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Vasoactive-inotropic score as a predictor of in-hospital mortality in out-of-hospital cardiac arrest

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ABSTRACT

Background. The Vasoactive-Inotropic Score (VIS) is an objective clinical tool used to quantify the need for cardiovascular support in children and adolescents after surgery and to predict prognosis of pediatric septic shock. Considering the post-cardiac arrest syndrome (PCAS) is a sepsis-like syndrome, we aimed to investigate the correlation between VIS and in-hospital mortality in out-of-hospital cardiac arrest (OHCA) patients who achieved a sustained return of spontaneous circulation (ROSC) and admitted to the intensive care unit (ICU).

Methods. A retrospective chart review of 504 OHCA patients who were admitted to the emergency room with OHCA from Jan 2015 to Dec 2016 was done. VIS was calculated with the recorded administration rate of the drugs on electronic medical record at the same time during the first 24 hours in ICU. The highest value of VIS in 24 hours (24hr-peak VIS) was used for investigating the correlation between VIS and in-hospital mortality.

Results. Among 504 OHCA patients, 166 patients were admitted to the intensive care unit and 116 patients died during hospital stay. The probability of in-hospital mortality was significantly higher when 24hr-peak VIS was higher than 33.3 [Odds ratio (OR) = 3.18, 95% CI = 1.22 – 8.29, p value = 0.018].

Conclusion. 24hr-Peak VIS could be a good scoring system for predicting in-hospital mortality in OHCA patients who admitted to ICU. The AUC was 0.762 (95% CI = 0.690 to 0.825) and the optimal cut-off values were 33.3 (sensitivity 0.764, specificity 0.610).

BACKGROUND

Sudden cardiac death (SCD), unexpected death from a cardiovascular cause that occurs outside of the hospital, remains a significant public health problem estimated to account for 15 - 20% of all deaths(1)]. Moreover, the survival to hospital discharge rate after out-of-hospital cardiac arrest (OHCA) has remained poor over 30 years despite the major advances in cardiopulmonary resuscitation (CPR) practice(2).

In OHCA patients, early prognostication is important in the aspects of medical ethics as well as planning treatment plans. Although there have been many efforts for predicting prognosis of OHCA patients, no single standard predictor was developed(3).

The Vasoactive-Inotropic Score (VIS) is an objective clinical tool used to quantify the need for cardiovascular support in children and adolescent after surgery(4-7) and to predict prognosis of pediatric septic shock(8).

Given that the post-cardiac arrest syndrome (PCAS) is a sepsis-like syndrome(9), and VIS can predict the prognosis of septic shock, we hypothesised that VIS could predict the prognosis of post-cardiac arrest patients. To the authors' knowledge, there was no study about the correlation of VIS and outcome of OHCA. Therefore, we conducted this study to investigate the association between VIS and OHCA outcomes.

METHODS

Study design and data collection

This was a retrospective and observational study. Consecutive Adult OHCA patients who achieved ROSC and were admitted to the hospital from Jan 2015 to Dec 2016, were included. Exclusion criteria were age < 18 years, traumatic cardiac arrest, history of terminal malignancy, cerebral performance category (CPC) ≥ 3 score prior to cardiac arrest.

Age, gender, the location of arrest, witnessed cardiac arrest, initial rhythm, and bystander CPR, the cause of cardiac arrest, CPR duration and targeted temperature management, the rate of survival to admission and neurologic outcome at discharge were collected from the emergency department cardiac arrest registry.

For calculating VIS, administration rate of vasoactive drugs and inotropes was reviewed from the electronic medical record (EMR). Two trained researchers reviewed the registry and EMR. If there was a conflict, one emergency medicine specialist reviewed that case.

Vasoactive-inotropic score (VIS)

Vasoactive drugs and inotropes were administered to maintain the mean arterial pressure above 65mmHg. The vital signs

and administration rate of vasoactive drugs and inotropes were recorded every hour unless there were unstable events. VIS was calculated with the recorded administration rate of the drugs at the same time during the first 24 hours in ICU using the following formulae(10-11):

At least 24 values of VIS were obtained per each patient and the highest value of VIS within 24 hours (24hr-peak VIS) after admission to the ICU was used for further analysis.

Primary and secondary outcomes

The primary outcome of this study was the probability of in-hospital mortality correlated with VIS. The secondary outcome was the probability of neurologically intact survival correlated with VIS. Neurologically intact survival (NIS) group was defined as the patients who were discharged alive with CPC score of 1-2(12) and non-NIS group was defined as the patients who died in hospital or were discharged alive with CPC score of 3-5.

Statistical analysis

Statistical analyses were performed using SPSS software for Windows (V.20.0 K, SPSS, Chicago, IL, USA). Nominal data are presented as frequencies and percentages, and continuous variables are presented as the mean and standard deviation (SD) and median and interquartile range (IQR) after assessments for normality using the Shapiro-Wilk test. The chi-square test or Fisher's exact test were used for comparisons of nominal variables, while the two-sample t-test and Mann-Whitney U-test were used to compare continuous variables. Predictors of poor prognosis were determined by logistic regression analysis, and optimal cut-off points of predictors were evaluated by receiver operation characteristic (ROC) curves and the Youden index. P-values less than 0.05 were considered statistically significant.

Multivariate logistic regression analysis was used to identify independent predictors of in-hospital mortality and neurologically intact survival at hospital discharge, as measured by the estimated odds ratio (OR) with 95% confidence intervals (CIs). Variables with a p-value less than 0.2 on univariate analyses as well as clinically relevant variables were entered into the forward stepwise multiple logistic regression models.

Power analysis

Statistical power was calculated using G*Power 3.1, and the primary outcome was the probability of in-hospital mortality correlated with VIS. Given the probabilities of in-hospital mortality were 0.779, 0.410 in the patients whose 24hr-peak VIS was 33.3 or higher and lower than 33.3 respectively, and sample size was 166, the type 1 error < 0.001 and power > 0.999 were calculated for a two-tail logistic regression.

RESULTS

504 OHCA patients were admitted to the emergency room (ER) during the study period. Among them, 285 patients were excluded due to age (n=11), traumatic cardiac arrest (n=57) and death at ER(n=217). A total of 219 patients were admitted to the ICU, and 53 patients were excluded because of terminal malignancy (n=37) and CPC 3-5 prior to cardiac arrest (n=16) (Fig. 1).

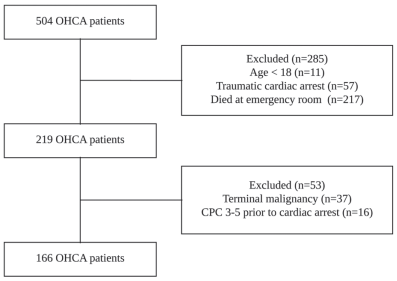

Figure 1. Flow diagram

OHCA: Out-of-hospital cardiac arrest, CPC: Cerebral performance category

As a result, 166 patients were included in this study. Among them, 60 patients survived at discharge, and 36 patients showed a neurologically intact survival. Forty-seven (73.4%) versus 55 patients (51.8%) were men and the mean age was 56.6 ± 18.3 versus 62.4 ± 16.4 in survivors and non-survivors respectively (p < 0.001 and p = 0.015, respectively). Also, there were significant differences between survivors and non-survivors regarding the cause of cardiac arrest, the location of cardiac arrest, initial shockable rhythm and CPR duration (Table 1).

Twenty-nine (80.6%) versus 73 patients (56.2%) were men, and the mean age was 47.8 ± 13.7 versus 63.3 ± 16.8 in the NIS group and the non-NIS group respectively (p = 0.011 and p < 0.001, respectively). The NIS group showed a higher rate of cardiac cause, public area, initial shockable rhythm

*Table 1. Clinical characteristics**

	Survivors (n=60)	Non-survivors (n=106)	p	NIS group (n=36)	Non-NIS group (n=130)	P
Age (years)	55.6 ± 18.3	62.4 ± 16.4	0.015*	47.8 ± 13.7	63.3 ± 16.8	< 0.001*
Male	47 (78.3)	55 (51.9)	0.001*	29 (80.6)	73 (56.2)	0.011*
Cardiac cause	34 (56.7)	25 (23.6)	< 0.001*	28 (77.8)	31 (23.8)	< 0.001*
Public area	30 (50.0)	36 (34.0)	0.047*	22 (61.1)	44 (33.8)	0.003*
Witnessed arrest	37 (61.7)	70 (66.0)	0.572	22 (61.1)	85 (65.4)	0.635
Bystander CPR	32 (53.3)	50 (47.2)	0.445	23 (63.9)	59 (45.4)	0.06
Shockable rhythm	27 (45.0)	16 (15.1)	< 0.001*	24 (66.7)	19 (14.6)	< 0.001*
24hr-peak VIS	29.2 (0 - 83.9)	97.6 (30.6 - 196.8)	< 0.001*	17.0 (0 – 66.5)	88.2 (28.6 – 183.0)	< 0.001*
CPR duration	27 ± 12	32 ± 13	0.019*	20 ± 9	32 ± 13	< 0.001*
TTM	19 (41.3)	27 (58.7)	0.471	32 (24.6)	14 (38.9)	0.097

Data are expressed as mean ± SD, number (%), or median (IQR), 24hr-peak VIS: The highest value of vasoactive-inotropic score in 24 hours, TTM: Target Temperature Management, NIS: Neurologically intact survival
*p value < 0.05

Table 2. Multivariate logistic regression analysis

	Neurologically intact survival at hospital discharge	
	OR (95% CI)	**P**
Male	1.91 (0.43-8.57)	0.397
Age ≥ 65	16.22 (2.73-96.43)	0.002*
Public area	0.86 (0.24-3.10)	0.819
Witnessed arrest	0.94 (0.28-3.20)	0.923
Bystander CPR	0.36 (0.09-1.44)	0.147
Shockable rhythm	0.08 (0.02-0.32)	<0.001*
Cardiac cause	1.40 (0.38-5.23)	0.613
CPR duration	0.97 (0.94-1.01)	0.121
24hr-peak VIS >33.3	1.18 (0.31-4.55)	0.811
TTM	1.05 (0.26-4.17)	0.951

24hr-peak VIS: The highest value of vasoactive-inotropic score in 24 hours, TTM: Target Temperature Management
*p value < 0.05

and shorter duration of CPR (Table 1).

Regarding VIS, the 24hr-peak VIS was significantly lower in survivors compared to non-survivors [29.2 (IQR 0-83.9) versus 97.6 (IQR 30.6-196.8), p < 0.001]. Also, the NIS group showed lower 24hr-peak VIS compared to the non-NIS group [17.0 (IQR 0 – 66.5) versus 88.2(IQR 28.6 – 183.0), p < 0.001] (Table 1).

The ROC curve analysis was performed for the prediction of in-hospital mortality and neurologically intact survival. The AUCs of the 24hr-peak VIS for the prediction of in-hospital mortality were 0.762 (95% CI = 0.690 to 0.825) and the optimal cut-off values were 33.3 (sensitivity 0.764, specificity 0.610) (Fig. 2). Regarding the neurologically intact survival, the AUC of 24hr-peak VIS was 0.763 (95% CI = 0.691 to 0.826) with the optimal cut-off value of 33.3 (sensitivity 0.694, specificity 0.721).

In the univariate logistic regression model, the probability of in-hospital mortality increases as 24hr-peak VIS increases [Odds ratio (OR) = 1.0107, 95% CI = 1.0056 – 1.0159, p < 0.001] (Fig. 3). In the multivariate logistic regression model, the probability of in-hospital mortality was significantly higher when 24hr-peak VIS was higher than 33.3 [Odds ratio (OR) = 3.18, 95% CI = 1.22 – 8.28, p value = 0.018] (Fig. 4). However, there was no significant correlation between 24hr-peak VIS and the neurologically intact survival (OR = 1.18, 95% CI = 0.26 – 4.17), p value = 0.951) (Table 2).

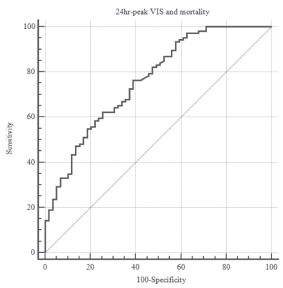

Figure 2a. ROC curve analysis for the prediction of in-hospital mortality

ROC: receiver operation characteristic, 24hr-peak VIS: the highest value of vasoactive-inotropic score in 24 hours, *p value < 0.05

24hr-peak VIS showed an AUC of 0.762 (95% CI = 0.690 to 0.825) and the optimal cut-off values were 33.3 (sensitivity 0.764, specificity 0.610).

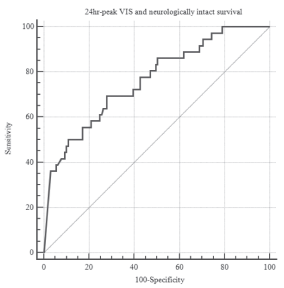

Figure 2b. ROC curve analysis for the prediction of neurologically intact survival at hospital discharge

ROC: receiver operation characteristic, 24hr-peak VIS: the highest value of vasoactive-inotropic score in 24 hours, *p value < 0.05

24hr-peak VIS showed an AUC of 0.763 (95% CI = 0.691 to 0.826) with the optimal cut-off value of 33.3 (sensitivity 0.694, specificity 0.721).

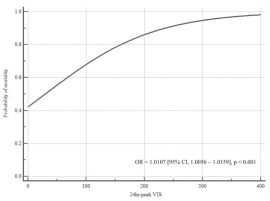

Figure 3. Univariate logistic regression for in-hospital mortality of OHCA patients

24hr-peak VIS: The highest value of vasoactive-inotropic score in 24 hours

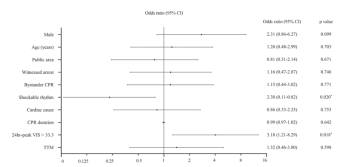

Figure 4. Multivariate logistic regression for in-hospital mortality of OHCA patients

24hr-peak VIS: The highest value of vasoactive-inotropic score in 24 hours, TTM: Target Temperature Management, *p value < 0.05

DISCUSSION

In the present study, we sought to investigate the association between VIS and outcomes of OHCA patients. As a result, we reported that the value of the 24hr-peak VIS higher than 33.3 showed a higher probability of in-hospital mortality.

Many efforts were made for predicting prognosis in OHCA patients which is essential for the treatment plan and ethics. However, no single method could predict the outcome. Moreover, only a few methods could be used in the early phase of the post-resuscitation period.

In the prehospital phase, the presence of the initial shockable rhythm and bystander CPR could predict the better outcome (13) After ROSC (return of spontaneous circulation), status myoclonus within 24 hours predicts unfavourable neurological outcome in comatose patients with OHCA treated with therapeutic hypothermia(14).

Regarding blood markers, serum ammonia and lactate levels on arrival are used as the prognostic factors(15), and higher copeptin at admission, DNI (delta neutrophil index), serial NSE (neuron-specific enolase) and S-100B protein were reported as being associated with poor outcome(16-19). In terms of image study, grey matter to white matter ratio (GWR) and optic nerve sheath diameter (ONSD) on initial brain CT correlated with the neurologic outcome of hypoxic-ischemic encephalopathy. (3,20) However, these blood markers and image studies could not be measured continuously or immediately.

There have been many studies for predicting the outcome using scoring systems such as SAPS III, OHCA score, RACA score(21-24). However, SAPS III could not predict mortality(23), and RACA score could predict only ROSC but not the Neurologically intact survival nor in-hospital mortality (25). OHCA score, one of the predictors of OHCA, has the limitation as it contains no-flow interval and low-flow interval which are difficult to be estimated or recorded in a large number of OHCA patients(1224) Recently, Argaud et al. reported that SOFA score at ICU admission was independently associated with 28-day mortality(26).

VIS is a clinical scoring system used to predict prognosis in the patients had cardiac surgery and with sepsis(4-8,10,11,27) . As PCAS is one of the sepsis-like syndromes and has the component of cardiac dysfunction, we investigated the correlation between VIS and in-hospital mortality of the post-resuscitated patients.

There are some limitations of the present study. First, this study was investigated in a single tertiary university hospital. Since our hospital had a protocol which was made to maintain the mean arterial pressure above 65 mmHg, other hospitals that have a higher blood pressure target protocol, may not be able to use the same cut-off value.

Second, though the NIS group showed lower 24hr-peak VIS than the non-NIS group, the long-term neurologic outcome should be investigated to make a strong conclussion.

CONCLUSION

24hr-Peak VIS could be used to predict in-hospital mortality in OHCA patients. The AUC was 0.762 (95% CI = 0.690 to 0.825) and the cut-off value was 33.3.

Conflicts of interest

None

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