

# Intravenous Fluid Administration and the Survival of Pre hospital Resuscitated out of Hospital Cardiac Arrest Patients in Thailand

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## ABSTRACT

**Introduction:** Out of Hospital Cardiac Arrest (OHCA) is a leading cause of death worldwide. The Emergency Medical Service (EMS) provides early care to critical OHCA patients. Pre hospital intervention has been improving OHCA survival rate, however it is still unclear for the recommendation of routine infusion of Intravenous (IV) fluids during cardiac arrest resuscitation.

**Aim:** This study aimed to determine whether IV fluid administration was associated with increasing survival of resuscitated OHCA patients and to assess the survival rate of resuscitated OHCA patients.

**Materials and Methods:** This cross-sectional analytical study was conducted among 33,006 resuscitated OHCA patients who received emergency medical service in Thailand. Data set from the EMS Registry of the OHCA patients who received Advanced Life Support (ALS) and Cardiopulmonary Resuscitation (CPR) during January 2011 to December 2015 was enrolled as per inclusion criteria. Data were analysed by using both descriptive statistic and multiple logistic regression.

**Results:** The result indicated that 27,270 OHCA patients (82.62%:95%CI=82.121-83.030%) survived until they reached hospital. In addition, after adjusting for effect modifiers and covariates, it was found that adult ( $\geq 18$  years) with IV fluid administration were more likely to survive (adjusted OR=4.389; 95% CI: 3.911-4.744) when compared to children (<18 years) with IV fluid administration (adjusted OR =2.952; 95% CI: 2.040-4.273). Other factors associated with OHCA patients' survival were female gender (adjusted OR =1.151; 95% CI: 1.067-1.241), response time per minutes (adjusted OR =0.993; 95% CI: 0.989-0.997), scene time per minutes (adjusted OR=0.948; 95% CI: 0.944-0.952) and transport time per minutes (adjusted OR=0.973, 95%CI: 0.968-0.978).

**Conclusion:** This study revealed that IV fluid administration was significantly associated with survival of OHCA patients while controlled other covariates including female gender, response time, scene time and transport time. Therefore, it is recommended that the IV fluid administration should be medicated for resuscitated OHCA patients.

**Keywords:** Advanced life support, Response time, Scene time, Transport time

## INTRODUCTION

OHCA is a leading cause of death worldwide. Over the past decade, the systems have been developed to improve the quality of OHCA care. However, the survival rate to hospital discharge for OHCA patients is still poor and it was reported that the survival rate was between 0.5%-10.4% [1-4]. Previous studies identified factors affecting survival of OHCA patients, including: CPR, gender, age, location where arrest occurred, time of the day on pre hospital care, response time, scene time, transport time, Automated External Defibrillator (AED) application, and IV fluid administration. In addition, these factors may be associated with survival rate of OHCA patients in rather complicated ways [5-12].

IV fluid loading is commonly performed during pre hospital resuscitation for OHCA patients in Thailand. Studies indicated that IV fluid administration was associated with improvement in survival rate to hospital discharge of children with OHCA and it improved one month survival of adult OHCA patients with non cardiac origin [9,10]. Studies among pediatric OHCA patients and non cardiac arrest origin of OHCA patients indicated that improving pre hospital survival was related to IV fluid administration and pre hospital intervention care [9,10]. It is, yet, unclear that IV fluid administration could improve survival rate of OHCA. There is insufficient evidence whether to recommend infusion of IV fluids during cardiac arrest resuscitation by ALS or not [13]. Investigation of the effect on IV fluid administration to survival of OHCA patients is still needed. Therefore, this study aimed to determine whether IV fluid administration was

associated with the improvement of survival rate of OHCA patients in Thailand.

## MATERIALS AND METHODS

### Ethical Consideration

An informed consent was taken from visitors of each respondent because it all respondents were critically ill. Ethical clearance was approved by Khon Kaen University Ethics Committee for human research with the reference number HE592021. Permission to undertake this study was obtained from National Institute for Emergency Medicine, Thailand.

### Study Design

This cross-sectional analytical study was conducted using data from the national emergency medical service registry of the National Institute for Emergency Medicine (NIEM), Thailand. Data considered in the present study were from OHCA patients receiving CPR by ALS teams between January, 2011 and December, 2015; OHCA patients receiving CPR but died before arrival to a hospital were excluded.

Patient's age and IV fluid were considered as potential effect modifiers of the outcome. Patients were stratified by age group of children and adult groups (<18, and  $\geq 18$ -year-old) and IV fluid (received or not). Variables considered in the present study were: (1) Patient factors: age, gender, period of pre hospital care (day/

night); (2) EMS factors: response time (from receiving a call to arrival at the scene), scene time (from arrival to departure from the scene), transport time (from scene to arrival at the hospital), were mentioned in minutes; and (3) Therapeutic factors: AED or Defibrillator (DF) and intravenous fluid administration.

The primary outcome of this study was survival rate to the hospital. Survival rate to the hospital was defined as OHCA patients who received resuscitation and did not pass away before arrival to the hospital and those patients who were dying on scene after the ALS team had arrived or during transportation after unsuccessful resuscitation were considered as "not survived" [14]. Thus, those who were passing away before the arrival of the ALS teams on the scene were excluded.

## STATISTICAL ANALYSIS

All variables were summarized by using descriptive statistics with frequencies (percentages) for categorical variables, and means standard deviations for continuous variables. The age categories (<18 and ≥18 years) were chosen based on clinical rationale and to match previous study [15-17]. Categories of time of day on pre hospital care (day: 8.30 am to 4.30 pm, night: 4.31 pm to 7.29 am) was defined by the time EMS personnel working, office hours of hospital and match previous study [7,18]. Crude OR as well as adjusted OR was obtained by using binary mixed effects logistic regression. The best model was identified using the purposeful selection of covariates approach [19]. Multivariable logistic regression was conducted by considering all covariates and interaction terms (age\* IV fluid). Purposeful Selection of Covariates (PSC) is later involved on the process. Briefly, PSC allowed all "potentially" important variables in to the model ( $p < 0.25$ ) then was sequentially excluded for reasons of non statistical significance and also rechecked their statistical significance in further steps along with their potential for inclusion as a confounders. As, IV fluid and age group were the study effect, these predictors were mandatory included into the model. All statistical analysis was conducted using Stata version 13.0 (Stata Corp, College Station, TX).

## RESULTS

The Thai EMS database of 2011-2015 reported 35,305 OHCA patients. However, only 33,006 OHCA patients received CPR. Therefore, only these patients were selected to include in this study. In the critical situation of death or alive of the patients, the rescue team were more focused on life saving and sending them to the hospital. Therefore, few data, such as age and sex were improperly recorded. Although, we have analysed the available data and the data were handled properly for missing values during analysis.

Of the total 33,006 OHCA patients who received CPR, 90.36% aged ≥18 years, 70.5% were male; 82.62% (95% CI= 82.121-83.030) survived to the hospital. Most of the OHCA occurred at night (61.29%). The mean response time was 10.9±8.9 minutes), mean scene time was 7.3 ±8.3 minutes), and mean transport time was 8.3±7.3 minutes). In addition, 7.4% had AED. Almost all (91.2%, 30,088 patients) received IV fluid [Table/Fig-1]. In bivariate analysis, patients who received IV fluids had higher odd of survival (OR=3.935, 95% CI: 3.631-4.263), as well as female patients OR=1.098, 95% CI: 1.026-1.175). The increased response time (per minute) (OR=0.984, 95% CI: 0.981-0.986), scene time (per minute) (OR=0.943, 95% CI:0.939-0.946), transport time (per minute) (OR=0.964, 95% CI: 0.961-0.968), AED/DF (OR=0.675, 95% CI: 0.611-0.745), and night time (OR=0.854, 95% CI: 0.805-0.906) decreased the odds of survival of the OHCA patients [Table/Fig-2].

Then, a multivariable logistic regression was used to examine the relationships between pre hospital IV fluid infusion and survival rate of the 33,006 patients with complete data. After adjustment of the covariates, pre hospital IV fluid infused patients had a significant

higher survival rate than those who didn't receive pre hospital IV infusion. The survival rate were associated with pre hospital IV fluid infusion both among children (adjusted OR=2.952; 95% CI: 2.040-4.273) and adult (adjusted OR=4.389; 95% CI: 3.911-4.744). Moreover, female had high survival rate than that of males (adjusted OR=1.151; 95% CI: 1.067-1.241). Every minute increase of response time, scene time and transport time significantly decreased the odd of survival among OHCA patients when they reached the hospital (adjusted OR=0.993; 95% CI: 0.989-0.997, adjusted OR =0.948, 95% CI: 0.944-0.952 and adjusted OR =0.973, 95% CI: 0.968-0.978) respectively [Table/Fig-3].

## DISCUSSION

The survival rate of OHCA patients when reached to the hospital in this study was 82.6% (95% CI=82.121-83.030). Previous studies documented that in Thailand, the survival rate of OHCA were 53%

Factors	n (%) or Mean ±SD	
<b>Patient factors</b>		
<b>Gender</b>		
Male	21,423	(70.5%)
Female	8,948	(29.5%)
<b>Age group</b>		
Children< 18 years	1,978	(6.2%)
Adult ≥ 18 years	29,825	(93.8%)
<b>Time of day on pre hospital care</b>		
Day	12,776	(38.7%)
Night	20,230	(61.3%)
<b>EMS factors</b>		
Response times (minutes)	10.9	± 8.9
Scene times (minutes)	7.3	± 8.3
Transport times (minutes)	8.3	± 7.3
<b>Therapeutic factors</b>		
AED/DF	2,452	(7.4%)
Intravenous fluid Administration	30,088	(91.2%)

**[Table/Fig-1]:** Characteristics of out-of-hospital cardiac arrest patients  
Remark: The total number of samples was 33,006 persons  
Some variables has missing values, therefore their summary were less than 33,006

Factors	Total Number (%)	OR Crude	95% CI	p-value
<b>Intravenous fluid administration</b>				
No	2,918 (8.9)	1		<0.001
Yes	30,088 (84.9)	3.935	3.631-4.263	
<b>AED/DF</b>				
No	30,554 (83.1)	1		<0.001
Yes	2,452 (7.8)	0.675	0.611-0.745	
<b>Gender</b>				
Male	21,423 (83.4)	1		0.007
Female	8,948 (84.7)	1.098	1.026-1.175	
<b>Age</b>				
< 18 Years	1,978 (85.0)	1		0.439
≥ 18 Years	29,825 (84.3)	0.951	0.838-1.080	
<b>EMS factors</b>				
Response times (minutes)	32,178 (84.0)	0.984	0.981-0.986	<0.001
Scene time (minutes)	31,797 (84.0)	0.943	0.939-0.946	<0.001
Transport time (minutes)	31,769 (84.8)	0.964	0.961-0.968	<0.001
<b>Time at day</b>				
Day (8.30 am to 4.30 pm)	12,776 (84.0)	1		<0.001
Night (4.31 pm to 7.29 am)	20,230 (81.8)	0.854	0.805-0.906	

**[Table/Fig-2]:** Survival rate to hospital and factors associated with survival rate of OHCA in bivariate analysis.  
Remark: The total number of samples was 33,006 persons  
Some variables has missing values, therefore their summary were less than 33,006

Factor	Total Number (%)	OR Crude	OR Adjusted	95% CI	p-value
<b>IV fluid administration in aged group</b>					
<b>Children (&lt; 18 years)</b>					
No	191 (70.2)	1	1		<0.001
Yes	1,787 (86.6)	2.742	2.952	2.040-4.273	
<b>Adult (≥ 18 years)</b>					
No	2,550 (59.7)	1	1		<0.001
Yes	27,275 (86.4)	4.389	4.308	3.911-4.744	
<b>Gender</b>					
Male	21,423 (83.4)	1	1		<0.001
Female	8,948 (84.7)	1.098	1.151	1.067-1.241	
<b>EMS factors</b>					
Response times (minutes)	32,178 (84.0)	0.984	0.993	0.989-0.997	<0.001
Scene time (minutes)	31,797 (84.0)	0.943	0.948	0.944-0.952	<0.001
Transport time (minutes)	31,769 (84.8)	0.964	0.973	0.968-0.978	<0.001

**[Table/Fig-3]:** Multivariable regression model for survival rate, with interaction of survival rate with intravenous fluid administration and age group.

Remark: The total number of samples was 33,006 persons

Some variables has missing values, therefore their summary were less than 33,006

[20,21]. This might be due to different EMS coverage, numbers of ALS team and CPR knowledge to people.

The result suggested that in Thailand, survival rate among OHCA patients is considerably higher than other countries [1-4]. Beside an improvement of ALS care for OHCA patients, other possible explanation might be that we used a short term patient outcome (survival until the patient reach to the hospital) which could reflect the quality pre hospital EMS better than long term survival. Long term survival of the patients covered the survival of the patients until they were discharged from the hospital. Therefore, quality of care in the hospital such as in emergency unit, intensive care unit or hospital wards has influences on the patient's long term survival.

This study investigated the association between IV fluid administration of resuscitated OHCA patients and survival rate of OHCA patients. The result of study showed an increasing odds of survival to the hospital for OHCA patients who received intravenous fluid. It was explained that IV fluid transfusion helps increasing intravascular volume, cardiac output and improve organ perfusion during cardiopulmonary resuscitation. In addition, after patient Return Of Spontaneous Circulation (ROSC), IV fluid transfusion does not only improve cardiac output but also increase patient's blood pressure [22-24]. Previous study also reported that isotonic crystalloids had a primary function for expanding the amount of intravascular fluid in an attempt to increase blood pressure and deliver the red blood cells and oxygen that they carried to body tissues [25]. Therefore, the OHCA patients who received IV fluid had an increasing survival rate to the hospital.

This study observed that the survival rate was associated to pre hospital IV fluid infusion for children. The fluid and vasoactive infusion were used for maintaining systolic blood pressure after ROSC in paediatric ALS [26]. Consistent with previous studies, administration of IV fluid was associated to improve survival rate to hospital discharge [10]. In addition, hypertonic saline infusion during resuscitation from OHCA was achieved from short term survival rates (admission to hospital with spontaneous circulation) [27]. The hospitalized children who received maintenance of IV fluid therapy, isotonic solutions had significantly decreased the risk of developing hyponatremia [28]. Isotonic crystalloids increased blood pressure and delivered the red blood cells and oxygen that they carried to body tissues [25].

These finding also showed that adult, who received IV fluid administration, had also an improvement in the survival rate of

OHCA patients, which was consistent with other study conducted in Japan [9]. Previous study focused on adult OHCA patients of non cardiac origin has long term survival rate [9]. This study assessed survival rate of OHCA patients when they reach to hospital, since its better to reflex quality of pre hospital EMS among critical patients. Long term survival depends on hospital treatment, including critical care and other advanced treatments of underlying diseases [29]. In addition, other studies have also found that the pre hospital use of lactate Ringer's solution was associated with survival of ROSC before hospital arrival [30]. Patients who received hypertonic saline showed a trend to have higher resuscitation success and hospital admission survival rates as well as a small improvement in neurological outcome among survivors on discharge [31,32].

This study also identified other factors associated with OHCA patient survival rate to the hospital such as response times, scene time, transport time and gender. However, these factors had a slight association with survival rate to the hospital. Although, spending more response time affected to the decreasing of survival rate to the hospital. Being consistent with several previous studies, early EMS and response time were associated with OHCA patient survival [9,33,34]. An increasing scene time affected to give even worse survival rate to the hospital. This finding is opposite to the previous study which demonstrated the survival discharge was at its highest in the first 10 to 35 minutes on scene time group compared to the >35 minutes group and the <10 minutes group [10]. This study demonstrated higher transport time was also associated with the decreasing chance of survival rate to the hospital. Other studies have found that transport time was not associated with survival rate to the hospital discharge [11]. This might be due to different EMS in Thailand that was a scoop and run approach whereas our study observed survival outcome in short term.

Moreover, female OHCA patients demonstrated a higher chance of survival rate compared to males. Being consistent with several previous studies, females had a higher chance of survival more than males [5,6,17,35]. In contrast, several previous studies also showed that males had a higher chance of survival rate than females. This might be due to different causes of cardiac arrest and severe critical conditions [33,36-38] which signified that both sex are equally associated with OHCA however the causes of cardiac arrest determine the results.

## LIMITATION

This nation wide cross-sectional analytical study had great advantage in term of having the country representative samples. However, few limitations are always associated in every study which has been illustrated as follows; first, data used in this study didn't record resuscitation drug. The pre hospital IV fluid was only isotonic crystalloids. A second potential limitation was that data used in this study were OHCA patients who were receiving care of ALS teams in 76 out of the 77 provinces of Thailand, with an exceptional province of Bangkok. This is due to an administrative issue found in this province, where several EMS systems were running simultaneously. In addition, only one of which has fallen under the supports of the National Institute for Emergency Medicine. Lastly, most of the previous studies of OHCA patients used the UT stein-style reporting templates [9,27,30,31,34], but data collection used in this study involved the use of a Case Record Form (CRF) of the EMS, Thailand. Consequently, some potentially important predictors have not yet measured (e.g., witnessed, bystander CPR, location of arrest).

## CONCLUSION

In Thailand, patients who experienced pre hospital resuscitated OHCA with the IV fluid infusion had increasing odd of survival to the hospital in the condition that quality of EMS was improved by reducing response, scene and transport times. The recommendation is improving the system to shortening the time used at scene and

transport and IV fluid transfusion for improving short term survival of OHCA.

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