Resuscitation

Original Article
External Validation of a Risk Classification at the Emergency Department of Post-cardiac Arrest Syndrome Patients Undergoing Targeted Temperature Management

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Abstract

Introduction: There are no established risk classification for post-cardiac arrest syndrome (PCAS) patients at the Emergency Department (ED) undergoing targeted temperature management (TTM). The aim of this study was to externally validate a simplified version of our prognostic score, the "post-Cardiac Arrest Syndrome for Therapeutic hypothermia score" (revised CAST [rCAST]) and estimate the predictive accuracy of the risk classification based on it.

Methods: For the external validation, we used data from an out-of-hospital cardiac arrest (OHCA) registry of the Japanese Association for Acute Medicine (JAAM), which is a multicenter, prospective registry of OHCA patients across Japan. Eligible patients were PCAS patients treated with TTM at 33ºC-36ºC between June 2014 and December 2015. We validated the accuracy of rCAST for predicting the neurological outcomes at 30 and 90 days.

Results: Among the 12,024 OHCA patients, the data of 460 PCAS patients treated by TTM were eligible for the validation. The areas under the curve of rCAST for predicting the neurological outcomes at 30 and 90 days were 0.892 and 0.895, respectively. The estimated sensitivity and specificity of the risk categories for the outcomes were as follows: 0.95 (95% CI: 0.92-0.98) and 0.47 (0.40-0.55) for the low (rCAST: ≤5.5), 0.62 (0.56-0.68) and 0.48 (0.40-0.55) for the moderate (rCAST: 6.0-14.0), and 0.57 (0.51-0.63) and 0.95

(0.91-0.98) for the high severity category (rCAST: ≥14.5).

Conclusions: The rCAST was useful for predicting the neurological outcomes with high accuracy in PCAS patients, and the three grades was developed for a risk classification based on the rCAST.

Keywords: post-cardiac arrest syndrome; neurological prognosis; therapeutic hypothermia; therapeutic normothermia; risk classification; rCAST; CAST

Introduction

Post-cardiac arrest syndrome (PCAS) patients represent a heterogeneous population, because the severity of PCAS is influenced by a variety of factors, including the cause of the cardiac arrest, differences in the down-time period until the return of spontaneous circulation (ROSC), and the quality of chest compressions. Risk classification of these patients at the Emergency Department (ED) may not only help in performing statistical comparisons in epidemiological studies, but also help in decision-making as to the appropriate management strategy for these patients. For example, the outcomes of PCAS patients classified into the “very severe” category at the ED could be potentially improved by very early and aggressive treatment after admission to the ICU.

There are a few reports of prognostic scoring systems for PCAS patients at the ED [1-3], however, all of these studies included PCAS patients regardless of whether they had undergone targeted temperature management (TTM) or not. Interestingly, a previous study showed that the predictive accuracy of these prognostic scoring systems was not as high when they were applied to the subgroup of PCAS patients who had undergone TTM [4]. At present, TTM is often undertaken for PCAS patients, according to guidelines, in an attempt to obtain good recovery of these patients [5-7], and it is important to create a

risk classification system specifically designed for PCAS patients undergoing TTM, not for all PCAS patients.

Previously, we developed the “post-Cardiac Arrest Syndrome for Therapeutic hypothermia score (CAST)” for predicting the 30-day neurologic outcome of PCAS patients at the ED, prior to the initiation of TTM [8, 9]. It was unique, in that it was created focusing on PCAS patients undergoing TTM, as well as was calculated at the ED prior to the initiation of TTM. It enabled estimation of the probability of a good neurological outcome at 30 days with high accuracy, suggesting that it would also be useful to devise a severity classification for PCAS patients undergoing TTM. However, some of the variables used for calculation of CAST were not entirely suitable for practical clinical use as items for risk classification, because they could not be easily obtained before the initiation of TTM, and the formula for calculation of the score was also rather complex (see Supplemental Fig. 1). To devise a classification system that would be practically useful, we simplified the model for calculation of the score, and developed the revised CAST (rCAST). The aim of this study was to develop a risk classification at the ED for PCAS patients undergoing TTM, by validating the predictive accuracy of rCAST for predicting poor neurological outcomes at 30 and 90 days.

Methods

Study Design

This study was an observational study conducted using data from an out-of-hospital cardiac arrest (OHCA) registry of the Japanese Association for Acute Medicine (JAAM), which is a multicenter, prospective registry of OHCA patients who are transported to critical care medical centers or hospitals with an emergency care department across Japan (a total of 73 institutions). The design and data collection methods for the JAAM-OHCA registry have been described in detail in previous reports [10]. In summary, emergency medical service (EMS) personnel collect pre-hospital data based on the Utstein-style template [11], and physicians at the participating institutions collect in-hospital data, including on the presumed etiology of the OHCA, and the patients' treatments and outcomes. Between June 2014 and December 2015, this registry included the data of 12,024 OHCA patients. This study was conducted with the approval of the Institutional Review Boards of all the participant institutions, which waived the requirement for obtention of informed patient consent to ensure participant anonymity, stipulated in the Japanese government guidelines.

Subjects

Adult patients with non-traumatic cardiac arrest who underwent TTM at 33ºC-36ºC were included in this study. Patients were excluded if they were less than 18 years old, underwent TTM at ≤32ºC (moderate therapeutic hypothermia), or required extracorporeal membrane oxygenation (ECMO), because of the hemodynamic instability. Patients with any missing values of the variables needed for the calculation of rCAST and/or for adjustments in the analyses were also excluded (complete case analyses).

Targeted Temperature Management

TTM is considered for cardiac arrest patients who are in coma (Glasgow Coma Scale (GCS) ≤ 8) after ROSC, according to the recommendation of the Japanese resuscitation guideline [6]. We defined mild therapeutic hypothermia as TTM at 33ºC-34ºC, and normothermia treatment as TTM at 35ºC-36ºC. The protocol for TTM adopted for the patients included in this study, including the setting core temperature, depended on the protocol followed at each participating hospital, but in most patients (93.8%, 348/371), it was maintained for 12-72 h, unless it had to be interrupted because of complications such as hemodynamic instability. Rewarming was performed gradually over a period of at least 24-72 h. The devices/methods used for the TTM in the subjects included surface cooling devices in 90.4% (416/460) of patients, cold saline infusion in 43.3% (199/460) of patients, gastric lavage in 16.7% (77/460) of patients, and blood

cooling devices in 7.6% (35/460) of patients; the method used was unknown in 0.7% (3/460) of patients.

Outcome Measurement

We set Cerebral Performance Categories (CPC) at 30 days as the primary outcome: CPC 1, full recovery; CPC 2, moderate disability; CPC 3, severe disability; CPC 4, coma or vegetative state; CPC 5, death. Categories 1-2 were considered as representing a good outcome, and categories 3-5 as representing a poor outcome [12]. As a secondary outcome, we also evaluated the CPC at 90 days, and the mortality rates at 30 and 90 days.

Definition of rCAST

In the study protocol, we used rCAST, a simplified version of the original CAST previously developed by us, taking account usage of the component factors in clinical practice [8, 9]. The calculation of the CAST score is summarized in Supplemental Fig. 1. In the process of creation of rCAST, we deleted several variables (serum albumin, serum hemoglobin, and the gray matter:white matter ratio on cranial CT) included in the original CAST. Also, the coefficients for the calculation of rCAST were created by simplifying the weights used for the original CAST (Fig.1).

Statistical Analysis

In this study, we validated the predictive accuracy of rCAST by plotting the receiver-operating characteristic (ROC) curve and evaluating the area under the ROC curve (AUC). High accuracy was defined as an AUC of more than 0.9, moderate accuracy as an AUC of less than 0.9 but greater than 0.7, and low accuracy as an AUC of less than 0.7 [13]. While we included the data of 460 PCAS patients for analysis of the neurological outcome at 30 days, data of only 366 patients were included for analysis of the neurological outcome at 90 days, because the outcome at 90 days of the remaining 94 patients were not available. For developing the classification comprising three severity grades based on the rCAST (low severity, moderate severity, and high severity), the cutoff points were defined as the score points yielding 95% sensitivity and 95% specificity, for which we referred to some previous studies [14, 15]. Here, specificity refers to the proportion of patients with poor outcomes who were correctly identified. We performed complete case analyses in this study. All the reported P values are two-sided, and $P < 0.05$ was regarded as denoting a statistically significant difference. All analyses were conducted using R, version 3.5.1, and SAS, version 9.4 (SAS Institute, Cary, NC).

Results

In a preliminary study conducted prior to this study, we confirmed that the predictive accuracy of rCAST was as high as that of the original CAST using the data of the 151 PCAS patients whose data we had used to develop CAST in our previous study (Supplemental Fig. 2) [9]. In this study, a total of 12,024 cardiac arrest patients were registered in the JAAM-OHCA registry between June 2014 and December 2015, and 758 of these PCAS patients underwent TTM after ROSC. Among these, 298 patients were excluded from this study, because they were pediatric patients aged under 18 years old (n = 16), had traumatic cardiac arrest (n = 6), underwent TTM at ≤32ºC (moderate therapeutic hypothermia; n = 4), needed ECMO (n = 207), or had missing values of variables needed for the analysis in this study (n = 65). Data of the remaining 460 PCAS patients were analyzed (Fig. 2).

The baseline characteristics of the eligible patients included in this study are summarized in Table 1. The distribution of the score points of rCAST in all patients are summarized in Supplemental Fig. 3. Using these data, we plotted the ROC curve of rCAST for predicting a poor neurological outcome at 30 and 90 days, and the mortality at 30 and 90 days; the analysis revealed values of the AUCs of 0.892, 0.895, 0.832 and 0.827, respectively (Fig. 3).

After confirming the predictive accuracies of the rCAST scores for the outcomes, we developed

the risk classification system based on the rCAST. Because they were cutoff values indicating 95% sensitivity and 95% specificity, the score points of 6 and 14.5, respectively, were set as the thresholds for classifying the subjects into three severity groups based on the rCAST; low severity category (rCAST ≤ 5.5), moderate severity category (rCAST, 6-14), and high severity category (rCAST ≥ 14.5) (Fig. 4). All predictive accuracies of rCAST for neurological outcome at 30 days in each cutoff point were also shown in Supplemental Table.1. Among the 460 subjects, 96, 192 and 172 patients were classified into the low severity, moderate severity and high severity categories, respectively. The estimated sensitivity and specificity were 0.95 (95% CI: 0.92-0.98) and 0.47 (0.40-0.55) for the low severity, 0.62 (0.56-0.68) and 0.48 (0.40-0.55) for the moderate severity, and 0.57 (0.51-0.63) and 0.95 (0.91-0.98) for the high severity categories. The percentages of patients in each category showing poor neurological outcomes and mortality are shown in Table 2.

Discussion

In this study, from data obtained from the database of a large-scale multicenter registry in Japan, we validated the predictive accuracy of the rCAST score, which was created by simplifying our previous prognostic score system developed for PCAS patients at the ED; the AUCs of the rCAST scores for the neurological outcomes at 30 and 90 days were 0.892 and 0.895, respectively. The patients were classified into three grades of severity according to the 95% sensitivity and 95% specificity of the score points of rCAST for predicting the neurological outcome at 30 days, as follows: low severity category (rCAST ≤ 5.5), moderate severity category (rCAST, 6.0-14.0), and high severity category (rCAST ≥ 14.5). To the best of our knowledge, this is the first study to conduct external validation of a risk classification at the ED for PCAS patients undergoing TTM, based on the data from a large multicenter registry. The rCAST may be a useful scoring system for risk classification at the ED of PCAS patients undergoing TTM.

In the process of creation of the rCAST, we deleted three variables (serum albumin, serum hemoglobin, and the gray matter:white matter ratio on cranial CT) included in the original CAST, because data on these variables could prove difficult to obtain before the initiation of TTM, and we assumed that they might depress the versatility of the rCAST as a risk classification tool. The remaining five variables of rCAST can be easily obtained at the ED before the initiation of TTM in the ICU. Interestingly, a few systems for prognostic scoring at the ED for PCAS patients undergoing TTM were recently reported,

however, none of these were subjected to external validation in large-scale multicenter trials [16-18]. In our study conducted for external validation of rCAST using the data of 460 PCAS patients from 73 institutions across Japan, the AUC of rCAST was nearly 0.90 (a value of the AUC of 0.90 is regarded as exhibiting a high discrimination ability according to the previous study [13]), which means rCAST can be useful for risk classification of PCAS patients at the ED.

Several studies have shown a significant therapeutic effect by focusing on a particular severity group among all patients if they had not been able to show for all patients [19]. Considering the diversity of the PCAS population, PCAS patients of particular subgroups may benefit more from any treatments such as mild therapeutic hypothermia [20], controlled reperfusion [21, 22], and other treatments [23, 24], which could not show a significant therapeutic effect for all PCAS patients. Previously, a few studies have attempted to evaluate the effects of therapies for PCAS patients according to the severity by using a single factor such as “time until ROSC” [25], but this may be insufficient for risk classification, because the severity could be influenced by a number of pre-hospital factors. If we developed an appropriate stratification system for PCAS based on the rCAST, it may be possible to identify a particular subgroup of PCAS patients who would benefit the most from treatment and show a better prognosis, although further studies are definitely needed.

There were several limitations of our study. First, we suggested the cutoff points of 6.0 and 14.5 as the points representing 95% specificity and 95% sensitivity. Although the usefulness of rCAST for risk classification was confirmed in this study by the high AUCs, further study would be needed to investigate whether these thresholds are indeed the most appropriate. We just suggested the possibility of grading based on the rCAST, and it may be better to set different cutoff points depending on the situation and the purpose. Second, in the development of rCAST, we modified the weights of the 5 variables used for calculating the original CAST by doubling and simplifying the values to multiples of 0.5. We think that this may also be one of the limitations of this study. Third, even though we assume that it is important to classify the severity of PCAS patients at the ED, it is also important to estimate their prognosis several days after their admission to the hospital by using these examinations. Of course, various kinds of intensive treatments given to the patients after their admission to the ICU could influence the outcomes. It should be noted that the purpose of the scoring system is not to provide prognostication regarding withdrawal of care decision and that prediction of the patients' precise neurological prognosis should also be made by decisive examinations such as electroencephalography or somatosensory evoked potential testing performed several days after admission [26]. Forth, we excluded PCAS patients who underwent ECMO support, because their hemodynamic status differs significantly from those not receiving such support. It would be of great interest

to devise a system for risk classification of PCAS patients receiving ECMO support.

Finally, in this study, we performed complete case analysis. In such a large-scale retrospective observational study, it is inevitable to have some missing values. The frequency of missing values in our study were as follows: 14/525 (2.7%) for the initial rhythm, 23/525 (4.4%) for time until ROSC, 11/525 (2.1%) for the pH values, 27/525 (5.1%) for the serum values of lactate, and 0/525 (0%) for the score on the motor scale of the GCS. We speculated the following as being among the causes for the missing values: loss of record, failure to input the data, failure to record the information, etc. However, we believe that these reasons for missing values did not influence the outcomes of the study, and that the biases were minimal. Our study has illustrated the importance of the information about these 5 variables for predicting the neurological outcomes of PCAS patients, suggesting the importance of collecting these data completely in actual clinical practice.

Conclusions

The rCAST was useful for predicting the neurological outcomes with high accuracy in PCAS patients, and the three grades was developed for a risk classification based on the rCAST.

Conflicts of Interest

The authors declare that there are no relationship or conflict to disclose.

Acknowledgements

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Figure legends

Fig. 1 Revised post-Cardiac Arrest Syndrome for Therapeutic hypothermia score (rCAST).

(A) For the development of rCAST, three variables (GWR, Alb, Hb) were deleted and other weights used for the original CAST were simplified. (B) Categorization of the variables was the same as in the original CAST. (C) Formula for determination of the rCAST score. The rCAST score was calculated by summing up the values obtained by multiplying each simplified weight with the corresponding categorical variable. *CAST,* post-Cardiac Arrest Syndrome for Therapeutic hypothermia score; *rCAST* revised CAST; time until *ROSC,* time from cardiac arrest until return of spontaneous circulation; *GCS M,* motor scale of Glasgow Coma Scale; *GWR,* gray matter:white matter ratio; *Alb*, albumin; *Hb*, hemoglobin.

Fig. 2 Patient flow chart illustrating the subject enrollment in this study.

OHCA, Out-of-hospital cardiac arrest; *TTM,* targeted temperature management; *PCAS*, post-cardiac arrest syndrome; *CA,* cardiac arrest; *ECMO,* extracorporeal membrane oxygenation.

Fig. 3 Receiver operating characteristic curve of rCAST for outcomes at 30 and 90 days.

The black line denotes the curve for poor neurological outcome, while the dotted gray line represents

mortality. Here, specificity measures the proportion of patients with poor outcomes who were correctly identified.

Fig. 4 Sensitivity and specificity of rCAST for predicting a poor neurological outcome at 30 days.

Supplemental Fig. 1 Summary of the original post-Cardiac Arrest Syndrome for induced Therapeutic hypothermia (CAST) score.

Using the categorized score points (A) and weights (B) in the 8 variables, the resultant scores and the probability of a good outcome were calculated (C).

Supplemental Fig. 2 Receiver-operating characteristic curve of CAST and rCAST.

The receiver operating characteristic curves of CAST and rCAST for the neurological outcome at 30 days were plotted using the data of the 151 PCAS patients whose data we had used to develop the CAST score in our previous study [9].

Supplemental Fig. 3 Distribution of rCAST scores and the prognostic performance of rCAST for the

neurological outcome at 30 days.

rCAST scores were set between 0 and 18.5, and the median was 12.0.

Figure.1

A

Variables	Weights CAST		Weights rCAST
Initial rhythm	0.57		1.0
Witness/until ROSC	1.08		2.0
pH	1.17	→ Simplify x2	2.5
Lactate	0.34		0.5
GCS M	2.23		4.5
GWR	1.48		(-)
Alb	1.08		(-)
Hb	0.60		(-)

C

Calculation formula for rCAST

1.0 x (Initial rhythm) + 2.0 x (Witness/until ROSC)

+ 2.5 x (pH) + 0.5 x (Lac) + 4.5 x (GCS M) = ☐ points

B

Variables \ *Score point*	*0*	*1*	*2*	*3*
Initial Rhythm	***Shockable***	***Non Shockable***		
Witness / until ROSC time	***< 20 min***	***20 min ≤***	***No Witness***	
pH	***≥ 7.31***	***7.30-7.16***	***7.15-7.01***	***7.00 ≥***
Lactate	***≤ 5.0***	***5.1-10.0***	***10.1-14.0***	***14.1 ≤***
GCS M	***≥ 2***	***1***		

Figure.2

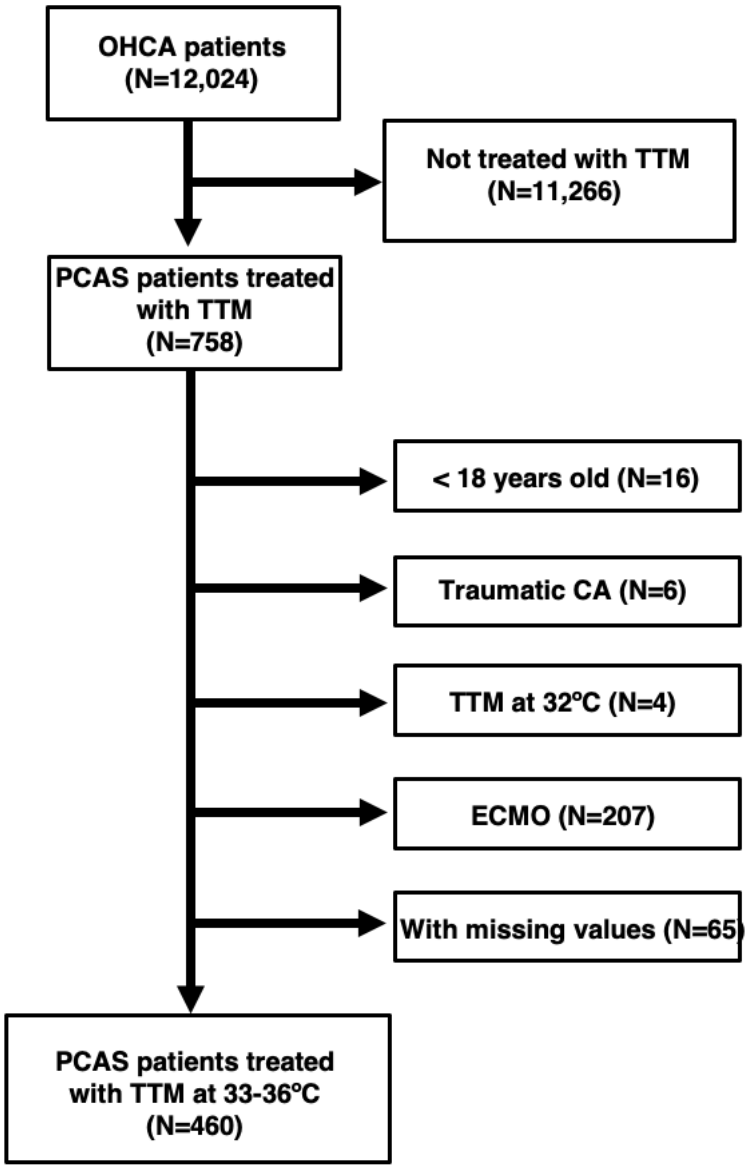

OHCA patients
(N=12,024)
Not treated with TTM
(N=11,266)
PCAS patients treated
with TTM
(N=758)
< 18 years old (N=16)
Traumatic CA (N=6)
TTM at 32°C (N=4)
ECMO (N=207)
With missing values (N=65)
PCAS patients treated
with TTM at 33-36°C
(N=460)

Figure.3

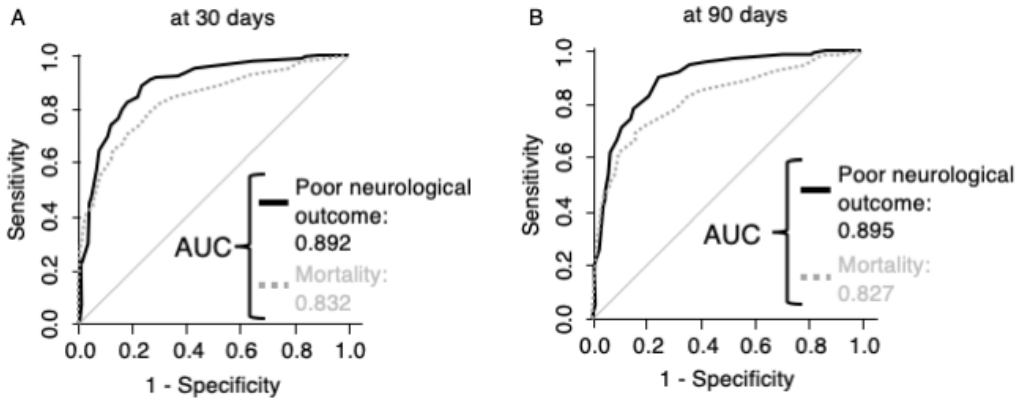

A
at 30 days
Sensitivity
0.0
0.2
0.4
0.6
0.8
1.0
1 - Specificity
AUC
Poor neurological outcome: 0.892
Mortality: 0.832
B
at 90 days
Sensitivity
1 - Specificity
AUC
Poor neurological outcome: 0.895
Mortality: 0.827

Figure.4

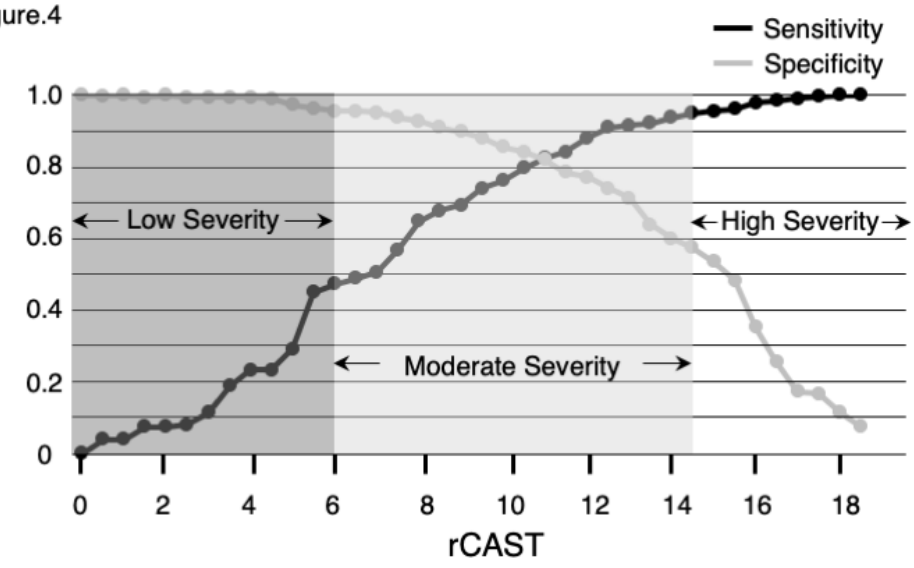

Sensitivity
Specificity
1.0
0.8
0.6
0.4
0.2
0
Low Severity
Moderate Severity
High Severity
0
2
4
6
8
10
12
14
16
18
rCAST

Table 1 Baseline characteristics of all subjects

Variable	All patients N = 460
Age, yr	66.0 (52.8-76.0)
Sex, Male, *n* (%)	345 (75.0)
Witness, *n* (%)	355 (77.2)
Bystander, *n* (%)	249 (54.1)
Initial rhythm, shockable, *n* (%)	201 (43.7)
Duration of resuscitation effort, min	23.0 (14.0-34.3)
Pre-hospital epinephrine administration, *n* (%)	116 (25.2)
GCS	3.0 (3.0-3.0)
GCM M, ≤2, *n* (%)	65 (14.1)
Serum pH	7.08 (0.21)
Serum lactate, mmol/dL	9.58 (4.23)
In-hospital epinephrine administration, *n* (%)	201 (43.7)
PCI, *n* (%)	100 (21.7)
Mild therapeutic hypothermia (TTM at 33ºC -34 ºC), *n* (%)	343 (74.6)
Normothermia treatment (TTM at 35ºC -36 ºC), *n* (%)	117 (25.4)
Outcome at 30 days	
Survival, *n* (%)	311 (67.6)
Good (CPC ≤ 2), *n* (%)	176 (38.3)
Outcome at 90 days (N = 366)*	
Survival, *n* (%)	201 (54.9)
Good (CPC ≤ 2), *n* (%)	135 (36.7)

Data are presented as the median and interquartile ranges (25-75% percentile), mean (standard deviation) or as absolute frequencies with percentages. *GCS* Glasgow Coma Scale, *PCI* Percutaneous Coronary Intervention, *TTM* targeted temperature management, *CPC* Cerebral Performance Category.

Table 2 Predicted probability of mortality and poor neurological prognosis in each grade of rCAST

Grade of rCAST (n= 460)	At 30 days		At 90 days*	
	Probability of poor neurological outcome	Probability of mortality	Probability of poor neurological outcome	Probability of mortality
High (n=96)	94.8 (90.4-97.2)	62.8 (55.4-69.7)	95.4 (90.9-97.8)	73.2 (65.7-79.6)
Moderate (n=192)	56.3 (49.2-63.1)	20.3 (15.2-26.6)	52.7 (44.7-60.7)	34.5 (27.2-42.5)
Low (n=172)	13.5 (8.1-21.8)	2.1 (0.6-7.3)	14.5 (8.1-24.7)	4.4 (1.5-12.2)

*We performed analysis by using data of 366 PCAS patients, whose data about the outcome were available.

Supplemental figure.1

A

Score	0	1	2	3
Initial Rhythm (X1)	Shockable	Non Shockable		
Witness / ROSC time (X2)	< 20 min	20 min ≤	No Witness	
pH (X3)	≥ 7.31	7.30-7.16	7.15-7.01	7.00 ≥
Lactate (X4)	≤ 5.0	5.1-10.0	10.1-14.0	14.1 ≤
GCS M (X5)	≥ 2	1		
GWR (X6)	≥ 1.201	1.200-1.151	1.150 ≥	
Alb (X7)	≥ 3.6	3.5-3.1	3.0 ≥	
Hb (X8)	≥ 13.1	13.0-11.1	11.0 ≥	

B

	Weight
Initial Rhythm	0.570 (α1)
Witness / ROSC time	1.040 (α2)
pH	1.167 (α3)
Lactate	0.338 (α4)
GCS M	2.225 (α5)
GWR	1.480 (α6)
Alb	1.077 (α7)
Hb	0.595 (α8)
intercept	-5.282 (α9)

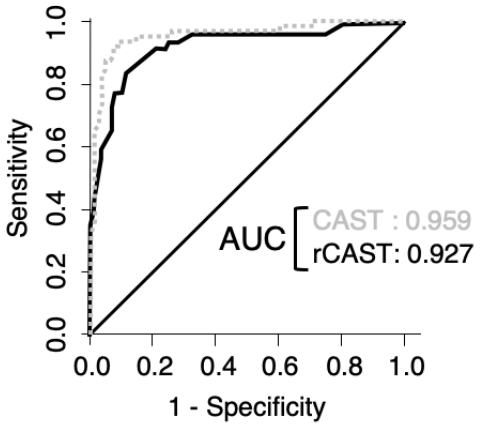
C

Score (A) = α1 x X1+ α2 x X2 …+ α9

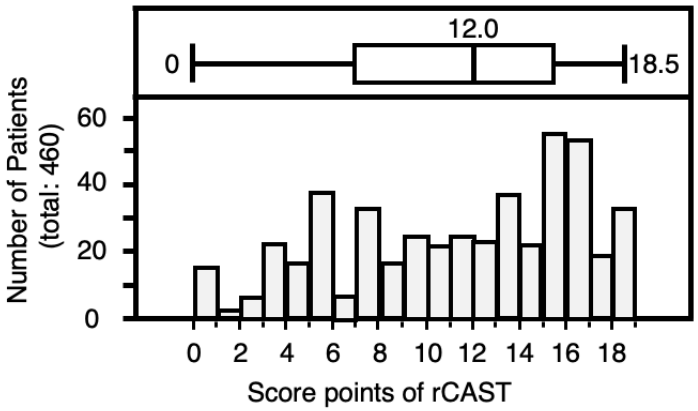
α: weight
X: categorized variables in C

$$\text{Probability for Good Outcome} = \frac{(e^{-A})}{1 + (e^{-A})}$$

Supplemental figure.2



Supplemental figure.3



Supplemental Table 1 Predictive accuracy of rCAST for neurological outcome at 30 days in each cutoff point

Cutoff points	Sensitivity	Specificity	Grade	Cutoff points	Sensitivity	Specificity	Grade
≥ 0.0	**1.00**	**0.00**	**Low**	≥ 9.5	0.88	0.74	Moderate
≥ 0.5	1.00	0.04	Low	≥ 10.0	0.86	0.76	Moderate
≥ 1.0	1.00	0.04	Low	≥ 10.5	0.84	0.80	Moderate
≥ 1.5	0.99	0.07	Low	≥ 11.0	0.82	0.82	Moderate
≥ 2.0	0.99	0.07	Low	≥ 11.5	0.79	0.84	Moderate
≥ 2.5	0.99	0.08	Low	≥ 12.0	0.77	0.88	Moderate
≥ 3.0	0.99	0.11	Low	≥ 12.5	0.74	0.91	Moderate
≥ 3.5	0.99	0.19	Low	≥ 13.0	0.71	0.91	Moderate
≥ 4.0	0.99	0.23	Low	≥ 13.5	0.64	0.92	Moderate
≥ 4.5	0.99	0.23	Low	≥ 14.0	0.60	0.94	Moderate
≥ 5.0	0.97	0.29	Low	**≥ 14.5**	**0.57**	**0.95**	**High**
≥ 5.5	0.96	0.45	Low	≥ 15.0	0.54	0.95	High
≥ 6.0	**0.95**	**0.47**	**Moderate**	≥ 15.5	0.48	0.96	High
≥ 6.5	0.95	0.49	Moderate	≥ 16.0	0.35	0.98	High
≥ 7.0	0.95	0.51	Moderate	≥ 16.5	0.25	0.98	High
≥ 7.5	0.94	0.57	Moderate	≥ 17.0	0.17	0.99	High
≥ 8.0	0.93	0.65	Moderate	≥ 17.5	0.17	0.99	High
≥ 8.5	0.91	0.68	Moderate	≥ 18.0	0.11	1.00	High
≥ 9.0	0.88	0.74	Moderate	≥ 18.5	0.07	1.00	High