Shock on Admission as a Potential Marker for ICU Mortality of Cardiac Arrest Patients

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Summary

To investigate the association of shock on admission with predicting intensive care unit (ICU) mortality, hospital mortality, and neurological outcomes of post cardiac arrest patients.

This was a retrospective study of cardiac arrest (CA) patients admitted to ICU. Student's t test and Chi-square test were performed to compare the difference of non-shock and shock group. Multivariable regression analysis was performed to investigate shock and its association with ICU mortality, hospital mortality, and neurologic outcomes and linear regression analysis to explore its correlation with length of stay in hospital.

A total of 374 CA patients were analyzed, with 200 (53.5%) patients in the presence of shock on admission. Shock was significantly associated with higher ICU mortality (OR 2.42, 95% CI 1.60 to 3.68; $P < 0.001$), hospital mortality (OR 2.33, 95% CI 1.54 to 3.54; $P < 0.001$), and more unfavorable neurological outcomes (OR 1.98, 95% CI 1.30 to 3.02; $P = 0.001$). After adjusting for confounding factors, shock was still an independent predictor of ICU mortality (OR 2.40, 95% CI 1.30 to 4.43; $P = 0.005$).

Shock on admission of CA patients was significantly associated with ICU mortality.

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Key words: Neurological outcome

Cardiac arrest (CA) is a leading cause of death worldwide, with half of million people suffered in the Europe and United States each year. Unfortunately, the post CA syndrome, including neurologic and cardiovascular injury, contributes to a poor prognosis, with only 2-20% of patients being discharged in good condition.¹⁻³⁾

Several studies confirmed several variables as a predictor of in-hospital mortality and out-hospital outcomes. A recent meta-analysis showed that acute kidney injury increased the likelihood of poor outcomes.⁴⁾ Similarly, Enrica, *et al.* found that the occurrence of acute liver failure and hypoxic hepatitis were independent predictors of neurologic outcomes among CA patients.⁵⁾ Interestingly, a recent study reported that initial serum cholesterol level was significantly associated with neurologic outcome (OR: 0.99).⁶⁾

The shock state during intensive care unit (ICU) stay of patients admitted to ICU will demonstrate an unfavorable impact on prognosis, due to the ischemia-reperfusion-ischemia injury accompanied. Early correction of shock in cardiac arrest, maintaining mean artery pressure higher

than 80 mmHg, played an important role in the treatment of CA patients.⁷⁾ However, limited studies were focused on the association between shock and mortality and neurologic outcomes of CA patients.

The aim of this study was to describe the presence of shock on admission among CA patients admitted to ICU as well as their association with patient outcomes.

Methods

Study population: This study was based on a retrospective study in the Department of Intensive Care at Erasme Hospital, Brussels (Belgium), approved by the local Ethical Committee (P2017/264). From January 2007 to December 2015, all comatose patients admitted after CA with Glasgow Coma Scale < 9 were included in the study.

Post CA care: The standard institutional protocol of post CA care was described elsewhere⁴⁾. Briefly, all CA patients were treated with targeted temperature management (TTM; 32-34°C) for 24 hours. Mean arterial pressure was maintained at > 65 -70 mmHg and intra-aortic balloon counterpulsation (IABP) or extracorporeal membrane oxy-

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Table I. Characteristics of the Study Population, According to Shock State

	ALL (n = 374)	Non-Shock (n = 174)	Shock (n = 200)	P value
Demographics				
Age, years	61.8 ± 15.4	62.1 ± 15.2	61.6 ± 15.5	0.968
Weight, kg	77.0 ± 14.7	76.8 ± 14.0	77.2 ± 15.4	0.136
Male, n (%)	270 (72.2)	130 (74.7)	140 (70.0)	0.310
APACHE II score	24.3 ± 7.0	7.1 ± 0.5	6.9 ± 0.5	0.872
SOFA score	11.2 ± 3.5	3.7 ± 0.3	3.4 ± 0.2	0.146
Witnessed, n (%)	320 (85.6)	140 (80.0)	180 (90.0)	0.009
Bystander CPR, n (%)	254 (67.9)	108 (62.1)	146 (73.0)	0.024
Time to ROSC, minutes	18.1 ± 14.1	15.6 ± 11.4	20.2 ± 15.8	0.001
Out-of-hospital, n (%)	207 (55.3)	118 (67.8)	89 (44.7)	< 0.001
TTM, n (%)	331 (88.5)	156 (89.7)	175 (87.9)	0.601
Non-cardiac cause, n (%)	153 (40.9)	67 (38.5)	86 (43.0)	0.378
Non-shockable rhythm, n (%)	221 (59.1)	87 (50.0)	134 (67.0)	0.001
ICU mortality, n (%)	194 (51.9)	70 (40.2)	124 (62.0)	< 0.001
Hospital mortality, n (%)	213 (57.0)	80 (46.0)	133 (66.5)	< 0.001
Favorable neurological outcome at 3 months, n (%)	148 (39.6)	84 (48.3)	64 (32.0)	0.001
ICU length of stay, days	7.9 ± 9.7	5.9 ± 6.5	9.7 ± 11.5	< 0.001
Comorbidities				
Chronic heart failure, n (%)	78 (20.9)	29 (16.7)	49 (24.5)	0.063
Hypertension, n (%)	159 (42.5)	85 (48.9)	74 (37.0)	0.021
Coronary artery disease, n (%)	146 (39.0)	66 (37.9)	80 (40.0)	0.682
Diabetes, n (%)	91 (24.3)	39 (22.4)	52 (26.0)	0.420
COPD, n (%)	63 (16.8)	28 (16.1)	35 (17.5)	0.717
Neurological disease, n (%)	54 (14.4)	32 (18.4)	22 (11.0)	0.043
Chronic renal failure, n (%)	62 (16.6)	20 (11.5)	42 (21.1)	0.013
Liver cirrhosis, n (%)	17 (4.5)	3 (1.7)	14 (7.0)	0.015
Medical operation				
IABP, n (%)	24 (6.4)	3 (1.7)	21 (10.5)	0.001
ECMO, n (%)	47 (12.6)	3 (1.7)	44 (22.0)	< 0.001
Vasopressor therapy, n (%)	283 (75.7)	86 (49.4)	197 (98.5)	< 0.001
Inotropic agents, n (%)	201 (53.7)	56 (32.2)	145 (72.5)	< 0.001
Mechanical ventilation, n (%)	369 (98.7)	172 (98.9)	197 (98.5)	0.768
CRRT	61 (16.3)	9 (5.2)	52 (26.0)	< 0.001
Laboratory examination on admission				
Lactate, mEq/L	6.2 ± 3.3	5.5 ± 2.3	6.9 ± 3.9	< 0.001
ScvO ₂ /SvO ₂ , %	69.2 ± 9.1	70.1 ± 8.9	68.5 ± 9.3	0.400
Proteins, mg/dL	7.2 ± 8.8	10.2 ± 0.8	7.4 ± 0.5	0.168
Glucose, mg/dL	234.8 ± 125.1	101.7 ± 7.7	142.4 ± 10.1	0.013
pH	7.32 ± 0.1	7.33 ± 0.1	7.31 ± 0.1	0.214
PaO ₂ , mmHg	151.1 ± 104.2	105.6 ± 8.0	103.3 ± 7.3	0.442
PaCO ₂ , mmHg	39.2 ± 10.9	9.6 ± 0.7	11.9 ± 0.8	0.267
MAP, mmHg	90.6 ± 21.4	96.1 ± 21.7	85.9 ± 20.0	0.053
Creatinine, mg/dL	1.5 ± 1.2	1.4 ± 1.2	1.6 ± 1.2	0.035
CRP, mg/dL	62.9 ± 72.6	49.9 ± 60.2	74.2 ± 80.3	0.002

ICU indicates intensive care unit; CPR, cardiopulmonary resuscitation; ROSC, return of spontaneous circulation; TTM, targeted temperature management; COPD, chronic pulmonary obstructive disease; IABP, intra-aortic balloon counterpulsation; ECMO, extracorporeal membrane oxygenation; CRRT, continuous renal replacement therapy; AKI, acute liver failure; ScvO₂/SvO₂, central venous oxygen saturation or mixed venous oxygen saturation; MAP, mean arterial pressure; CRP, C-reactive protein; APACHE, Acute Physiology and Chronic Health Evaluation; SOFA, Sequential Organ Failure Assessment, CI, Confidence Interval. * $P < 0.05$.

generation (ECMO) in cases of severe cardiogenic shock. SpO₂ was maintained higher than 94% by ventilation, and blood glucose was kept between 110 and 150 mg/dL using a continuous insulin infusion.

Data collection: Data on demographics, pre-existing chronic diseases and cardiopulmonary resuscitation (CPR) (initial rhythm, bystander CPR, and time to ROSC), were collected by electric health records. Severity of disease was assessed using Acute Physiology and Chronic Health Evaluation (APACHE) II score⁸⁾ and the Sequential Organ

Failure Assessment (SOFA) score⁹⁾ on the day of admission. Use of mechanical ventilation, continuous renal replacement therapy (CRRT) and length of ICU stay were recorded.

Shock was defined as the need for vasopressor agents for more than six hours.

Neurological evaluation was assessed at three months after CA using the cerebral performance categories score (CPC; 1 = no or mild neurological disability, 2 = moderate neurological disability, 3 = severe neurological impairment).

Table II. Logistic Regression Analysis of Shock for ICU Mortality, Hospital Mortality, and Unfavorable Neurological Outcome

	OR	95% CI	P value
ICU mortality			
Model 1	2.42	1.60 to 3.68	< 0.001
Model 2	2.53	1.58 to 4.07	< 0.001
Model 3	2.40	1.30 to 4.43	0.005
Hospital mortality			
Model 1	2.33	1.54 to 3.54	< 0.001
Model 2	2.25	1.40 to 3.60	0.001
Model 3	1.81	0.97 to 3.35	0.061
Unfavorable neurological outcomes			
Model 1	1.98	1.30 to 3.02	0.001
Model 2	1.81	1.13 to 2.91	0.013
Model 3	1.43	0.77 to 2.65	0.264

Model 1: univariate logistic regression; Model 2: adjusted for Witnessed CA, Time to ROSC, Bystander CPR, Non-shockable rhythm; Model 3: adjusted for Model 2 plus Liver cirrhosis, Chronic renal failure, IABP, ECMO, Vasopressor therapy, Inotropic agents, CRRT, lactate and CRP.

ment, 4 = vegetative states, 5 = death).⁹⁾ A favorable neurological outcome was considered as a CPC 1-2 with an unfavorable neurological outcome as CPC 3-5.¹⁰⁾

Statistical analysis: Continuous variables were reported as mean and standard deviation, and categorical variables were expressed as frequencies and percentages. The two-tailed student's *t* test was used to compare continuous variables, and Chi-square test was used to compare categorical variables. Only variables with a *P* value < 0.01 in the univariate analysis were considered in the multivariable logistic regression, and odds ratios (OR) were estimated. Data were analyzed using IBM SPSS 25.0. A *P* value < 0.05 was considered as statistically significant.

Results

Characteristics of study subjects: Of 374 CA patients, 200 (53.5%) patients presented with shock on admission (Table I). Compared with the no-shock group, a higher ICU mortality (62.0% versus 40.2%; *P* < 0.001), hospital mortality (66.5% versus 46.0%; *P* < 0.001) and more presence of neurological outcomes (68.0% versus 51.7%; *P* = 0.001) was found at the 3-month follow-up. With regard to the medical operation, patients with shock received more positive therapy, such as more presence of IABP, ECMO, vasopressor therapy, inotropic agents, and CRRT.

Shock and clinical outcomes: Univariate logistic regression analysis (Table II) revealed that shock was significantly associated with ICU mortality (OR 2.42, 95% CI 1.60 to 3.68; *P* < 0.001), hospital mortality (OR 2.33, 95% CI 1.54 to 3.54; *P* < 0.001), and unfavorable neurological outcomes (OR 1.98, 95% CI 1.30 to 3.02; *P* = 0.001). After adjusting for witnessed CA, time to ROSC, bystander CPR, and non-shockable rhythm, shock still increased ICU mortality (OR 2.53, 95% CI 1.58 to 4.07; *P* < 0.001), hospital mortality (OR 2.25, 95% CI 1.40 to 3.60; *P* = 0.001), and the occurrence of unfavorable neurological outcomes (OR 1.81, 95% CI 1.13 to 2.91; *P* = 0.013). To exclude the possible influence of medical op-

Table III. Liner Regression Analysis of Shock for ICU Stay

Variable	β	95% CI	P value
Model 1	0.19	1.80 to 5.70	< 0.001
Model 2	0.16	1.17 to 5.15	0.002
Model 3	0.07	-1.29 to 3.86	0.327

Model 1: univariate logistic regression; Model 2: adjusted for Witnessed CA, Time to ROSC, Bystander CPR, Non-shockable rhythm; Model 3: adjusted for Model 2 plus Liver cirrhosis, Chronic renal failure, IABP, ECMO, Vasopressor therapy, Inotropic agents, CRRT, lactate and CRP.

eration, we adjusted for liver cirrhosis, chronic renal failure, IABP, ECMO, vasopressor therapy, inotropic agents, and CRRT. Shock was also significantly related to ICU mortality (OR 2.40, 95% CI 1.30 to 4.43; *P* = 0.005). However, shock was not significantly associated with hospital mortality, and unfavorable neurological outcomes adjusted for other covariates.

Shock and length of stay: As seen in Table I, the length of stay was longer in the shock group (9.7 ± 11.5 versus 5.9 ± 6.5 ; *P* < 0.001). So, we evaluated the association of shock and length of stay. As shown in Table III, shock was significantly associated with the length of stay (β 0.19, 95% CI 1.80 to 5.70; *P* < 0.001). After adjusting for witnessed CA, time to ROSC, bystander CPR, and non-shockable rhythm, the relation still existed (β 0.16, 95% CI 1.17 to 5.15), while the association disappeared after being adjusted for comorbidities and medical operations.

Discussion

Our study found that the presence of shock on admission was significantly associated with higher ICU mortality, higher hospital mortality, and more unfavorable neurological outcomes of CA patients. After adjusting for demographics and medical operation, shock was also an independent predictor of ICU mortality and hospital mortality. Besides, the presence of shock was associated with length of stay of CA patients. Even though shock correlated with unfavorable neurological outcomes in model 1 and model 2, this association was not significant after adjusting for medical operation in model 3, which could be attributed to the aggressive operations such as ECMO or other neurological monitoring for brain protection, suggesting that timely intervention decreased out-of-hospital brain damage.

The etiologies of CA were categorized into cardiac or noncardiac. The former includes myocardial infarction, arrhythmia, or heart failure, with a prevalence of approximately 50% to 60%.^{11,12)} Poor functional statuses prior to the CA, such as pneumonia, renal dysfunction, and hepatic dysfunction, were identified as significant predictors of poor survival.^{13,14)} Previous studies demonstrated that hypotension, most arising from septic shock, is related to worse outcome,¹⁵⁾ which could partly explain our findings. However, when adjusted for blood pressure, the relation between shock and clinical outcomes was still statistically significant. To analyze of shock for ICU/hospital mortality

in each etiology, we examined the association in subgroup analysis. We found that shock independently associated with ICU/ hospital mortality only in cardiac CA patients, not in CA patients with noncardiac cause. These results suggested that correction of shock of CA due to cardiac cause was particular important. However, the subgroup data were relatively small, which deserved further investigation.

During shock, whole body ischemia was aggravated, and following reperfusion injury would persist for days with reactive oxidative species burst and inflammatory cytokine production. Some measures including defibrillation, CPR, or inotropic agents should be implemented as soon as possible for the purpose of relieving shock and restoring brain recovery.¹⁶⁾ If the shock was not timely corrected, the chance to develop unfavorable neurologic outcomes will be greatly increased.

In summary, our study confirmed that shock on admission was significantly associated with ICU mortality, hospital mortality, and unfavorable neurological outcomes. Early correction of shock will contribute to a good prognosis.

Disclosure

Conflicts of interest: The authors have no conflict of interest to declare.

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