

A Comparison of the Performance of Out-of-hospital Cardiac Arrest Score and Standard Severity Scores in Predicting Hospital Mortality and Neurological Consequence in Out-of-hospital Cardiac Arrest Patients

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Abstract:

Objective: There is limited data to determine the performance of general and specific severity score in out-of-hospital cardiac arrest (OHCA) patients. Hence, we compared the performance of the OHCA score with Acute Physiology and Chronic Health Evaluation (APACHE) and Simplified Acute Physiology Score (SAPS) to predict outcome in OHCA patients.

Material and Methods: A retrospective study was conducted in a mixed intensive care unit of a tertiary hospital. The primary outcome was in-hospital mortality. The secondary outcome was poor neurological outcome.

Results: A total of 190 OHCA patients were enrolled. The OHCA score had moderate discrimination with an area under the receiver operating characteristic curve (AUC) 0.77 (95% CI 0.7–0.837) whereas discrimination of APACHE II–IV, SAPS II, and SAPS 3 were good with an AUC more than 0.8. The actual hospital mortality rate was 64.7%. The OHCA score predicted hospital mortality of 95.3 ± 8.4 , which significantly overestimated the mortality with standardized mortality ratio 0.68 (95% CI 0.56–0.81). However, all severity scores revealed poor calibration. Additionally, overall performance of APACHE II–IV, SAPS II and SAPS 3 were better than the OHCA score. For secondary outcome, discrimination of the OHCA score was moderate with an AUC 0.790 (95% CI 0.700–0.878) whereas other severity scores demonstrated good discrimination with AUC more than 0.8.

Conclusion: APACHE II–IV, SAPS II, and SAPS 3 indicated superior overall performance and demonstrated good discrimination for predicting hospital mortality and unfavorable neurological consequence better than the OHCA score. However, all severity scores attested poor calibration, therefore, specific scores for OHCA patients should be modified.

Keywords: APACHE, SAPS, outcome, risk prediction

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Introduction

Out-of-hospital cardiac arrest (OHCA) is a major global medical problem. The overall prognosis of OHCA varies among studies, with a low median survival rate of 2.0–20.0%.^{1–4} The survival improvement is considerable as well as the neurological outcome with less than 10.0% able to return their previous status.^{5–7} The prediction of neurological consequence in the survivor after cardiac arrest is extremely crucial for counselling patients' families, reducing unnecessary costs and facilitating organ donation. The discipline of intensive care medicine is particularly concerned with mortality prediction. Severity scoring system is a crucial tool for patients admitted in the intensive care unit (ICU) in order to predict hospital mortality, characterize disease severity, and compare ICU quality between time and unit performance.^{8–13} The non-disease specific severity scores including the Acute Physiology and Chronic Health Evaluation (APACHE) and Simplified Acute Physiology Score (SAPS) are two models currently in common use for accessing severity of ICU patients.^{9,13–16} Those were designed for general patients, not specific for post cardiac arrest populations. Therefore, the OHCA score was derived. The OHCA score needs only five parameters comprising estimated no-flow and low-flow intervals, initial rhythm, serum creatinine level and blood lactate, whereas APACHE and SAPS need many variables for calculation. A previous study found that the OHCA score demonstrated good discrimination and calibration for hospital mortality prediction.¹⁷

Although severity could be evaluated by either general or specific scoring system, the applications of these measurements (APACHE, SAPS, the OHCA score) depend on the clinical conditions of patients and different settings of management, and few studies have determined their performance for prognosticating in-hospital mortality and neurological consequence in patients with OHCA. Therefore, the object of this study was to verify the performance

between the OHCA score versus APACHE II–IV^{18–21}, SAPS II²², and SAPS 3²³, in patients with OHCA and return of spontaneous circulation (ROSC).

Material and Methods

A retrospective analysis of data all adult OHCA patients admitted in the mixed ICUs of a referral medical center in Southern Thailand was conducted. The study was approved by our institutional ethics committee (REC. 62–301–14–1).

Consecutive critically ill adult patients (>18 years) were diagnosed OHCA with ROSC admitted to our ICUs from January 2011 to September 2019 and enrolled. Cardiac arrest is defined as the absence of palpable pulse with the absence of spontaneous breathing. ROSC was defined as recovery of blood pressure and pulse for more than one hour, with or without administration of vasopressor or inotropic agents.¹⁷ Patients who did not have serum lactate level within twenty-four hours after admission were excluded because it is one of the parameters for calculating the OHCA score. Besides, patients whose cause of cardiac arrest was due to trauma were excluded.

The outcomes were survival status on hospital discharge and Cerebral Performance Category (CPC) of the Glasgow–Pittsburgh Outcome Categories. All parameters required by APACHE, SAPS and OHCA scores as determined in the original articles were collected for analysis. The physiological variables in APACHE II–IV^{18–21} and SAPS II²² were calculated based on the worst values within the first 24 hour after ICU admission, in contrast to the physiological data of SAPS 3²³, which were based on the worst values before or after the first hour of ICU admission. The biochemical variables for OHCA score were obtained at ICU admission in patients who return to spontaneous circulation, before the further interventions were performed. The primary outcome was hospital mortality. Poor neurological consequence assessed by

using CPC was the secondary outcome. Poor neurological outcome was identified by CPC score of 3 to 5.^{6,24,25}

To estimate the sample size, we assumed the performance of the OHCA score may not differ more than 15.0% when compared to other non-disease specific scores such as APACHE and SAPS. Based on the original study, the area under the receiver operating characteristic curve (AUC) of the OHCA score was 0.88.¹⁷ This study needed 135 patients to achieve 80.0% power and 5.0% type I error.

Continuous variables were presented as means with standard deviations or median with interquartile range, and categorical variables were reported as numbers and percentages. Chi-square and Wilcoxon rank sum test were used to compare category variables and continuous variables, respectively. The performance of the severity scores was appraised by discrimination, calibration, and overall performance. The discrimination refers to the ability of the score to discriminate between survivors and non-survivors. This index was evaluated by using the AUC.¹⁵ An AUC greater than 0.8 indicates good discrimination, while 0.7–0.8 indicates moderate discrimination, and 0.5–0.7 indicates low discrimination.²⁶ Calibration evaluates the rank of agreement between expected probabilities of mortality and actual mortality across all of the strata of probabilities of death. Calibration was examined by the Hosmer–Lemeshow (H–L) goodness-of-fit H and C statistics, and standardized mortality ratio (SMR).^{10,15} Patients were rank-ordered in five groups according to their probability of death to calculate the H statistic. To evaluate the C-statistic, the patients were divided into quintiles of predicted risk, $p\text{-value} > 0.100$ indicated goodness-of-fit.¹⁷ The SMR is a ratio that is calculated by dividing the observed number of non-survivors in the study group and the number of non-survivors which would be anticipated from severity score. Therefore, $\text{SMR} > 1$ is an underestimation, whereas $\text{SMR} < 1$ is an overestimation of the mortality by the severity scoring system prediction. The Brier score refers overall performance including both

discrimination and calibration.¹⁰ The lower Brier score is shown, the higher accuracy of severity score is represented. All statistical analysis was performed using Stata version 11.

Results

There were 271 OHCA with ROSC patients admitted in ICU during the study period. After applying the exclusion criteria, 81 patients were excluded because of lack of serum lactate level ($n=47$) and traumatic patients ($n=34$). Overall, 190 patients were included for analysis.

There was some difference in the baseline characteristics of the patients between survivors and non-survivors in terms of age, assumed arrest due to cardiac cause, revascularization in myocardial infarction, duration of no flow time, shockable rhythm and serum lactate (Table 1).

A total of 190 patients were analyzed, survivors were 67 cases and non-survivors were 123 cases. The quantity of male gender was higher than female gender in both groups. The majority situation of cardiac arrest occurred at home (65.8%). Myocardial infarction was the most common cause of arrest in survivors (40.3%), whereas it was the second most common cause in non-survivors (27.6%), and hypoxic arrest was the main cause in non-survivors (30.0%). The proportion of myocardial infarction patients which received revascularization was 19/27 (70.4%) in survivors and 9/34 (26.5%) in non-survivors. Therapeutic hypothermia was provided in 20 cases of survivors (29.9%) and 28 cases (22.8%) in non-survivors. The percentage of VA ECMO was equipped 3 and 3.3 in survivors and non-survivors, correspondingly.

Hospital mortality rate as sorted by the OHCA score are shown in Figure 1. The mortality rate substantially increased in patients with higher scores. The OHCA score of 31–50 had percentage of mortality rate at fifty-four. Furthermore, the OHCA score of 51–60 had a mortality rate of 76.5%, rising to 91.0% in cases of OHCA score more

than 60. Discrimination of the OHCA score was moderate with the AUC 0.77 (95% CI 0.7–0.837). On the contrary, the non-disease specific severity scores such as APACHE II–IV, SAPS II and SAPS 3 had good discrimination with the AUC more than 0.8 (Figure 2).

Table 1 Clinical demographic data

Parameters	All patients (n=190)	Survivors (n=67)	Non-survivors (n=123)	p-value
Age, years (IQR)	60 (47.0–77.0)	58 (43.0–68.0)	62 (52.0–75.0)	0.030
Male [n (%)]	122 (64.2)	42 (62.7)	80 (65.0)	0.750
Witness arrest [n (%)]	170 (89.5)	64 (95.5)	106 (86.2)	0.050
Place of event [n (%)]				
Home	125 (65.8)	37 (55.2)	88 (71.5)	0.023
Public	51 (26.8)	24 (35.8)	27 (22.0)	0.039
During transfer with personnel	14 (7.4)	6 (9.0)	8 (6.5)	0.537
Bystander [n (%)]	52 (27.4)	21 (31.3)	31 (25.2)	0.360
Assume cardiac cause [n (%)]	85 (44.7)	40 (59.7)	45 (36.6)	0.002
Cause [n (%)]				
Myocardial Infarction	61 (32.1)	27 (40.3)	34 (27.6)	0.074
Hypoxic	52 (27.4)	15 (22.4)	37 (30.0)	0.256
Arrhythmia	17 (8.9)	10 (14.9)	7 (5.7)	0.033
Sepsis	16 (8.4)	1 (1.5)	15 (12.2)	0.011
Other*	38 (20.0)	14 (20.9)	24 (19.5)	0.820
Unknown	6 (3.2)	0 (0.0)	6 (5.0)	0.066
Adrenaline dose before ROSC, mg (IQR)	3 (2.0–7.0)	3 (2.0–9.0)	3 (3.0–7.0)	0.210
Therapeutic temperature management [n (%)]	48 (25.3)	20 (29.9)	28 (22.8)	0.280
Myocardial infarction with revascularization [n (%)]	28 (45.9)	19 (70.4)	9 (26.5)	<0.001
VA ECMO [n (%)]	6 (3.2)	2 (3.0)	4 (3.3)	0.920
ICU LOS, days (IQR)	3 (2.0–7.0)	6 (3.0–10.0)	3 (1.0–6.0)	<0.001
Hospital LOS, days (IQR)	8 (3.0–19.0)	20 (10.0–35.0)	4 (1.0–9.0)	<0.001
Serum Cr, mmol/L (IQR)	1.4 (1.0–2.2)	1.3 (1.0–1.6)	1.5 (1.1–2.4)	0.004
No-flow interval, min (IQR)	10 (5.0–15.0)	8 (2.0–10.0)	10 (5.0–15.0)	0.020
Low-flow interval, min (IQR)	18 (9.0–31.0)	16 (6.0–29.0)	18 (11.0–33.0)	0.050
Shockable rhythm [n (%)]	49 (25.8)	27 (40.3)	22 (17.9)	0.001
Serum lactate, mmol/L (IQR)	7.75 (4.4–11.4)	4.6 (3–8)	9.2 (6.4–12.4)	<0.001
OHCA score (IQR)	50.4 (41.2–59.4)	43.2 (30.5–50.0)	55.6 (46.4–62.7)	<0.001
APACHE II score	34 (26.0–39.0)	26 (19.0–30.0)	38 (32.0–41.0)	<0.001
APACHE III score	106 (74.0–125.0)	63 (48.0–86.0)	118 (102.0–133.0)	<0.001
SAPS II score	60 (49.0–71.0)	44 (36.0–55.0)	67 (58.0–76.0)	<0.001
SAPS 3 score	77 (63.0–87.0)	59 (55.0–69.0)	83 (75.0–89.0)	<0.001

IQR=interquartile range, *Other: cardiomyopathy, pulmonary embolism, electrical injury, hypovolemia, metabolic disturbance, cardiac tamponade, ROSC=return of spontaneous circulation, VA ECMO=veno-arterial extracorporeal membrane oxygenator, ICU LOS=intensive care unit length of stay, Cr=creatinine, mmol/L=millimoles per liter, OHCA=out-of-hospital cardiac arrest, APACHE=Acute Physiology and Chronic Health Evaluation, SAPS=Simplified Acute Physiology Score

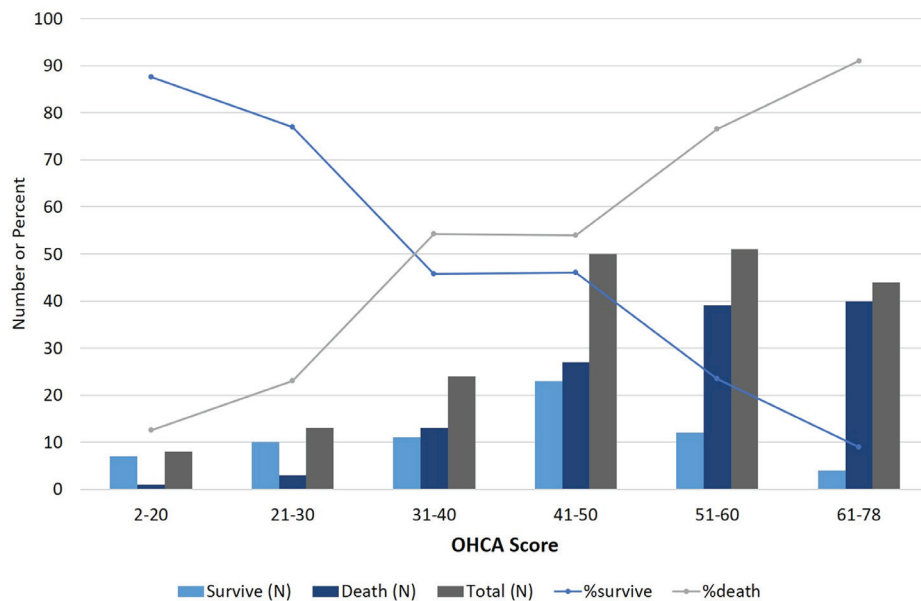
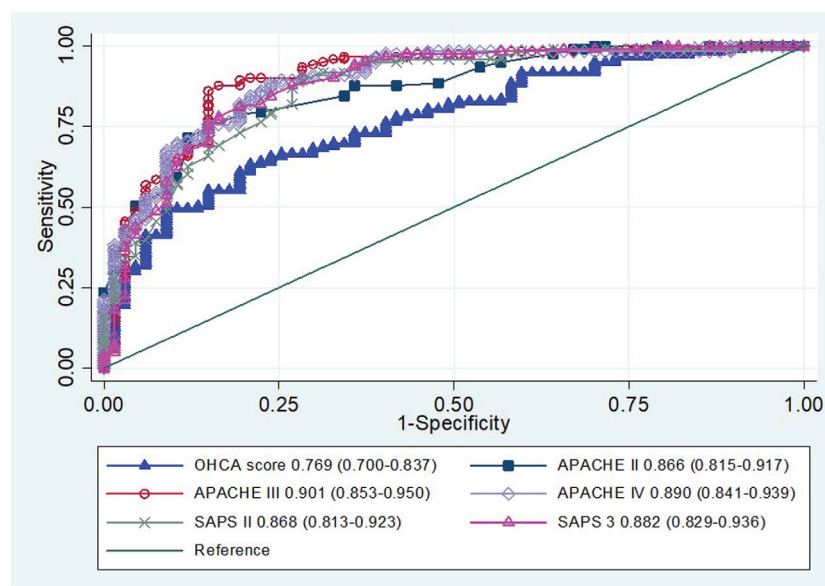


Figure 1 Hospital mortality rate arranged by the out-of-hospital cardiac arrest score



APACHE=Acute Physiology and Chronic Health Evaluation, SAPS=Simplified Acute Physiology Score, OHCA=out-of-hospital cardiac arrest

Figure 2 Comparison of the area under the receiver operating characteristic curves of the out-of-hospital cardiac arrest score with other severity scores for hospital mortality prediction in out-of-hospital cardiac arrest with return of spontaneous circulation patients admitted in intensive care unit.

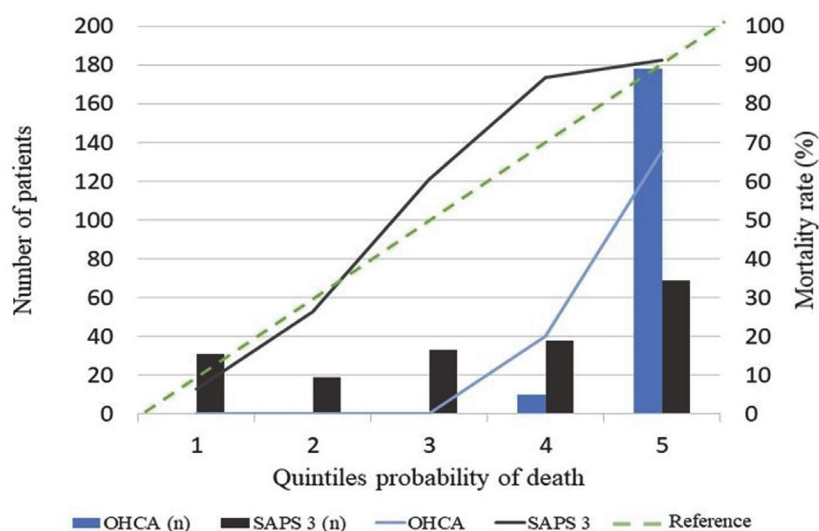
The actual hospital mortality rate was 64.7%. The OHCA score predicted hospital mortality of 95.3 ± 8.4 , which significantly overestimated the mortality with SMR 0.68 (95% CI 0.56–0.81). Meanwhile, the non-disease specific severity scores; APACHE II overestimated hospital mortality with SMR 0.83 (95% CI 0.69–0.99), in contrast, APACHE

IV underestimated hospital mortality with SMR 1.29 (1.07–1.54). The others (APACHE III, SAPS II and SAPS 3) presented good mortality prediction with 95% CI of SMR between 1. The calibration of the OHCA score and other non-disease specific severity scores were poor due to the H-L goodness-of-fit test <0.1 (Table 2 and Figure 3).

Table 2 The performance of Out-of-Hospital Cardiac Arrest score, Acute Physiology and Chronic Health Evaluation II, III, IV, Simplified Acute Physiology Score II, and Simplified Acute Physiology Score

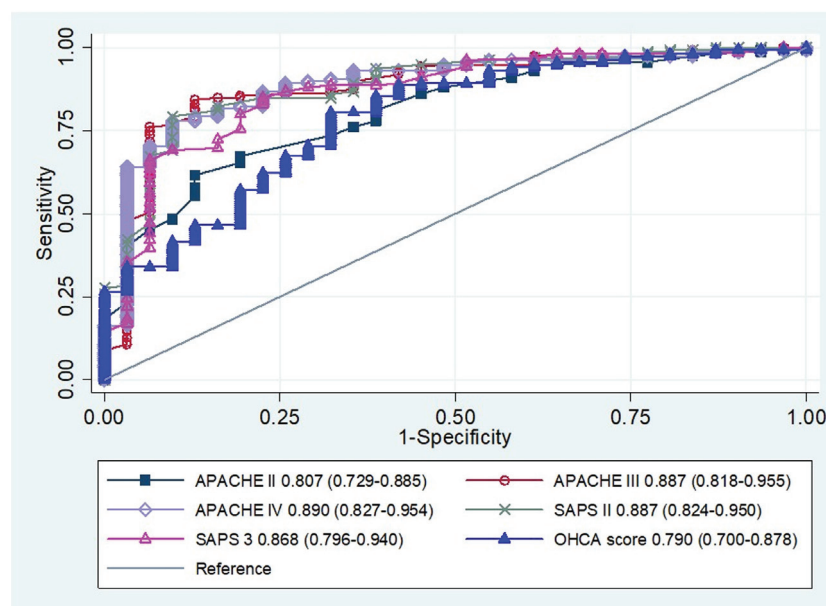
	AUC (95% CI)	SMR (95% CI)	H Chi-2, p-value	C Chi-2, p-value	Brier score
OHCA score	0.769 (0.700–0.837)	0.68 (0.56–0.81)	550.18, <0.001	692.80, <0.001	0.299
APACHE II	0.866 (0.815–0.917)	0.83 (0.69–0.99)	28.70, <0.001	42.40, <0.001	0.170
APACHE III	0.901 (0.853–0.950)	0.93 (0.77–1.11)	7.46, 0.190	19.95, 0.001	0.144
APACHE IV	0.890 (0.841–0.939)	1.29 (1.07–1.54)	29.87, <0.001	29.85, <0.001	0.153
SAPS II	0.868 (0.813–0.923)	1.04 (0.87–1.24)	4.95, 0.420	15.60, 0.008	0.136
SAPS 3	0.882 (0.829–0.936)	1.08 (0.90–1.29)	6.93, 0.220	14.75, 0.010	0.127

APACHE=Acute Physiology and Chronic Health Evaluation, AUC=area under the receiver operating characteristic, C=Hosmer–Lemeshow goodness-of-fit C test, CI=confidence interval, H=Hosmer–Lemeshow goodness-of-fit H test, OHCA score=Out-of-Hospital Cardiac Arrest score, SAPS=Simplified Acute Physiology Score, SMR=standardized mortality ratio



OHCA=out-of-hospital cardiac arrest, SAPS 3=Simplified Acute Physiology Score 3

Figure 3 Calibration curve for the out-of-hospital cardiac arrest score and Simplified Acute Physiology Score 3.



APACHE=Acute Physiology and Chronic Health Evaluation, SAPS=Simplified Acute Physiology Score, OHCA=out-of-hospital cardiac arrest

Figure 4 Comparison of the area under the receiver operating characteristic curves of the out-of-hospital cardiac arrest score with other severity scores for unfavorable neurological outcome in out-of-hospital cardiac arrest with return of spontaneous circulation patients admitted in intensive care unit.

Overall performance was evaluated by Brier scores, representing that OHCA score was objectionable, with the highest Brier score being 0.299. Meanwhile, SAPS 3 revealed the best overall performance with a Brier score of 0.127. The remaining ranking of overall performance was SAPS II, APACHE III, APACHE IV, APACHE II with Brier scores of 0.136, 0.144, 0.153, 0.170, respectively.

We obtained a secondary outcome to predict unfavorable neurological consequence categorized by CPC, the OHCA score had moderate discrimination to predict poor neurological consequence with the AUC 0.790 (95% CI 0.700–0.878). Other non-disease specific severity scores had good discrimination with the AUC more than 0.8, APACHE IV had the best discrimination with the AUC 0.890 (95% CI 0.827–0.954) (Figure 4).

Discussion

Our study found the OHCA score had moderate discrimination for predicting hospital mortality in case of OHCA with ROSC admitted to ICU. The OHCA score was originated by Adrie et al., they reported AUCs of 0.82 in the development cohort and 0.88 in the validation cohort and showed well calibration by the goodness-of-fit test.¹⁷ Our results of the OHCA score were different compared to the original OHCA research that may be due to time difference in terms of no flow and low flow intervals. The original study revealed that the mean of no-flow interval was 3 and 8 minutes, and mean of low-flow interval was 7.5 and 15 minutes in good and poor outcome groups, respectively. In contrast, our study showed that the mean of no-flow interval was 8 and 10 minutes, and mean of

low-flow interval was 16 and 18 minutes in survivors and non-survivors, consecutively. It was clearly seen that the population in our study experienced more prolonged resuscitation duration than the original study population. However, the hospital mortality in the present study was lower, which may be due to the improvement of knowledge and physicians' experience in each time period and the CPR guideline which was launched in a different time period. The CPR guideline is always updated every five years. In the original study, the data was collected from 1999 to 2003 while, the data in our study was collected from 2011 to 2019. Moreover, the population in this study may be less severe than in the original study because of lower severity score SAPS II.

Furthermore, in our study, APACHE II-IV, SAPS II and SAPS 3 had good discrimination. APACHE III had the best discrimination for predicting hospital mortality and SAPS 3 had the best overall performance. For secondary outcome, all non-disease specific severity scores had good discrimination. The reason why the OHCA score had lower discrimination for predicting mortality and poor neurological outcome than the other non-disease specific severity scores was the diversity in categorical variables. The OHCA score had only five variables with shockable rhythm, no flow time, low flow time, serum creatinine and lactate level. Meanwhile, the other non-disease specific severity scores had more variables comprise of several physiological parameters such as vital signs, severity of organ dysfunction, age, and co-morbid diseases.

The AUC of the OHCA in the present study had moderate discrimination to predict hospital mortality, which was similar to two previous studies. In the studies by Skrifvars et al.²⁷ and Choi et al.²⁸, the AUC of the OHCA score showed the AUC 0.77 and 0.74, respectively. Skrifvars et al. investigated the survival and outcome using the APACHE III and the OHCA score in patients treated

in the ICU following out-of-hospital, in-hospital or ICU cardiac arrest²⁷. Choi et al. investigated the performance on the APACHE II, SAPS II, SOFA and the OHCA score of post-cardiac arrest patients treated with therapeutic hypothermia²⁸. However, the APACHE III in our study was better than the OHCA in discrimination, calibration and overall performance in contrast to the result by Skrifvars et al., in which the AUC of the OHCA was slightly better than the APACHE III. The reason may be caused by the different of study population, as Skrifvars et al. enrolled out-of-hospital, in-hospital and ICU cardiac arrest patients, whereas the present study included only OHCA patients following the original article developed for OHCA population. OHCA patients had several different factors compared to in-hospital or ICU cardiac arrest patients such as facilities, medical personal, and time detection to cardiac arrest. Furthermore, the APACHE II-IV, SAPS II and SAPS 3 in our study had good discrimination in both aspects of predicting mortality and unfavorable neurological consequence that were different to the previous study by Choi et al., which found that APACHE II and SAPS II revealed moderate discrimination for predicting mortality in post cardiac arrest patients treated with therapeutic hypothermia.²⁸ The APACHE II and SAPS II were originated based on the worst values within the first 24 hours after ICU admission, but in the previous study by Choi et al.²⁸, the APACHE II and SAPS II were calculated at the time of admission (0 hour), 24 and 48 hours from the admission time.

Our study suggested that SAPS 3 should be used for OHCA patients because of the best overall performance, good discrimination to predict hospital mortality and poor neurological outcome. In addition, this score was accessed simply by search engine and the variables were less sophisticated than APACHE III, despite the best discrimination to predict hospital mortality of APACHE III. In addition, the performance of the OHCA score may be

ameliorated by secondary customization applying new variable parameters such as vital signs, age, preexisting comorbidities and new physiological variables.

The strength of the present study was, so far as we know, this is the first study that investigated all versions of broad commonly used severity scores such as APACHE II, III, IV, SAPS II and SAPS 3, for the general intensive care population compared to disease specific OHCA score. Secondly, the present study is the first attempt to examine not only discrimination but also calibration and overall performance of each severity score. Furthermore, this study endeavored to examine entire patients with and without target temperature management.

There were some limitations of this study. Firstly, this was a retrospective study and may have risk of bias to verify outcome. Secondly, the calibration examined by H-L goodness-of-fit test, this test may be underpowered especially when fewer than six groups are formed.²⁹ Thirdly, usual knowledge during a different time period may be effect ICU standard care, the latest CPR guideline was modified and launched in 2015, meanwhile our study enrolled the population from January 2011 to September 2019.

Conclusion

All non-disease specific severity scores indicated superior overall performance and demonstrated good discrimination for predicting hospital mortality and unfavorable neurological consequence better than the OHCA score. SAPS 3 indicated the best overall performance. However, all scores revealed poor calibration. Therefore, specific scores for OHCA patients should be modified for predicting mortality and neurological consequence in patients.

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Conflict of interest

There are no potential conflicts of interest to declare.

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