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Clinical paper

Prognostic performance of simplified out-of-hospital cardiac arrest (OHCA) and cardiac arrest hospital prognosis (CAHP) scores in an East Asian population: A prospective cohort study

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Abstract

Aim: The out-of-hospital cardiac arrest (OHCA) and cardiac arrest hospital prognosis (CAHP) scores were developed for early neuroprognostication after OHCA. Calculation of both scores requires estimation of the no-flow interval, which may be imprecise. We aimed to validate simplified OHCA and CAHP scores, which exclude the no-flow interval, in an East Asian cohort.

Methods: This was a single-centre prospective observational study. Consecutive OHCA patients were screened between January 2011 and March 2017. Simplified OHCA and CAHP scores (sOHCA, sCAHP) were calculated as the original scores with the no-flow interval omitted. Association between independent variables and outcomes was examined by multivariate logistic regression analysis, and area under the receiver operating characteristics curve (AUC) values were compared by paired DeLong test.

Results: A total of 412 patients were included. An inverse association between sOHCA and sCAHP scores and neurological outcome was confirmed, and most of the variables included in the simplified score calculations were also independently associated with neurological outcomes in our cohort. The AUC values for the simplified scores were similar, and both had excellent discriminatory performance for favourable neurologic outcome (AUC = 0.82, 95% confidence interval 0.77–0.86 for sOHCA and 0.84 with 95% confidence interval 0.80–0.89 for sCAHP, *p*-value = 0.19).

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Conclusion: The simplified OHCA and CAHP scores predicted neurological outcomes in successfully resuscitated East Asian OHCA patients with similar and excellent accuracy. The simplified OHCA and CAHP scores could potentially serve alongside the original scores as risk-adjustment tools for comparison of outcomes between regional OHCA registries worldwide.
Keywords: Out-of-hospital cardiac arrest, Neuroprognostication, Risk score, Validation

Introduction

Worldwide, out-of-hospital cardiac arrest (OHCA) strikes an estimated 28–44 people per 100,000 population annually.[1] Outcomes after OHCA remain poor despite ongoing efforts to improve the chain of survival. According to recent data from the Pan Asian Resuscitation Outcomes Study (PAROS) Clinical Research Network, the overall survival rate to hospital discharge after OHCA in Asian patients was 5.4%, and the survival rate with good neurological function was 2.7%.[2]

The out-of-hospital cardiac arrest (OHCA)[3] and cardiac arrest hospital prognosis (CAHP)[4] scores are risk scores that were developed in France specifically for patients who have ROSC after OHCA. Both scores allow early risk-stratification because they are based on variables that are immediately available upon admission to the intensive care unit (ICU). The OHCA score[3] is based on parameters including the presence of a shockable rhythm, the no-flow interval (time from collapse to initiation of cardiopulmonary resuscitate [CPR]), the low-flow interval (time from CPR to ROSC), the serum creatinine level, and the arterial lactate level. The CAHP score[4] considers the no-flow interval, the low-flow interval, the total dose of adrenaline required during CPR, the patient's age, the arrest setting, the presence of a shockable rhythm, and the arterial pH. Both scores were internally validated and showed strong discriminatory performance for poor outcomes (area under the receiver operating characteristics curve [AUC] for the OHCA score = 0.82 and for the CAHP score = 0.93).[3,4]

Although both scores were well-validated internally in the original studies,[3,4] the wide variation in the characteristics and outcomes of OHCA patients worldwide[1] requires external validation of the scores before they can be widely applied.[5] Furthermore, the updated Utstein template[6] no longer requires recording the time of collapse, and therefore, the duration of the no-flow interval could not be calculated. This raises problems for applying both scores to future patients. Accordingly, we have proposed simplified OHCA and CAHP scores (sOHCA and sCAHP scores) that remove the no-flow interval from the calculation. To test these scores, we first identified the independent risk factors affecting neurologic outcomes in East Asian patients after OHCA. We then assessed and compared the prognostic performance of the sOHCA and sCAHP scores in the same cohort.

Materials and methods

Setting

This prospective observational study was performed at the National Taiwan University Hospital (NTUH), which is a tertiary medical centre. The study was conducted in accordance with the Declaration of Helsinki and was approved by the NTUH Research Ethics Committee (reference number: 201708013RIND). Patients or their surrogates gave written informed consent for enrolment.

NTUH has 2600 beds, including 220 ICU beds, and there are approximately 100,000 patient visits to the NTUH emergency department (ED) each year. Resuscitation and post-resuscitation protocols for OHCA patients, including percutaneous coronary intervention and targeted temperature management (TTM), are performed in accordance with guideline recommendations.[7,8] If there is ROSC, neuroprognostication is based on daily assessments of brainstem reflexes along with electroencephalography on days 3 and 7. Because withdrawal of life-sustaining therapy (WLST) for post-cardiac arrest patients was not permitted by law in Taiwan until 2015, the main purpose of neuroprognostication was to assist surrogates and clinicians in deciding whether further aggressive life-sustaining therapy should be added.

Patients

Consecutive OHCA patients between January 2011 and March 2017 were screened, and those who met the following criteria were included in the study: (1) age 18 years or older; (2) non-traumatic arrest; (3) no documentation of a do-not-resuscitate order before arrest; and (4) sustained ROSC after CPR, which was defined as ROSC lasting for at least 20 min without resumption of chest compressions. If multiple cardiac arrest events occurred in a single patient, only the first event was recorded.

Data collection and outcome measures

Details of the OHCA events were recorded in the Utstein style,[6] and data were extracted from the electronic medical and ambulance records, including patient characteristics, interventions provided, and outcomes. Study data for each patient included age, sex, comorbidities, variables derived from the Utstein template, and laboratory results on admission to the ICU. The sOHCA and sCAHP scores were calculated by the same method as the original OHCA[3] and CAHP[4] scores (Supplemental Table 1), except that, because the time of arrest was not routinely recorded or estimated by emergency medical technicians or treating clinicians, the no-flow interval (time from arrest to initiation of CPR) was omitted. The low-flow interval was defined as the interval from the initiation of CPR to ROSC, and early recovery of consciousness was defined as appropriate response to verbal commands within the first 4 h after ROSC (i.e. before TTM).

The primary outcome was favourable neurological status at hospital discharge, defined as Cerebral Performance Category (CPC) 1 or 2.[9] The CPC score is a validated 5-point scale of neurological disability: CPC 1 indicates good cerebral performance; CPC 2, moderate cerebral disability; CPC 3, severe cerebral disability; CPC 4, coma/vegetative state; and CPC 5, brain death. Patients with a CPC score of 1 or 2 generally have sufficient cerebral function to live independently.

Statistical analysis

Data were analysed using R 3.3.1 software (R Foundation for Statistical Computing, Vienna, Austria). Categorical data are expressed as counts and proportions, and continuous data are expressed as means and standard deviations. Categorical variables

Table 1 – Baseline characteristics of study patients.

Variable	All patients (n = 412)	Patients with favourable neurological outcome at hospital discharge (n = 94)	Patients with unfavourable neurological outcome at hospital discharge (n = 318)	p-Value
Age, years (SD[a])	65.2 (16.8)	56.8 (16.3)	67.7 (16.2)	<0.001
Male, n (%)	282 (68.4)	67 (71.3)	215 (67.6)	0.53
Comorbidities, n (%)				
Diabetes mellitus	135 (32.8)	25 (26.6)	110 (34.6)	0.17
Hypertension	207 (50.2)	38 (40.4)	169 (53.1)	0.03
Coronary artery disease	133 (32.3)	28 (29.8)	105 (33.0)	0.62
Heart failure	37 (9.0)	11 (11.7)	26 (8.2)	0.31
Arrhythmia	37 (9.0)	13 (13.8)	24 (7.5)	0.07
Chronic obstructive pulmonary disease or asthma	25 (6.1)	2 (2.1)	23 (7.2)	0.08
End-stage renal disease	30 (7.3)	6 (6.4)	24 (7.5)	0.82
Cirrhosis	11 (2.7)	0 (0)	11 (3.5)	0.08
Stroke	30 (7.3)	6 (6.4)	24 (7.5)	0.82
Malignancy	68 (16.5)	7 (7.4)	61 (19.2)	0.007
Witnessed arrest, n (%)	305 (74.0)	84 (89.4)	221 (69.5)	<0.001
Arrest at home, n (%)	191 (46.4)	27 (28.7)	164 (51.6)	<0.001
Shockable rhythm, n (%)	124 (30.1)	56 (59.6)	68 (21.4)	<0.001
Adrenaline dose, n (%)				<0.001
0	87 (21.1)	43 (45.7)	44 (13.8)	
1 to 2 mg	105 (25.5)	29 (30.9)	76 (23.9)	
≥3 mg	220 (53.3)	22 (23.4)	198 (62.3)	
Time from CPR[b] to ROSC[c] (min) (SD)	33.9 (22.8)	25.9 (25.8)	36.2 (21.4)	<0.001
Laboratory tests (SD)				
pH	7.1 (0.2)	7.2 (0.2)	7.1 (0.2)	<0.001
$PaCO_2$ (mmHg)	63.3 (28.3)	52.4 (26.3)	66.5 (28.1)	<0.001
HCO_3^- (mmol/L)	19.6 (6.2)	19.8 (5.8)	19.5 (6.3)	0.55
Lactate (mmol/L)	10.1 (4.6)	7.9 (4.4)	10.7 (4.5)	<0.001
Creatinine (mg/dL)	2.5 (3.0)	2.3 (3.0)	2.6 (3.0)	0.009
Early recovery of consciousness following ROSC, n (%)	33 (8.0)	25 (26.6)	8 (2.5)	<0.001
Simplified OHCA[d] score (SD)	31.6 (13.8)	20.1 (11.4)	34.9 (12.6)	<0.001
Simplified CAHP[e] score (SD)	186.3 (49.9)	139.3 (42.1)	200.1 (43.2)	<0.001

[a] SD, standard deviation.
[b] CPR, cardiopulmonary resuscitation.
[c] ROSC, return of spontaneous circulation.
[d] OHCA, Out of Hospital Cardiac Arrest score.
[e] CAHP, Cardiac Arrest Hospital Prognosis score.

were compared using Fisher's exact test and continuous variables were examined using Wilcoxon's rank-sum test. A two-tailed *p*-value of <0.05 was considered significant.

We first sought to identify the independent variables that were associated with the primary outcome and to determine which of them, other than those included in the risk scores, might impact the primary outcome in our population. To do this, we built two separate prediction models by multivariate logistic regression analyses, with the odds ratio (OR) as the outcome measure. The first model included all statistically significant variables, except for the sOHCA and sCAHP scores, in the prediction model. The second model allowed the sOHCA and sCAHP scores to compete with the other independent variables in the model-building process so that we could discover which variables would stay in the prediction model when the influence of the risk scores had been accounted for. Next, we validated the sOHCA and sCAHP scores in our population by univariate logistic regression analyses to obtain their respective ORs and AUC values. The AUC values were then compared by paired DeLong test.

The details of the model-fitting process of the multivariate logistic regression are as follows. All available independent variables were considered in the regression model, regardless of whether they were scored as significant by univariate analyses. The stepwise variable selection procedure (with iterations between the forward and backward steps) was applied to obtain the final regression model. Significance levels for entry and to stay were set at 0.15 to avoid exclusion of potential candidate variables. The final regression model was identified by sequentially excluding individual variables with *p*-value >0.05 until all regression coefficients were statistically significant. Generalised additive models (GAMs)[10] were used to examine nonlinear effects of the continuous variables and, if necessary, to identify the appropriate cut-off point(s) for dichotomising a continuous variable during the variable selection procedure. The goodness-of-fit of the fitted regression model was tested using the AUC value, the adjusted generalised R^2, and the Hosmer–Lemeshow goodness-of-fit test.

Results

A total of 936 adult non-traumatic OHCA patients were sent to the NTUH ED during the study period; among these patients, 524 patients did not achieve sustained ROSC and were excluded from analysis. The remaining 412 patients who achieve sustained ROSC were included in the analysis.

Table 1 provides the details of the OHCA events before, during, and after CPR for all patients in the cohort. The mean age of the patients was 65.2 years. The majority (74.0%) of the arrests were witnessed, and most of the initial rhythms were shockable (59.6%). The average duration of the low-flow interval (time from the start of CPR to ROSC) was 33.9 min. The average sOHCA score was 31.6 and the average sCAHP score was 186.3. Ninety-four patients (22.8%) survived to hospital discharge with favourable neurological status.

We placed all of the independent variables listed in Table 1 in the multivariate logistic regression analysis for variable selection. As shown in Table 2, the model 1 demonstrated that most of the variables incorporated in the sOHCA and sCAHP scores (Supplemental Table 1), including age, shockable rhythm, adrenaline dosage, low-flow interval, pH, and lactate level, were also significantly associated with neurological outcomes in our cohort; the model 2 demonstrated that when sOHCA and sCAHP scores were put into competition with other variables during model-fitting process, these two scores replaced most of the individual factors identified in the model 1 with only four other individual variables left in the model, including early recovery of consciousness following ROSC and malignancy. Moreover, the discriminatory performance of both model 1 and 2 remained similarly excellent (AUC = 0.91 for both models), which suggested that either sOHCA or sCAHP score alone may be used to predict neurological outcomes in OHCA patients.

The univariate logistic regression analysis indicated that both the sOHCA and sCAHP scores were inversely associated with favourable neurological outcome (Table 3), and both scores demonstrated excellent discriminatory performance (AUC = 0.82; 95% confidence interval [CI] 0.77–0.86, sOHCA, and 0.84; 95% CI 0.80–0.89, sCAHP). There was no significant difference between the AUC values for the sOHCA and sCAHP scores on the paired DeLong test ($p = 0.19$).

Discussion

Main findings

In this prospective observational study, we found that most of the prognostic factors after OHCA are similar in East Asian and Western patients. As such, the sOHCA and sCAHP scores, which exclude the no-flow interval from the calculation of the OHCA and CAHP scores, were still significantly associated with neurological outcomes after ROSC in an East Asian OHCA cohort. The AUC values for both sOHCA and sCAHP indicated similarly excellent accuracy for predicting neurological outcome in this population.

Individual predictors of neurological outcome

In concert with the original studies developing the OHCA[3] and CAHP[4] scores in France, our results showed that age, shockable rhythm, adrenaline dosage, low-flow interval, pH, and lactate levels were significantly associated with neurological outcomes in a Taiwanese

Table 2 – Multiple logistic regression model with favourable neurological outcome at hospital discharge as the dependent variable.

Independent variable[a]	Odds ratio	95% confidence interval	*p*-Value
Model 1: Regression model without simplified OHCA or CAHP scores			
Early recovery of consciousness following ROSC[b]	16.69	5.23–53.25	<0.001
Time from CPR[c] to ROSC < 32 min	5.02	2.39–10.54	<0.001
Shockable rhythm	4.02	2.05–2.89	<0.001
Age	0.96	0.94–0.98	<0.001
pH > 7.1	3.06	1.41–6.67	0.005
Lactate <7.5 mmol/L	2.41	1.25–4.65	0.009
Adrenaline dose	0.59	0.39–0.89	0.01
Malignancy	0.26	0.09–0.75	0.01
Model 2: Regression model with simplified OHCA and CAHP scores			
Early recovery of consciousness following ROSC	13.83	4.67–40.94	<0.001
Simplified CAHP score	0.98	0.97–0.99	<0.001
Simplified OHCA score	0.95	0.92–0.98	0.001
pH between 7.1 and 7.4	3.11	1.48–6.53	0.003
Malignancy	0.24	0.08–0.71	0.01
Arrhythmia	3.20	1.09–9.39	0.03

Model 1: Goodness-of-fit assessment: n = 412; adjusted generalized $R^2 = 0.55$; estimated area under the receiver operating characteristic curve = 0.91 (95% confidence interval: 0.88–0.94); and Hosmer–Lemeshow goodness-of-fit Chi-squared test $p = 0.92$.
Model 2: Goodness-of-fit assessment: n = 412; adjusted generalized $R^2 = 0.55$; estimated area under the receiver operating characteristic curve = 0.91 (95% confidence interval: 0.87–0.94); and Hosmer–Lemeshow goodness-of-fit Chi-squared test $p = 0.79$.
OHCA score: out-of-hospital cardiac arrest score.
CAHP score: cardiac arrest hospital prognosis score.
[a] The independent variables are arranged in order of ascending *p*-values. The bold-type indicates variables which were also components of the simplified OHCA or CAHP scores.
[b] ROSC, return of spontaneous circulation.
[c] CPR, cardiopulmonary resuscitation.

Table 3 – Performance of out-of-hospital cardiac arrest (OHCA) and cardiac arrest hospital prognosis (CAHP) scores as predictive variables for favourable neurological outcome at hospital discharge.

Variable	Odds ratio (95% confidence interval)	Area under the ROC[a] curve (95% confidence interval)
Simplified OHCA score	0.91 (0.89–0.93)	0.82 (0.77–0.86)
Simplified CAHP score	0.97 (0.96–0.98)	0.84 (0.80–0.89)

[a] ROC, receiver operating characteristic.

cohort. All of these variables were components of the sOHCA or sCAHP scores, and we therefore expected that these scores would also be predictive. Additionally, we found that early recovery of consciousness and malignancy were significantly associated with positive and negative outcomes, respectively, in our study, even after controlling for the influence of the sOHCA and sCAHP scores in the regression model. Similarly, Hirlekar et al.[11] found that metastatic carcinoma was inversely associated with 30-day survival for OHCA patients in a nationwide study in Sweden, and although this adverse relationship between malignancy and favourable neurologic outcomes has not been detected uniformly[12,13], Kang et al.[12] have also found an inverse relationship between 1-year survival and malignancy in a cohort of Korean OHCA patients. Patients with malignancy may be less likely to undergo TTM or coronary angiography.[12,13] As such, in our study, the inverse association between malignancy and favourable neurological outcomes may be confounded by the uncontrolled influence of these post-resuscitation procedures.

Regarding our finding that of a positive association between early recovery of consciousness after ROSC and a favourable neurological outcome at discharge, most trials investigating post-cardiac arrest care[14] have excluded patients who have early recovery of consciousness after ROSC, and the incidence and significance of this variable are not yet clear. In the original studies developing the OHCA[3] and CAHP[4] scores, the number of patients with early recovery of consciousness after ROSC was not reported, nor were these patients explicitly excluded from the analysis. Although clinicians might not consider neuroprognostication for this unique group of patients, our findings suggest that the sOHCA and sCAHP scores should be calculated in these cases, because 24% (8/33) of patients with early recovery of consciousness (Table 1) were discharged with poor neurological outcomes. Calculation of sOHCA and sCAHP scores after early recovery of consciousness is useful for risk-stratification and possibly to temper the expectations of family members.

Validation of the simplified OHCA and CAHP scores

An advantage of using OHCA or sOHCA and CAHP or sCAHP scores for early neuroprognostication after OHCA is that these risk scores are based on variables that are immediately available after admission to the ICU. The basic characteristics of the patients in our study, including age and sex, were similar to those of the patients in the original OHCA[3] and CAHP[4] cohorts. However, there was a marked difference in the rate of witnessed arrests between our study (74%) and the original CAHP-score study in France (91%).[4] The rate of witnessed arrests (81.1%) among patients with ROSC in a North American OHCA cohort was also higher than ours,[15] while rates of witnessed arrests in studies in other Asian countries have been close to or lower than ours. In Japanese[16] and Korean[17] registries, approximately 60% and 64% of arrests among resuscitated OHCA patients were witnessed.

It may quite difficult, if not impossible, for clinicians to estimate the time of collapse in an unwitnessed OHCA, and the updated Utstein template no longer requires recording this time[6]. Imprecision in estimating a no-flow interval after unwitnessed OHCA might actually undermine the prognostic consistency of calculated OHCA or CAHP scores. The rate of witnessed arrests was approximately 76.9% when Choi et al.[18] validated OHCA scores in a Korean cohort of 173 OHCA survivors after TTM, and the accuracy of the score in these circumstances was only fair (AUC: 0.764). On the other hand, when OHCA scores were validated in U.S.[19] and Swiss cohorts [20] with rates of witnessed arrest of 73% and 82.8%, the AUC values were better (0.85, and 0.80, respectively). When we removed the no-flow intervals from our calculations, the AUC values for the sOHCA and sCAHP scores improved to 0.82 and 0.84, and were comparable to the previously-validated OHCA and CAHP scores in the U.S.[19] and Swiss cohorts.[20] Because in East Asian countries, about 30–40% of resuscitated OHCA patients experienced unwitnessed collapse,[16,17] sOHCA and sCAHP scores may be more applicable in these areas by removing "no-flow interval, an imprecise estimate, from the calculation.

Application of sOHCA and sCAHP scores in East Asia

Many registries have been developed and implemented to measure and improve the process and outcomes of care for OHCA patients. Besides the well-known OHCA registries in the US, such as CARES and ROC,[21] numerous OHCA registries are evolving, including PAROS in Asia[2] and EuReCa in Europe.[22] By analysing big data collected in registries, researchers can provide feedback to healthcare providers to reflect on their performance to encourage change in their behaviour or in the system. However, because of the diverse baseline characteristics across different regions, it would be difficult to attribute the outcome differences into care process when different systems were compared. With validated risk-adjustment tools, such as the original or simplified OHCA and CAHP scores, researchers could compare outcomes between different registries on a fair basis and gain insight into unmet needs, which could assist in developing strategies in improving system performance.

Besides the epidemiological application, sOHCA and sCAHP scores might also be used in early neuroprognostication for OHCA patients, which may be of particular importance in East Asia. During early post-resuscitation period, most patients are still intubated and sedated, and their treatment decisions rely on the discussion between their families and clinicians. There is a strong emphasis on filial piety and family-centred end-of-life care in East Asian society,[23] and families may wish to take all available measures to treat their loved ones, even when the predicted outcome is bleak. A survey of physicians in Asian ICUs found that most, but not all (69.7%), would withhold CPR for patients with no real chance of recovering a meaningful life.[24] As the focus of care shifts to personalised medicine, the ability to provide timely and objective probabilities of neurologically intact survival following OHCA may be of great help in managing the expectations of families and making critical decisions, such as whether or not to withhold repeated resuscitation attempts.

However, it should be emphasized that when assessing individual patient risk, the discriminatory performance of sOHCA or sCAHP score is not yet sufficiently robust and should not be used for major decisions such as WLST, although in most Asian countries WLST is not permitted by law.[24] Formal individual neuroprognostication should still be performed according to the recommended guidelines,[25] which suggested that the false positive rate of the neuroprognostication should ideally be nearly 0% for unfavourable neurological outcomes. As suggested by the original developers of the OHCA[3] and CAHP[4] scores, the risk scoring system should better be applied in the context of an OHCA population.

Study limitations

This study was observational in design. Therefore, we could only establish associations rather than causal relationships between the independent variables and the outcomes. Also, even though we used multivariate analysis to account for the influence of existing confounding factors, unmeasured confounding factors may still bias the association between sOHCA of sCAHP score and outcomes. Although the sOHCA and sCAHP scores were not used in clinical practice to determine the treatment strategy, the components of both scores, such as age, shockable rhythm, and certain laboratory test results, are well known to be associated with patient outcomes and may still influence clinical decision-making. Nevertheless, in Taiwan, WLST was not legal until 2015, which may reduce the possible bias of self-fulfilling prophecy.

Conclusions

Patients in East Asia societies shared most of the common post-OHCA prognosticators with those in Western countries. The simplified OHCA and CAHP scores predicted neurological outcomes with excellent accuracy among successfully resuscitated OHCA patients in an East Asian population, and the discriminatory performance did not differ between these two scores. Either original or simplified OHCA and CAHP scores may serve as risk-adjustment tools to compare outcomes among regional OHCA registries worldwide.

Conflicts of interests

The authors declare that they have no conflict of interest.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.resuscitation.2019.02.015.

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