Successful resuscitation of out of hospital cardiac arrest patients in the emergency department

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ABSTRACT

Background. We examined factors associated with the successful resuscitation, in the emergency department (ED), of adult, out-of-hospital cardiac arrest (OHCA) patients.

Methods. The study cohort consisted of adult patients (over 18 years of age) who presented to the ED in 2009 with a diagnosis of cardiac arrest. Data were retrieved from the institutional database.

Results. A total of 122 adult, non-traumatic, OHCA patients were enrolled in the study. There were no significant differences between the sustained return of spontaneous circulation (ROSC) and non-sustained ROSC groups in initial body temperature (P = 0.420), time to successful intubation (P = 0.524), time to first intravenous epinephrine injection (P = 0.108), blood sugar levels (P = 0.122), hematocrit (P = 0.977), cardiac enzymes (P = 0.116) and serum sodium level (P = 0.429). Leukocytosis (P = 0.047) and cardiac rhythm of pulseless ventricular tachycardia/ ventricular fibrillation and pulseless electrical activity (P = 0.022), were significantly associated with sustained ROSC. In contrast, patients with more severe acidosis (P = 0.003) and hyperkalemia (P < 0.001) had a reduced likelihood of achieving sustained ROSC. After multiple variable logistic regression analysis adjusting for variables, the correlation between sustained ROSC and leukocytosis and hyperkalemia remained high (leukocytosis, P = 0.007, odds ratio [OR] 3.655, 95% CI 1.422-9.395; hyperkalemia, P = 0.001, OR 0.169, 95% CI 0.057-0.500)

Conclusion. Patients suffering an OHCA were appropriately resuscitated after arriving at the ED. Successful resuscitation in adult OHCA victims was determined by the patient's status, in particular their white blood cell count and potassium level.

Introduction

Background

Out-of-hospital cardiac arrest (OHCA) poses a difficult challenge for emergency physicians. The survival rate of out-of-hospital cardiac arrest patients is low, ranging from 1.7% to 6.1%. (1–4) Identification of the factors associated with sustained return of spontaneous circulation (ROSC) in adult OHCA victims may help emergency physicians to deal more effectively with such cases. Predictors of sustained ROSC in cases of adult OHCA include witness of collapse, initial cardiac rhythm, bystander cardiopulmonary resuscitation (CPR), early start of emergency medical system (EMS), early defibrillation, and a short duration of transportation. (5–9) These predictors have been studied during the pre-hospital phase and may not be available when patients arrive at the emergency department (ED). However, no previous reports have examined factors associated with ROSC in adult OHCA patients during the in-hospital phase, which may be useful as parameters for predicting the effects of resuscitation, and may aid in the further improvement of treatment methods or interventions.

Therefore, the aim of our study is to determine the factors associated with sustained ROSC in adult OHCA patients during the in-hospital phase. We hypothesized that the factors associated with sustained ROSC in adult OHCA victims, after arriving at the ED, could help physicians improve resuscitation and predict the outcome.

Methods

Study Design and Setting

This was a retrospective cohort study conducted at a university-affiliated teaching hospital with an annual ED case load of 227,000 visits. This study was approved by the Hospital Ethics Committee on Human Research. The study protocol was reviewed and
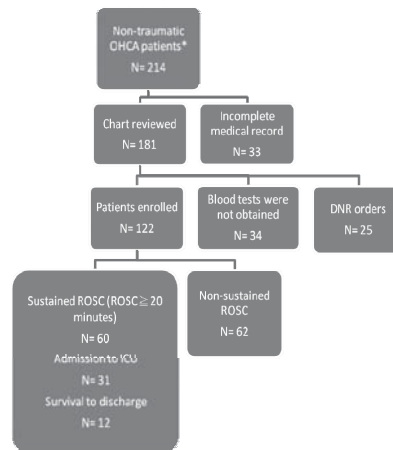
DNR, Do-not-resuscitate; ICU, Intensive care unit; OHCA, out of hospital cardiac arrest; ROSC, return of spontaneous circulation.

Figure 1. Patient eligibility. Numbers of patients included and excluded from the study.
*Adults, over 18 years of age, with ICD-9CM codes for cardiac arrest 7981, 7982 and 7989, were included. Patients who were not resuscitated due to 'do-not-resuscitate (DNR)' orders and those with incomplete or lost documentation were excluded.

deemed exempt from the requirement to obtain informed consent.

Patient selection

The study cohort consisted of adult patients over 18 years of age who presented to the ED of a teaching hospital between January 1, 2009, and December 31, 2009 with the main diagnosis of cardiac arrest. Patients with International Classification of Disease, 9th revision and Clinically Modified (ICD-9-CM) Diagnosis Code 798 Cardiac Arrest were included in the study. Patients with ICD-9CM Diagnosis Code 798.0 (Sudden Infant Death Syndrome), those who received no resuscitation due to 'do-not-resuscitate (DNR)'orders, and those for whom documentation was incomplete or had been lost were excluded from the study. We reviewed 214 cases and excluded 92 patients based on the exclusion criteria; thus, 122 patients were enrolled in this study. Sustained ROSC was achieved in 60 (49.1%) patients, and 31 (25.4%) were admitted to the intensive care unit, with 12 (9.8%) surviving to discharge. Among the 92
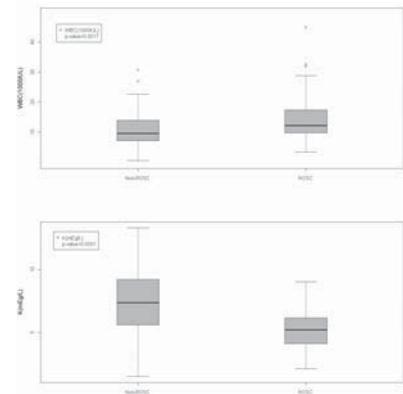
Figure 2. White blood cell count and serum potassium level in non-ROSC and sustained ROSC groups. (Gray box: 1st quartile - 3rd quartile, Thick line: median, Lower end line: 1st quartile-1.5 median, Upper end line: 3rd quartile+1.5 median, point: outlier).

excluded patients, 33 had incomplete medical records, 25 had DNR orders, and blood tests were not obtained in 34 (figure 1).

Study protocol

OHCA patients were identified at triage or based on information provided by the EMS. Advance cardiac life support (ACLS) was implemented according to the 2005 America Heart Association (AHA) guidelines and included chest compression and emergent endotracheal intubation with mechanical ventilator support, intravenous injection of epinephrine, and cardioversion accordingly. (10) A blood sample was collected and sent for laboratory tests, including blood gas analysis, complete blood cell count, and biochemical studies. Sustained ROSC is defined as 20 consecutive minutes of signs of circulation without chest compression. (11) Patients with sustained ROSC are then transferred to intensive care units for further care as indicated. Survival to discharge was defined as being discharged alive or able to be transferred to a long-term care centre.

Measurements

We reviewed the charts and collected the following variables in relation to the subjects' ED visits: patient demographics (age, sex, transportation, and

Table 1. Patient characteristics between sustained and non-sustained ROSC groups in non- traumatic OHCA patients.

Sustained ROSC	No (n=62)	Yes (n=60)	p-value
Gender			0.064
Male	46	35	
Female	16	25	
Median age in years (IQR)	71.5 (56 – 83)	73.5 (59 – 84)	0.424
Mode of transportation			0.12
EMS	42	34	
Family	17	12	
Other	3	14	
Witness collapse	28	42	0.006
Bystander CPR	9	15	0.145
Cardiac rhythm at ED			0.022
Asystole	54	40	
VF/ pulseless VT	2	8	
PEA	6	12	

CPR, cardiopulmonary resuscitation; ED, emergency department; EMS, emergency medical service; IQR, interquartile range; OHCA, out of hospital cardiac arrest; PEA, pulseless electrical activity; ROSC, return of spontaneous circulation; VF, ventricular fibrillation; VT, ventricular tachycardia.
Categorized variables are given as number of patients.
Variable test using Chi-square test (Gender, Mode of transportation, Witness collapse, Bystander CPR, Cardiac rhythm), and Two sample t-test (Age).

Table 2. Findings and timing of resuscitation interventions between sustained and non-sustained ROSC groups in non-traumatic OHCA patients after arriving at the ED.

Sustained ROSC	No (n=62)	Yes (n=60)	p-value
Mean initial Body temperature, (SD)	35.2 (1.92)	35.4 (1.15)	0.420
Timing of resuscitation interventions			
Median time to successful intubation, minutes (IQR)	2 (1 – 5)	2 (1 - 3)	0.524
Median time to intravenous adrenaline injection, minutes (IQR)	2 (1 – 5)	2 (1 – 3)	0.108
Median time to Blood drawing, minutes (IQR)	10 (6 -12)	7 (2 - 14)	0.838
Laboratory tests			
Blood gas, mean (SD)			
pH	6.9 (0.24)	7.0 (0.21)	0.003
$PaCO_2$, mmHg	79.1 (49.03)	66.3 (29.26)	0.338
Bicarbonate, mm/L	14.5 (7.60)	17.8 (9.69)	0.090
Capillary blood glucose , mg/dL	224.1 (147.54)	261.2 (127.26)	0.122
White blood cell (WBC), 1000/uL	10.7 (5.56)	14.6 (7.61)	0.001
Hematocrit, %	32.0 (12.32)	31.9 (7.78)	0.977
Creatinine, mg/dL	3.3 (6.19)	1.9 (1.29)	0.040
Sodium, mEq/L	140.0 (9.80)	139.6 (11.23)	0.449
Potassium, mEq/L	7.4 (2.45)	5.3 (1.56)	<0.001
AST, U/L	409.9 (983.48)	313.2 (1289.25)	0.068
Creatine Kinase-MB, ng/mL	11.9 (30.18)	6.9 (8.94)	0.488
Troponin I, ng/mL	0.8 (2.18)	0.4 (0.98)	0.116

AST, aspartate aminotransferase; ED, emergency department; IQR, interquartile range; OHCA, out of hospital cardiac arrest; ROSC, return of spontaneous circulation; SD, standard deviation; WBC, white blood cell.
Variable test using Mann-Whitney U test (time to successful intubation, time to intravenous adrenaline injection, PaCO2, bicarbonate, capillary blood glucose , white blood cell, creatinine, AST, creatine kinase-MB, troponin I), and two sample t-test (initial body temperature, time to blood drawing, pH, hematocrit, sodium, potassium).

Table 3. Logistic regression analysis of factors related to sustained ROSC (ROSC 20 minutes) in non-traumatic OHCA patients.

	Odds ratio	95% Confidence Interval	P-value
Cardiac rhythm in the ED			
Pulseless VT/VF	2.472	0.379-16.131	0.344[a]
PEA	1.849	0.518-6.602	0.344[b]
Witness of collapse	2.294	0.922-5.705	0.074
pH determined by blood gas analysis	1.446	0.158-13.276	0.744
Leukocytosis*	3.655	1.422-9.395	0.007
Creatinine	0.943	0.776-1.145	0.552
Hyperkalemia*	0.169	0.057-0.500	0.001

ED, emergency department; OHCA, out of hospital cardiac arrest; PEA, pulseless electrical activity; ROSC, return of spontaneous circulation; VF, ventricular fibrillation; VT, ventricular tachycardia.
a The comparison between asystole and VF/VT
b The comparison between asystole and PEA
*Leukocytosis : WBC count > 11000/uL, Hyperkalemia: serum potassium level > 5.5 mEq/L

underlying disease), witness of collapse, bystander CPR, mode of transportation to the hospital (sent by family, start EMS with ambulance, or others), initial cardiac rhythm at the ED, initial body temperature, time to successful intubation (minutes), time to intravenous epinephrine injection (minutes), time to blood drawing for laboratory tests (minutes), laboratory test results including capillary blood glucose , pH, bicarbonate, $PaCO_2$ determined by blood gas analysis, white blood cell count, hematocrit, serum sodium, serum potassium, aspartate aminotransferase (AST), creatinine, serum creatine kinase-MB, and serum troponin-I.

Statistical Tests

The data were analysed using SPSS 13.0 for Windows (SPSS, Chicago, IL). Factors associated with sustained ROSC were analysed using the Pearson Chi-square test. The two-tailed t-test or Mann–Whitney U-test was used for continuous variables as indicated. Multivariate binary logistic regression analysis was used to identify independent factors associated with sustained ROSC. In all analyses, $P < 0.05$ was taken to indicate statistical significance.

Results

A total of 122 adult, non-traumatic, OHCA patients were enrolled in this study. Table 1 demonstrates patient characteristics of the sustained and non-sustained ROSC group. The median age of the patients was 73 years (interquartile range, IQR: 56 - 83 years), and the cohort included predominantly men (81 patients, 66.4%). Witness of collapse occurred in 70 (57.4%) cases, with 24 (19.6%) patients receiving bystander CPR. EMS was started in 76 (62.3%) cases. An automatic external defibrillator (AED) was applied in 50 cases, with electrical defibrillation in only one case. The most common initial rhythm seen at the ED was asystole (77.0%), followed by pulseless electrical activity (PEA) (14.8%) and pulseless ventricular tachycardia (VT) or ventricular fibrillation (VF) (8.2%). The underlying diseases among the enrolled patients were as follows: stroke, 28.9%; diabetes mellitus, 28.7%; lung disease, 23%; heart disease, 22.1%; chronic kidney disease, 16.3%; and liver disease, 7.3%. A witnessed collapse ($P = 0.006$) and pulseless VT, VF, and PEA in the ED ($P = 0.022$) were significantly different between the two groups. More patients had received bystander CPR in the sustained ROSC group, but the difference was not statistically significant ($P = 0.145$).

The findings and timing of resuscitation interventions between the two groups after arriving at the ED are shown in table 2. There were no significant differences in initial body temperature at triage ($P = 0.42$), timing of successful intubation ($P = 0.524$), timing of the first intravenous epinephrine injection ($P = 0.108$), hematocrit ($P = 0.977$), and serum sodium level ($P = 0.429$) between the groups. Initial blood tests during resuscitation revealed a significant correlation between white blood cell count (WBC) count ($P = 0.001$), serum potassium level ($P < 0.001$), serum creatinine level ($P = 0.04$), pH value by blood gas analysis ($P = 0.003$), and sustained ROSC. More patients with leukocytosis (WBC count > 11000/uL) were noted in the sustained ROSC group with a statistically significant difference ($P = 0.047$). In contrast, patients with hyperkalemia (serum potassium level > 5.5 mEq/L) had a reduced likelihood of achieving sustained ROSC ($P <0.001$).

Higher blood sugar (mean ± SD: 224.1 ± 147.54 vs. 261.2 ± 127.26 mg/dL, $P = 0.122$) and lower cardiac enzyme levels (CK-MB, mean ± SD: 11.9 ± 30.18 vs. 6.9 ± 8.94 ng/mL, $P = 0.488$; troponin I, mean ± SD: 0.8 ± 2.18 vs. 0.4 ± 0.98 ng/mL, $P = 0.116$) were associated with sustained ROSC, but the relationships were not statistically significant.

Multiple variable logistic regression was used to analyse the factors related to sustained ROSC, including witness of collapse, cardiac rhythm at ED, pH determined by blood gas analysis, leukocytosis, hyperkalemia, and cre-

atinine levels (table 3). After logistic regression analysis adjusting for the variables mentioned above, the correlations of sustained ROSC and leukocytosis or hyperkalemia remained high (leukocytosis, $P = 0.007$, odds ratio [OR] 3.655, 95% confidence interval [CI] 1.422-9.395; hyperkalemia, $P = 0.001$, OR 0.169, 95% CI 0.057-0.500) (figure 2).

Discussion

In our study, victims of non-traumatic OHCA had received resuscitation adherent to guidelines equally after arriving at the ED. Airway management, chest compressions and establishment of peripheral venous access, with an epinephrine bolus, were done efficiently and without significant delay between the groups. There were several factors associated with sustained ROSC. First of all, although the precise time of onset of OHCA was mostly unavailable from the records, witness of collapse may indicate early resuscitation and was associated with sustained ROSC. We failed to demonstrate the effects of bystander CPR between the groups which may be due to the relatively low percentage of bystander CPR in our study population. Previous studies indicated that the percentage of bystander CPR in non-traumatic OHCA is around 32.5–36%. (1,12)

Second, despite the small proportion of PEA and pulseless VT/VF in non-traumatic OHCA on arrival at the ED, we found a correlation with sustained ROSC.

Hu et al. reported that only 4.1% of victims presented with pulseless VT and VF after arriving at hospital. (13) Ko et al. reported pulseless VT and VF as the initial rhythm in 11.8% of OHCA in Taipei, Taiwan. (14) The prevalence of coronary heart disease is lower in Taiwan in comparison with other studies. (15,16)

Third, there was a high prevalence of hyperkalemia in our study population. Those patients without hyperkalemia were more likely to achieve sustained ROSC. Potassium plays an important role in cardiac electri-

cal and contractile activity. Previous studies have shown that an increase in serum potassium occurs during cardiac arrest and prolonged CPR both in humans and animal models. (17–19) Several factors contribute to hyperkalemia in OHCA: 1) loss of intracellular high-energy phosphates, which occurs rapidly after the onset of ischemia, resulting in dysfunctional transcellular ionic exchange mechanisms; (20) 2) global hypoperfusion after cardiac arrest induces acidosis, which leads to potassium movement into the extracellular fluid; and 3) increased tissue breakdown by chest compression and electrical defibrillation could result in the release of potassium into the extracellular fluid. (19) Despite advances in cardiac life support, a vicious circle of hyperkalemia and cardiac arrest results in resuscitation failure. Current treatment of hyperkalemia includes calcium and sodium bicarbonate infusion, β_2-adrenergic agonist inhalation, insulin plus glucose water injection, and haemodialysis. Previous investigations failed to demonstrate a beneficial effect on resuscitation outcome of elemental calcium administration or sodium bicarbonate therapy during resuscitation. (21-24) However, there have been several reports of successful resuscitation and survival of hyperkalemia cardiac arrest in patients undergoing haemodialysis during cardiopulmonary resuscitation. (25,26) Although hyperkalemia may be the result of prolonged tissue ischemia, we propose reconsidering elemental calcium administration and sodium bicarbonate therapy during resuscitation. A further prospective randomised control study should be conducted to verify this proposal. Serum potassium level on arrival at the ED predicts prognosis and may be useful as a parameter to monitor the efficiency of resuscitative interventions.

Fourth, leukocytosis is a marker of inflammation and is commonly seen in infection or stress, such as myocardial infarction. (27–29) In our study, leukocytosis was significantly associated with sustained ROSC. None of

the previous reports addressed the relationship between WBC count and ROSC in OHCA. The present finding suggests that patients who were able to respond to acute stress with an inflammatory reaction may respond to resuscitation.

In contrast, we found no significant relationship between the severity of acidosis and sustained ROSC after adjusting for the variables mentioned above by binary logistic regression analysis. Combined respiratory and metabolic acidosis develops during cardiopulmonary arrest. Hypoxia-induced anaerobic metabolism generates lactic acid, and ventilatory failure causes carbon dioxide retention. The severity of acidosis worsens as the arrested state continues and may indicate the period of ischemia. (30) The severity of acidosis was reciprocally influenced by many factors, which may not be independent factors of sustained ROSC in OHCA.

According to the results of our study, the factors associated with sustained ROSC in adult OHCA victims were mainly determined by the patient's status of severity of illness. Initial serum potassium level and WBC count, after arriving at the ED, could serve as parameters of efficiency of pre-hospital resuscitation and predict the prognosis. The therapeutic implications of these observations remain to be determined. Further studies should focus on public awareness, bystander CPR and how to shorten the duration of transportation.

Limitations

The present study should be interpreted in the context of the following limitations. First, our study was retrospective, and the data were collected from a computer database and chart review. Although we made every effort to remain objective, possible errors may have been introduced. Second, this study was conducted in a university-affiliated teaching hospital, which may limit the general applicability of our findings. A comparative study with other systems would be of interest. Third, there was sampling bias due

to the large proportion of excluded patients who received no resuscitation due to DNR orders, failure to obtain blood test results, or incomplete documentation. Nevertheless, the characteristics of the patients enrolled and the results of resuscitation were similar to those in previous studies.

Conclusions

Non-traumatic OHCA patients were appropriately resuscitated, without significant delay, after arriving at the ED. Factors associated with sustained ROSC in adult OHCA were determined by the patient's status after arriving at the ED, in particular their white blood cell count and potassium level.

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