

Early blood pH as an independent predictor of neurological outcome in patients with out-of-hospital cardiac arrest

A retrospective observational study

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Abstract

Metabolic acidosis is observed in 98% of patients with out-of-hospital cardiac arrest (OHCA). The longer the no-flow or low-flow duration, the more severe is the acidosis in these patients. This study explored whether blood pH in early stages of advanced life support (ALS) was an independent predictor of neurological prognosis in patients with OHCA.

We retrospectively enrolled patients with OHCA from January 2012 to June 2018 in a single-medical tertiary hospital in Taiwan. Patients with OHCA whose blood gas analyses within 5 minutes after receiving ALS at the emergency department (ED) were enrolled. Patients younger than 20 years old, with cardiac arrest resulting from traumatic or circumstantial causes, with return of spontaneous circulation (ROSC) before ED arrival, lacking record of initial blood gas analysis, and with do-not-resuscitate orders were excluded. The primary outcome of this study was neurological status at hospital discharge.

In total, 2034 patients with OHCA were enrolled. The majority were male (61.89%), and the average age was 67.8 ± 17.0 years. Witnessed OHCA was noted in 571 cases, cardiopulmonary resuscitation was performed before paramedic arrival in 512 (25.2%) cases, and a shockable rhythm was observed in 269 (13.2%). Blood pH from initial blood gas analysis remained an independent predictor of neurological outcome after multivariate regression.

Blood pH at early stages of ALS was an independent prognostic factor of post-OHCA neurological outcome. Blood gas analysis on arrival at the ED may provide additional information about the prognosis of patients with OHCA.

Abbreviations: ALS = advanced life support, CPC = cerebral performance category, CPR = cardiopulmonary resuscitation, ED = emergency department, OHCA = out-of-hospital cardiac arrest, ROC = receiver operating characteristic, ROSC = return of spontaneous circulation.

Keywords: blood gas analysis, blood pH value, cardiopulmonary resuscitation, neurological outcome, out-hospital cardiac arrest, return of spontaneous circulation

1. Introduction

The incidence rate of out-of-hospital cardiac arrests (OHCA) was approximately 9.11 per 10,000 person-years in Taiwan, with the survival rate after OHCA being approximately 3.9% to 4.6%.^[1-3] Advances in cardiopulmonary resuscitation (CPR) and postcardiac

arrest care have improved neurological outcomes in some patient cohorts.^[4-6] Depending on the underlying cause, survival rates with good neurological outcomes after OHCA varies from 0.9% to 14%.^[7] Many factors are associated with the prognosis of patients with OHCA, such as witnessed arrest, bystander CPR, and presence of shockable cardiac rhythm.^[8] OHCA survivors

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CHL and SHY contributed equally to the work.

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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experience high mortality if they have severe acidosis, as detected in blood gas analysis.^[9] Studies have mainly investigated the predictive value of blood pH after return of spontaneous circulation (ROSC). This application of blood pH during very early stages of CPR has rarely been discussed.

The current single-center retrospective observational study aimed to assess whether initial blood gas pH can predict neurological outcome in patients with OHCA. Factors associated with neurological outcomes of patients with OHCA were analyzed. The difference in the pH among subgroups were compared to explore the possible relationships between pH and OHCA.

2. Methods

2.1. Study design and setting

We conducted a retrospective observational study in the emergency department (ED) of China Medical University Hospital, an urban tertiary care hospital in Taichung, Central Taiwan. There are approximately 1625 general wards and 130 intensive care unit beds, and the ED received more than 160,000 visits in 2018. The population of Taichung was >2.8 million in 2018.

In Taichung, emergency medical technicians mainly provide airway and ventilation management with basic life support to patients with OHCA by using bag valve masks and laryngeal mask airways. Patients are shocked with automated external defibrillators at suggested cardiac rhythms. Moreover, advanced life support (ALS) is not performed in the prehospital resuscitation settings, and no prehospital epinephrine or sodium bicarbonate are administered. Patients with OHCA received ALS resuscitation after they arrive the ED. Patients with OHCA in this study had blood gas drawn within 5 minutes after ALS began. The physicians considered administering sodium bicarbonate according to initial blood gas analysis screening for metabolic acidosis and hyperkalemia. All patients received standard CPR following international guidelines of American Heart Association.^[10]

This study was approved by the Institutional Review Board of China Medical University Hospital.

2.2. Study population and data collection

All patients with OHCA who were sent to the ED of China Medical University Hospital from January 1, 2012, to June 30, 2018, were enrolled for the initial analysis. Patient information was recorded according to the Utstein template. Information was collected retrospectively, including age, sex, patient visiting date and time, initial cardiac rhythm, CPR duration, time of ROSC, whether the patient received bystander CPR, whether an AED was used, initial blood gas pH value, and neurological functional status at hospital discharge. These data were collected by a nurse of ED and were verified by another ED's nurse practitioner for accuracy. Exclusion criteria were as follows: age younger than 20 years; cardiac arrest from specific causes, such as trauma, hanging, drowning, intoxication, or asphyxia; ROSC before ED arrival; no record of initial blood gas analysis; and presence of do-not-resuscitate orders. These criteria were implemented by the study assistant from tertiary center.

2.3. Outcome measurement

The primary outcome of this study was neurological status at hospital discharge. Neurological status was assessed using the

cerebral performance category (CPC) system.^[11] Neurological status was described based on CPC scores of 1 to 5: good cerebral performance (score 1), moderate cerebral disability (score 2), severe cerebral disability (score 3), coma or vegetative state (score 4), and death (score 5).^[12] Favorable and unfavorable neurological outcomes were defined as CPC 1 to 2 and CPC 3 to 5, respectively. Neurological functional status was recorded in the hospital's electrical medical record for all patients with OHCA on discharge. The secondary outcome of this study was the proportion of sustained ROSC and survival hospital discharge. Sustained ROSC is the return of circulation in the ED for at least 2 hours.

2.4. Statistical analysis

To analyze the relationship between variables and neurological outcomes, patients were divided into 2 groups according to their neurological outcomes. Differences between the 2 groups were analyzed through χ^2 testing for categorical variables and independent-sample *t* testing for continuous variables. Furthermore, univariate analysis was used to identify the variables associated with neurological outcome. Significant variables were entered into a stepwise backward logistic regression analysis. Independent Student *t* testing was used to assess different pH values among subgroups.

To measure concordance levels of pH values on neurological outcome in patients with OHCA, we constructed a receiver operating characteristic (ROC) curve and calculated the corresponding area under the curve. Youden J statistic was used to select the optimum cut off for continuous variables.^[13] All statistical assessments involved two-tailed testing. Statistical significance was defined as $P < .05$. All statistical analyses were performed with SAS (version 9.4; SAS Institute, Cary, NC).

3. Results

In total, 3135 patients with OHCA were referred to China Medical University Hospital from January 2012 to June 2018, as shown in Figure 1. Among the 2872 patients who received CPR, 96 (3.1%) were excluded because they were younger than 20 years, 249 (7.9%) were excluded because they had ROSC before entering the ED, 180 (5.7%) because their cardiac arrests were related to caused excluded from the study, and 275 (8.8%) because they lacked initial blood gas results. Missing data resulted in 38 patients being excluded. In total, 2034 patients with OHCA were enrolled for outcome analysis, of which 1564 (76.9%) had cardiac arrests at home, 571 (28.1%) were witnessed, and 512 (25.2%) received bystander CPR. In addition, 269 (13.2%) cardiac arrests were shockable; moreover, in 609 (34.3%) cases, ROSC after ED treatment was noted. Finally, 189 (9.3%) patients were discharged alive, and 70 (3.4%) had favorable neurological outcomes.

Of the 2034 patients with OHCA, 698 patients achieved ROSC and 70 patients had favorable neurological outcomes. The 70 patients with favorable outcomes were younger than the 1964 patients with unfavorable outcomes (55.29 ± 15.54 vs 68.24 ± 16.82 years, $P < .001$) and had higher prevalence of initial shockable rhythm (53% vs 12%), witnessed cardiac arrest (64% vs 27%), and higher initial pH values (7.13 ± 0.19 vs 6.98 ± 0.17 ; all $P < .001$; Table 1).

According to the univariate analysis, age, sex, initial heart rhythm, cardiac arrest location, whether the cardiac arrest was

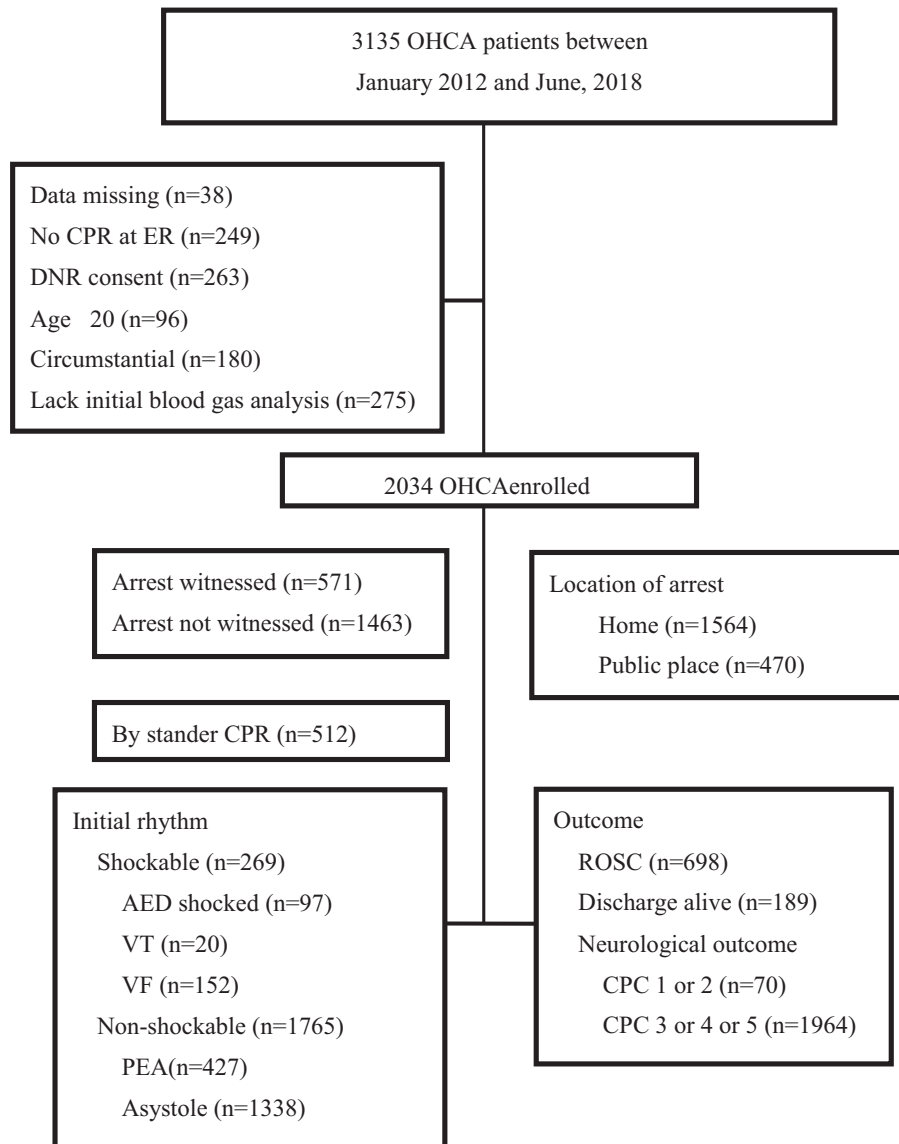


Figure 1. Patients enrollment. CPC = cerebral performance category, CPR = cardiopulmonary resuscitation, DNR = do-not- resuscitate, OHCA = out-of-hospital cardiac arrest, PEA = pulseless electrical activity, ROSC = return of spontaneous circulation, VF = ventricular fibrillation, VT = ventricular tachycardia.

witnessed, whether the patient received bystander CPR, and initial ED blood gas pH were associated with neurological outcomes after OHCA. Furthermore, age, initial heart rhythm, whether the cardiac arrest was witnessed, and initial ED blood gas pH remained significant in multivariate analysis after logistic regression. Multivariate analysis indicated no significance between sex, cardiac arrest location, and bystander CPR and neurological outcome (Table 2).

We compared initial blood pH among subgroups (shown in Table 3.) demonstrates that blood gas pH analysis was significantly associated with sustained ROSC, survival discharge, and favorable neurological outcomes of patients with OHCA.

We calculated levels of sustained ROSC, survival hospital discharge, and favorable neurological outcome among blood pH intervals. As displayed in Figure 2, the prognosis of patients with OHCA improved as the pH approached 7.4.

The ROC curve of pH on neurological outcome in patients with OHCA is presented in Figure 3. The corresponding area

under the ROC curve was 0.7316, which indicated good predictive value for early pH. The best cut off of pH using Youden J statistic was 7.0, with 71.43% sensitivity and 61.76% specificity.

4. Discussion

This study revealed that pH obtained from blood gas analysis at ALS onset is associated with the prognosis of patients with OHCA. Studies have rarely reported on the predictive value of early blood pH in patients with OHCA. Patients with higher pH are more likely to have better ROSC rates, surviving discharge rates, and favorable neurological outcomes than were patients with lower blood pH.

A key factor affecting the neurological outcomes of patients with OHCA is the duration of low-flow and no-flow durations.^[5,14] Respiratory acidosis and hypoperfusion induces lactic acidosis after cardiac arrest, which directly reflect on initial ED

Table 1
Demographic data of different neurological outcomes.

Variable	CPC level		P value
	1-2 (n=70)	3-5 or mortality (n=1964)	
*Age	55.29 ± 15.54	68.24 ± 16.82	<.001
*Gender			.003
Male	55 (4.37)	1204 (95.63)	
Female	15 (1.94)	760 (98.06)	
*Initial rhythm			<.001
Asystole/PEA	33 (1.87)	1732 (98.13)	
VT/VF	37 (13.75)	232 (86.25)	
Home arrest			<.001
No	30 (6.38)	440 (93.62)	
Yes	40 (2.56)	1524 (97.44)	
Witness			<.001
No	25 (1.71)	1438 (98.29)	
Yes	45 (7.88)	526 (92.12)	
Bystander CPR			.018
No	44 (2.89)	1478 (97.11)	
Yes	26 (5.08)	486 (94.92)	
pH	7.13 ± 0.19	6.98 ± 0.17	<.001

* P < .05.
VT = ventricular tachycardia, VF = ventricular fibrillation.

blood gas pH values.^[6,9,15-17] The pCO₂ level obtained within 4 minutes of initiating CPR is an independent predictor of sustained ROSC in patients with OHCA.^[17] Among patients with ROSC after OHCA, patients with favorable outcomes had lower lactate and higher pH than did those with unfavorable outcomes.^[15] We also found that initial blood pH was an independent predictor of neurological outcome in patients with OHCA. Moreover, patients with initial shockable rhythm, who experienced cardiac arrest in public places, and whose cardiac arrests were witnessed had higher blood pH. Therefore, blood pH can represent a low-flow and no-flow durations in patients with OHCA and could influenced the neurological outcomes of patients with OHCA.

Table 2
Univariate and multivariate logistic regression analysis of predictors for unfavorable neurological outcomes.

Variables	Univariate		Multivariate	
	OR (95% CI)	P value	Adjusted-OR (95% CI)	P value
*Age	1.04 (1.03-1.06)	<.001	1.04 (1.02-1.05)	<.001
Gender				
Female	Ref.	-	Ref.	-
Male	0.43 (0.24-0.77)	.004	0.71 (0.38-1.32)	.282
*Rhythm				
VT/VF	Ref.	-	Ref.	-
Asystole/PEA	8.37 (5.13-13.65)	<.001	3.99 (2.33-6.81)	<.001
*pH	0.02 (0.01-0.05)	<.001	0.03 (0.01-0.13)	<.001
Home arrest				
No	Ref.	-	Ref.	-
Yes	2.60 (1.60-4.22)	<.001	1.34 (0.78-2.29)	.284
*Witness				
Yes	Ref.	-	Ref.	-
No	4.92 (2.99-8.11)	<.001	3.29 (1.89-5.71)	<.001
Bystander CPR				
Yes	Ref.	-	Ref.	-
No	1.80 (1.10-2.95)	.020	0.97 (0.55-1.72)	.920

* P < .05.
VT = ventricular tachycardia, VF = ventricular fibrillation.

Table 3
Subgroup analysis.

Subgroup	pH	P value
First rhythm		<.001
non-Shockable (N=1765)	6.97 ± 0.16	
Shockable (N=269)	7.06 ± 0.18	
Location		<.001
Home (N=1564)	6.97 ± 0.17	
Public place (N=470)	7.02 ± 0.17	
Witness		<.001
No (N=1463)	6.97 ± 0.16	
Yes (N=571)	7.03 ± 0.17	
Bystander CPR		.424
No (N=1522)	6.99 ± 0.17	
Yes (N=512)	6.98 ± 0.17	
Sustained ROSC		<.001
No (N=1336)	6.96 ± 0.16	
Yes (N=698)	7.03 ± 0.17	
Survival discharge		<.001
No (N=1845)	6.98 ± 0.17	
Yes (N=189)	7.08 ± 0.17	
Good CPC outcome		<.001
No (N=1964)	6.98 ± 0.17	
Yes (N=70)	7.13 ± 0.19	

* P < .05.

Older age was associated with less favorable neurological outcomes in patients with OHCA after adjustment for covariates in 2 studies.^[18,19] Those whose cardiac arrests were unwitnessed and asystole before and after hospital arrival experienced poor outcomes.^[20,21] The current study noted that age, initial rhythm, and whether cardiac arrest was witnessed were independent predictors, as reported previously.^[14,18-20,22-24] Studies have emphasized the value of bystander CPR and dispatcher-assisted CPR.^[15,20,25,26] However, the rate of bystander CPR and cardiac arrest in public locations in Taichung was lower than that reported previously. Quality of bystander CPR differed among

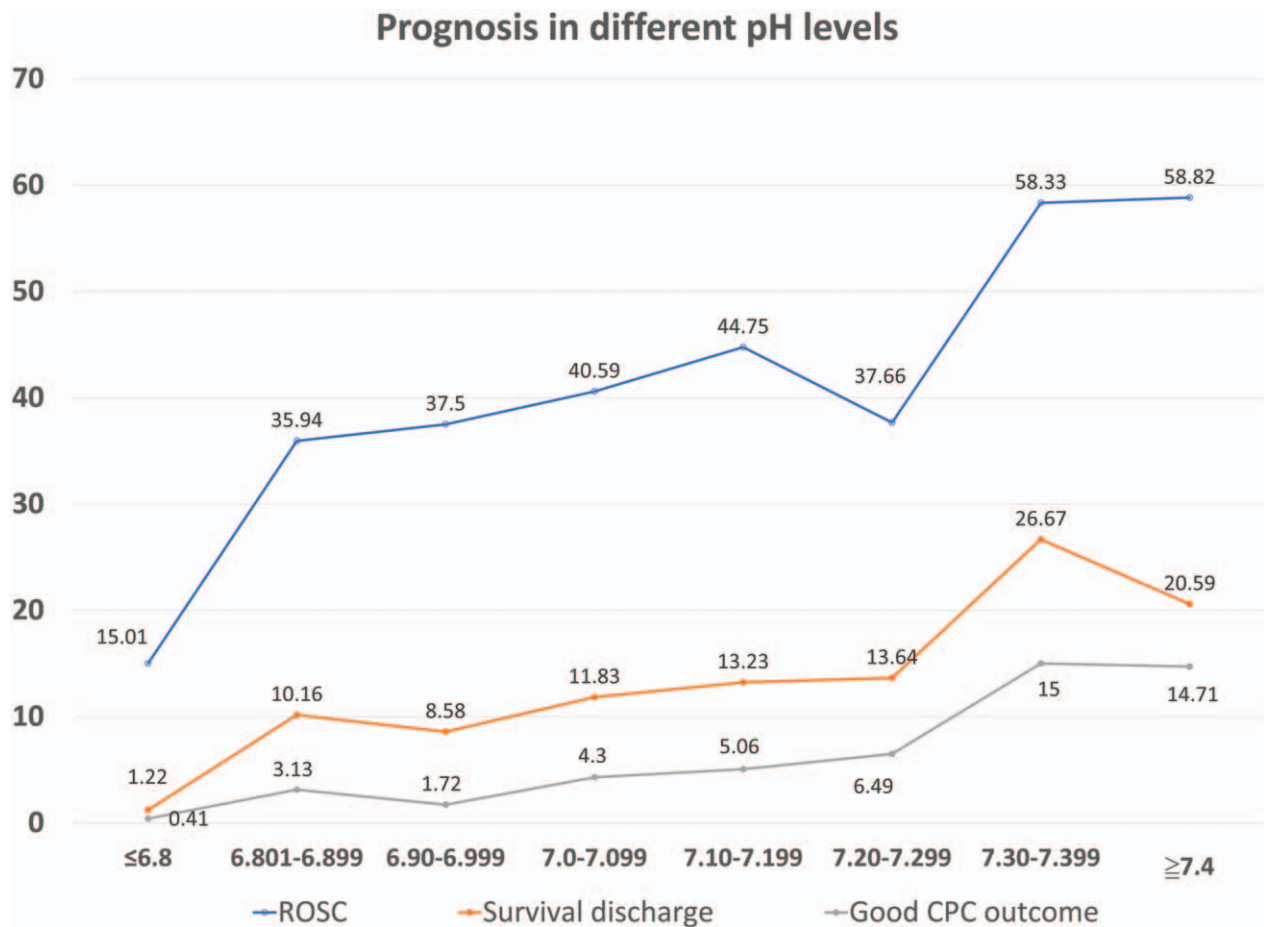


Figure 2. Patient’s prognosis in different pH levels from early stage of advanced life support OHCA patients are stratified according to the different pH values obtained from blood gas analysis within 5 minutes after the start of advanced life support. The chance of return of spontaneous circulation in patients with a pH value of less than 6.8 is 15.01%, while that of patients with a pH value of greater than 7.4 is 58.82%. Of the patients whose initial pH value was greater than 7.4, 20.59% survived to hospital discharge. However, only 1.22% of patients survived with an initial pH value less than 6.8. Among patients with an initial pH value greater than 7.4, 14.71% patients had favorable neurological prognosis. When the initial pH value was lower than 6.8, only 0.41% of patients had favorable neurological prognosis.

individuals and was difficult to assess. Public health information differs between urban and rural areas. For various reasons, bystander CPR contributed to the prognosis of patients with OHCA; however, no significant difference was noted after multivariate adjustment.

Our study has several limitations. First, we studied a single urban tertiary care hospital in Central Taiwan. The diversity and severity of patients in this single center were limited. We only enrolled patients with blood gas analysis within 5 minutes of ALS. These restrictions may have led to selection bias. However, the relatively large study population may minimize the effects of such selection bias. Second, in our research protocol, arterial or venous blood samples may be used for blood gas analysis during resuscitation. The degree of metabolic acidosis between arterial blood and venous blood may be slightly different, which may affect the results of the study. However, some previous studies have concluded that the venous and arterial pH and bicarbonate are reasonably consistent at all values.^[21,27] Even though specific causes of cardiac arrest, such as asphyxia and drowning, were excluded, the magnitude of neurological influence on respiratory acidosis could not be determined. Third, 275 (8.8%) patients

were excluded because of a lack of initial blood gas analysis, which may have led to information bias. Finally, we excluded patients who had ROSC before arrival at the ED, which led to a relatively low ROSC rate and a low proportion of favorable neurological outcomes. However, excluding these patients allowed us to understand the effects of pH on prognosis in patients with OHCA that received ALS.

Researchers have reported that sodium bicarbonate affected the metabolic acidosis of patients with OHCA.^[28–30] A study reported that of 13,865 patients with OHCA, 5165 treated with prehospital sodium bicarbonate had lower survival rates and poorer neurological outcomes at hospital discharge.^[28] Administration of sodium bicarbonate during ED resuscitation was significantly associated with an increased rate of survival to hospital admission in another nationwide study in Taiwan.^[29] However, the clinical benefits of sodium bicarbonate on neurological outcomes for patients with OHCA have not been established. The efficacy of sodium bicarbonate in patients with OHCA remains uncertain. We aim to conduct future studies to explore the effects of sodium bicarbonate on patients with different pH values.

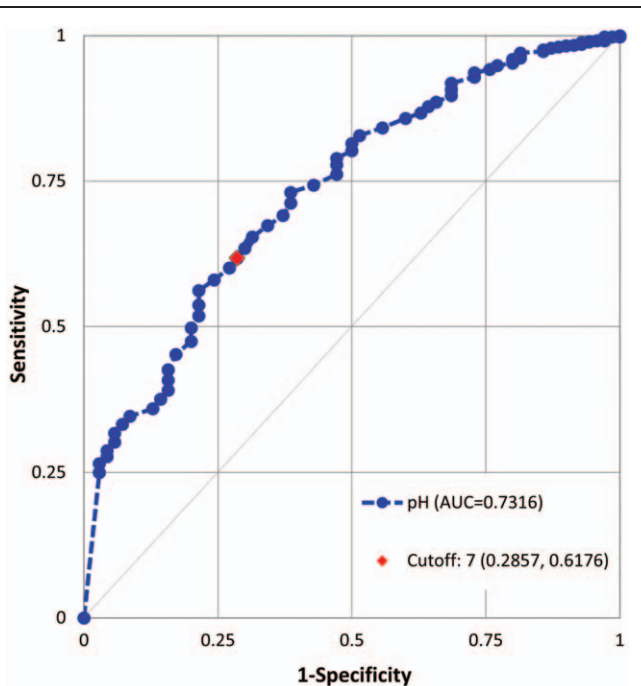


Figure 3. Receiver operating characteristic curve. The receiver operating characteristic (ROC) curve for good neurological outcome and initial blood pH value. The Area under the Curve is 0.7316. The best cut off pH by Youden index is 7.0.

5. Conclusions

Blood pH at early stage of ALS on ED arrival could be an independent prognostic factor of neurological outcome after OHCA. Blood gas analysis on ED arrival may provide additional information on the prognosis of patients with OHCA.

Author contributions

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Project administration: Hong-Mo Shih.
Resources: Shao-Hua Yu.
Supervision: Wei-Kung Chen.
Validation: Hong-Mo Shih.
Writing – original draft: Chin-Han Lin, Shao-Hua Yu.
Writing – review & editing: Chih-Yu Chen, Hong-Mo Shih.

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