG administration is routine practice in patients with OHCA and in patients with hypoglycemia, which is easily corrected in the prehospital context by 50% glucose intravenous administration and normal blood glucose level was tried to be maintained during CPR. This was believed to help improve clinical outcomes. This study revealed that patients with OHCA who had pupillary light reflex had more chances of sustained ROSC than patients without pupillary light reflex. The finding was consistent with a previous study reporting that pupillary light reflex could be used to predict outcomes after cardiac arrest, especially increased ROSC rate. In contrast, patients without pupillary light reflex would have significantly increased mortality rate (36), which contradicts the results of a recent study reporting that measurement of pupil size and pupillary light reflex could not be used to predict ROSC and the measurements were not associated with neurological outcomes in patients with cardiac arrest (37). Another factor used in the prediction of sustained ROSC was response time ≤ 8 min, which was defined as the interval between emergency call to ambulance arrival at the scene. This result was consistent with those of previous studies reporting that response time was associated with a sustained ROSC at the scene and neurological outcome, and with each minute increase in response time, the chance of ROSC would decrease in patients with OHCA (5, 15). In the study area, response time was guaranteed to be at most 8 min in patients identified with un-

consciousness or cardiac arrest. In patients with cardiac arrest, staff at the dispatch center advised callers to perform dispatcher-assisted bystander CPR (DA-CPR) before the ambulance arriving at the scene, and in the study area, the traffic police were coordinated to ensure the traffic route of ambulances and reduce response time.

Third, this study developed a simple tool for prediction of sustained ROSC at the scene, helping prehospital emergency medical personnel, such as EPs, paramedics, and ENPs, to identify predictors of sustained ROSC in patients with OHCA, and patients' relatives could know the prognosis in emergency situations. Factors that influence the management of patients with OHCA at the scene could be used in the prediction of sustained ROSC. This study developed a simple tool for the prediction of sustained ROSC in patients with OHCA, called PRAD-CCPR score, including six factors, namely, pupil reflex, response time, airway management, defibrillation, CBG, and CPR duration. The total score ranged from 0 to 15, with simplicity and convenience in remembrance and clinical application and appropriate to prehospital context. The score of at least 6 was the most suitable cutoff point in prediction of sustained ROSC at the scene with AUC of 0.759 (95% CI 0.715–0.802, $p < 0.001$), sensitivity of 62.0% (95% CI 51.2–71.9), specificity of 75.7% (95% CI 69.4–81.2), PPV of 51.8% (95% CI 40.9–62.3), and NPV of 79.5% (95% CI 73.5–84.6). To the authors' knowledge, so far, four scores have been developed for immediate prediction of ROSC outcome, comprising WATCH-CPR score (including witnessed arrest, time from arrest to chest compression, and CPR duration) (7). WATCH-CPR score ≥ 2 could be used to predict a chance of sustained ROSC in the emergency department. This study collected data in prehospital and ED settings. Notwithstanding, the WATCH-CPR score would be easy to apply, and many important data were still believed to be missed in the context of management by the EMS team in specific situations, for example, management of patients with OHCA, such as response time and prehospital advanced airway management. The RACA score had AUC of 0.710 (95% CI 0.697–0.724) including factors such as sex, age ≥ 80 years, witnessed arrest, asystole, arrest location, presumable etiology of cardiac arrest, bystander CPR, and time until professional arrival (13). However, the RACA score was difficult, complex, and inappropriate to apply in emergency conditions in the context of prehospital management. Besides, the interpretation of the score was complex and unfit for application. The NULL-PLEASE score variables included non-shockable rhythm, unwitnessed arrest, long no-flow period, long low flow period, pH < 7.2 , lactate > 7 , end-stage renal failure on dialysis, age > 85 years, on-going CPR, and extracardiac cause; and it had AUC of 0.632 (95% CI 0.523–0.741) (14). The NULL-PLEASE score was thought to be suitable for the hospital context. However, since obtaining the results of some included pa-

rameters took time, and because no blood gas test and lactate test are available outside the hospital and in the context of prehospital EMS in Thailand, it could not be applied in this setting. The P-ROSC score is made up of variables including age, time to EMS arrival, first rhythm, arrest witnessed, and prehospital drug administration, and has an AUC of 0.806 (95% CI 0.799–0.814) (15). Nevertheless, the P-ROSC score only used prehospital parameters in the prediction of ROSC in patients with OHCA using only five parameters. The P-ROSC score had a total score of 100, and the score proportion was divided for each parameter with complexity, inappropriate to apply in emergencies, and pressured conditions as the management of patients with OHCA. Therefore, the PRAD-CCPR score was proposed, which was a simple tool for the prediction of sustained ROSC at the scene including practical parameters in the context of prehospital management, comprising treatment at the scene by an EMS team, for assisting EPs, paramedics, and ENPs when making critical decisions for patients with OHCA regarding survival prediction.

5. Limitations

This study has several limitations. First, it was a retrospective observational study, collecting data in a single center, an advanced emergency medical operation unit in Bangkok, Thailand, a middle-income country. Thus, due to differences between areas, the study results may not be indicative in other areas and it is required to assess the external validity of the score. Second, this study only analyzed sustained ROSC at the scene. Additional studies are needed on the predictive performance of the score regarding long-term outcomes, such as survival to hospital discharge and neurological function outcome in patients with OHCA. Third, all data were retrospectively collected from the EMS patient care report; although neutrality was tried to be maintained in every way possible, there might be a risk of selection bias.

6. Conclusion

In this study, a score called PRAD-CCPR was developed and validated for predicting sustained ROSC in patients with OHCA at the scene in a middle-income country. An optimal score of ≥ 6 provides an acceptable area under the ROC curve of 0.759 with sensitivity and specificity of 62.0% and 75.7%, respectively. This predictive score might help CPR commanders to prognosticate the outcome of patients with OHCA at the scene.

7. Declarations

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Table 3: Screening performance characteristics of the PRADD-CPR model for predicting the sustained return of spontaneous circulation (ROSC) after out of hospital cardiac arrest in different cutoff points

| Score | Sensitivity (95% CI) | Specificity (95% CI) | PPV (95% CI) | NPV (95% CI) | LR+ (95% CI) | LR- (95% CI) |
|------------------|-------------------------|-------------------------|-----------------|-----------------|-----------------|-----------------|
| 1.0 | 100(96.1–100) | 1.8(0.5–4.6) | 30.1(25–35.5) | 100(39.8–100) | 1.02(1–1.04) | 0 |
| 2.0 | 100(96.1–100) | 3.7(1.6–7.1) | 30.5(25.3–36) | 100(63.1–100) | 1.04(1.01–1.07) | 0 |
| 2.5 | 100(96.1–100) | 4.1(1.9–7.7) | 30.6(25.4–36.1) | 100(66.4–100) | 1.04(1.01–1.07) | 0 |
| 3.0 | 100(96.1–100) | 11.5(7.6–16.5) | 32.3(26.9–38) | 100(86.3–100) | 1.13(1.08–1.18) | 0 |
| 3.5 | 100(96.1–100) | 12.4(8.3–17.5) | 32.5(27.1–38.3) | 100(87.2–100) | 1.14(1.09–1.2) | 0 |
| 4.0 | 90.2(82.2–95.4) | 32.1(26–38.7) | 35.9(29.7–42.5) | 88.6(79.5–94.7) | 1.33(1.19–1.49) | 0.31(0.16–0.58) |
| 4.5 | 89.1(80.9–94.7) | 34.9(28.6–41.6) | 36.6(30.3–43.3) | 88.4(79.7–94.3) | 1.37(1.21–1.54) | 0.31(0.17–0.58) |
| 5.0 | 73.9(63.7–82.5) | 60.6(53.7–67.1) | 44.2(36.2–52.4) | 84.6(78–89.9) | 1.87(1.53–2.3) | 0.43(0.3–0.62) |
| 5.5 | 69.6(59.1–78.7) | 65.1(58.4–71.4) | 45.7(37.3–54.3) | 83.5(77.1–88.8) | 2(1.59–2.5) | 0.47(0.34–0.65) |
| 6.0 ^a | 62.0(51.2–71.9) | 75.7(69.4–81.2) | 51.8(42.1–61.4) | 82.5(76.5–87.5) | 2.55(1.92–3.38) | 0.5(0.38–0.66) |
| 6.5 | 51.1(40.4–1.7) | 79.8(73.9–84.9) | 51.6(40.9–62.3) | 79.5(73.5–84.6) | 2.53(1.82–3.52) | 0.61(0.49–0.76) |
| 7.0 | 39.1(29.1–49.9) | 85.3(79.9–9.7) | 52.9(40.4–65.2) | 76.9(71–82) | 2.67(1.77–4.01) | 0.71(0.6–0.85) |
| 7.5 | 33.7(24.2–44.3) | 87.6(82.5–91.7) | 53.4(39.9–66.7) | 75.8(70–80.9) | 2.72(1.73–4.29) | 0.76(0.65–0.88) |
| 8.0 | 20.7(12.9–30.4) | 95.4(91.7–97.8) | 65.5(45.7–82.1) | 74(68.5–79) | 4.5(2.18–9.3) | 0.83(0.75–0.93) |
| 8.5 | 18.5(11.1–27.9) | 96.8(93.5–98.7) | 70.8(48.9–87.4) | 73.8(68.3–78.8) | 5.75(2.47–13.4) | 0.84(0.76–0.93) |
| 9.0 | 12(6.1–20.4) | 99.1(96.7–99.9) | 84.6(54.6–98.1) | 72.7(67.3–77.7) | 13(2.95–57.6) | 0.89(0.82–0.96) |
| 9.5 | 5.4(1.8–2.2) | 99.5(97.5–100) | 83.3(35.9–99.6) | 71.4(65.9–76.4) | 11.8(1.4–100) | 0.95(0.9–1) |
| 10.0 | 5.4(1.8–12.2) | 99.5(97.5–100) | 83.3(35.9–99.6) | 71.4(65.9–76.4) | 11.8(1.4–100) | 0.95(0.9–1) |

Data are presented with 95% confidence interval (CI). LR: likelihood ratio; NPV: negative predictive value; PPV: positive predictive value.

^aThe best threshold value was determined using Youden's index (Youden index J = Sensitivity + Specificity – 1).

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7.2. Conflict of interest

The authors have no conflicting interests to declare.

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7.4. Authors' contribution

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 Supervision: Thongpitak Huabangyang;
 Project administration: Thongpitak Huabangyang; Funding acquisition: Thongpitak Huabangyang.
 All authors read and approved the final version of manuscript.

7.5. Data Availability

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

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