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Original Article

Analysis of pre-hospital factors associated with survival to discharge in patients with successful out-of-hospital cardiopulmonary resuscitation

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Abstract: Cardiac arrest may occur in the hospital setting (in-hospital cardiac arrest) or outside the hospital [out-of-hospital cardiac arrest (OHCA)]. Cardiac arrest is a time-critical condition, such that each minute of delay in initiating key treatments, such as chest compressions and defibrillation, is associated with a significant decrease in survival. Improving survival to discharge from OHCA is a continuing challenge. This challenge is emphasized by the fact that reported survival ranges from 2% to 40% across different countries and continents. Most previous studies were focused on the factors affecting cardiac arrest in the hospital. However, there are relatively few studies about pre-hospital influencing factors. The pre-hospital parameters affecting the successful discharge were statistically analyzed, which was aimed to improve the successful discharge rate of out-of-hospital CPR. Patients with ECG presenting ventricular fibrillation before resuscitation and the on-site rescue time of less than 30 min had higher discharge rate. The moderate use of epinephrine may be beneficial to further enhance survival in patients with successful out-of-hospital CPR. We should not lose confidence of CPR in older people. Standardized high-quality CPR training before first-aid practice in first-aid staff is very important for improving the rate of successful discharge.

Keywords: Out-of-hospital cardiac arrest, cardiopulmonary resuscitation, on-site rescue time, pre-hospital first aid, survival

Introduction

Cardiac arrest describes the sudden cessation of heart function. Cardiac arrests may occur in the hospital setting (in-hospital cardiac arrest) or outside the hospital (OHCA) [1]. Cardiac arrest is a time-critical condition, such that each minute of delay in initiating key treatments, such as chest compressions and defibrillation, is associated with a significant decrease in survival [2, 3]. Survival following cardiac arrest can be categorized as either return of spontaneous circulation (ROSC), which describes the resumption of effective cardiac activity, or longer-term survival, often measured at discharge or 30 days following the cardiac arrest event [4]. In clinical work, the longer-term survival is more meaningful. Therefore, in this study, the result of a successful discharge is used to evaluate the prognosis. Reducing variability in survival provides the opportunity to save more lives if outcomes can be improved, which reflects the best performing systems.

The importance of OHCA as a health priority has been recognized in a series of government publications [5]. Improving survival to discharge from OHCA is a continuing challenge. This challenge is emphasized by the fact that reported survival ranges from 2% to 40% across different countries and continents [6-8]. On-site cardiopulmonary resuscitation (CPR) is an important component of emergency medicine, which is critical for longer-term survival. Successful pre-hospital CPR is the first step in rescuing patients with OHCA. Although pre-hospital CPR is successful, the rate of successful discharge is still low [6]. With in-hospital CPR, the chances of survival-to-discharge are 15-20%, while out-of-hospital CPR carries an even lower rate of survival-to-discharge [8-11]. Most previous studies were focused on the factors affecting

in-hospital cardiac arrest. However, there were relatively few studies about pre-hospital influencing factors of OHCA. In particular, there was even less research in developing countries. Therefore, we conducted this study on this subject. The pre-hospital parameters affecting successful discharge were statistically analyzed, which is aimed to improve the successful discharge rate of OHCA.

Material and methods

Subjects

A prospectively maintained database in Minhang emergency center of Shanghai was reviewed for all patients with successful out-of-hospital CPR between January 2013 and December 2017. Written informed consent was obtained from all patients or their families, according to institutional guidelines. All methods were carried out in accordance with relevant guidelines and regulations. All protocols were approved by the Licensing Committee of the Second Military Medical University. All patients had a detailed medical history, rescue document, and follow-up records.

Diagnostic criteria for out-of-hospital cardiac arrest

The diagnostic criteria included sudden loss of consciousness, bilateral dilated pupils, loss of light reflex, disappearance of aortic pulsation (carotid or femoral artery), and respiratory arrest. ECG was characterized by ventricular fibrillation (VF), pulseless ventricular tachycardia (VT), and ventricular arrest (VA). All cardiac arrest occurred outside the hospital.

Criteria for successful CPR

As soon as the diagnosis of cardiac arrest was given, standard CPR was given [12]. CPR is an emergency procedure, including chest compression, artificial respiration or defibrillation. Successful CPR was defined according to the reference of the 2017 International Consensus on Cardiopulmonary Resuscitation [13].

Standard of successful discharge

Receiving pre-hospital CPR and in-hospital treatment, the patients survived to be discharge from the hospital. After discharge, their cardiopulmonary function was basically restored to the pre-onset condition.

Statistical method

Comparisons were performed using Student's t-test for parametric data and Mann-Whitney U-test for non-parametric data. Chi-square test was used for categorical data. When the number of lattices with the theoretical frequency $1 \leq T < 5$ was more than 1/5 of the total number, Fisher exact probability test was used. The Cochran-Armitage trend test was used to investigate whether the rate of successful discharge was associated with patients' age, first-aid response time, transfusion time, on-site rescue time, dose of adrenaline, floor distribution and physicians' working years. Independent influencing factors for survival to discharge were performed using multivariate logistic regression analysis. $P<0.05$ was considered statistically significant. Calculations were done using SPSS Version 17.0 for Windows (SPSS, Inc., Chicago, IL, USA).

Results

General information

From January 2013 to December 2017, 351 cases of successful out-of-hospital CPR were prospectively collected. Among them, 212 were males, accounting for 60.4%. The mean age was 67.2 ± 17.9 years, ranging from 4 to 98 years. Of the 351 cases, 39 were successfully discharged from the hospital, accounting for 11.11%.

*Age distribution (**Table 1**)*

Among the 351 cases, the age group over 80 years old accounted for the highest proportion (29.91%). The rate of successful discharge was the highest in the two age groups of (4-20) and (30-40) years old, accounting for 33.33% and 31.58%, respectively. Cochran-Armitage trend test showed that with the increase of the patients' age, the rate of successful discharge decreased. However, the difference was not statistically significant (P=0.123).

*Disease spectrum (**Table 2**)*

Among the 351 cases, the main etiological diseases were circulatory diseases and respira-

Table 1. Age distribution of the total 351 cases

Age group	Successful CPR (n=351)	Died without discharge (n=312)	Survived to discharge (n=39)	Discharge rate (%)
0~20	3	2	1	33.33
20~30	11	9	2	18.18
30~40	19	13	6	31.58
40~50	24	19	5	20.83
50~60	49	45	4	8.16
60~70	67	58	9	13.43
70~80	73	68	5	6.85
≥80	105	98	7	6.67

Table 2. Disease spectrum of the total 351 cases

Disease spectrum	Successful CPR (n=351)	Died without discharge (n=312)	Survived to discharge (n=39)	Discharge rate (%)
Circulatory system	124	102	22	17.74
Respiratory system	44	42	2	4.55
Nervous system	18	16	2	11.11
Trauma	21	20	1	4.76
Electric shock	4	2	2	50.00
Asphyxia	18	15	3	16.67
Others	122	115	7	5.74

Others included malignant tumors, digestive system, urinary system, suicide, poisoning.

tory diseases, accounting for 35.33% and 12.54%, respectively. The highest rate of successful discharge was achieved with electric shock, which was 50%, followed by circulatory diseases. There was statistical significacet between the rate of successful discharge and etiological spectrum (P=0.005).

*ECG before and after resuscitation (**Table 3**)*

The analysis of ECG before resuscitation found that the rate of successful discharge was highest in patients with ventricular fibrillation. The rate of successful discharge was lowest in patients with ventricular arrest. There was a statistical difference of successful discharge rate according to ECG before resuscitation (P< 0.001). The analysis of ECG after resuscitation found that sinus rhythm recovery was found in 162 cases. There was a significant difference of successful discharge rate according to ECG after resuscitation (P=0.033), which indicated that ECG before and after resuscitation was significantly associated with successful discharge.

*The first-aid response time (**Table 4**)*

The first-aid response time of OHCA (the time interval from receiving emergency calls to arriving at the scene) was 14.38 ± 8.14 minutes (min), ranging from 1 min to 60 min. The average first-aid response time of patients who were successfully discharged from the hospital was 11.19 ± 7.83 min. The Cochran-Armitage trend test showed no direct relationship between the successful discharge rate and the first-aid response time (P=0.340).

*Transfusion time (**Table 5**)*

If the transfusion time was within 15 min, the discharge rate was 16.82%. The rate of successful discharge was the highest with transfusion within 5 min, and the lowest rate was with transfusion of more than 30 min. There were 239 cases without defibrillation, in which the heartbeat was recovered by chest compression and drug administration. The Cochran-Armitage trend test showed that there was no significant relationship between the rate of successful discharge and the transfusion time (P=0.178).

*The on-site rescue time (**Table 6**)*

The average on-site rescue time is 32.38 ± 20.72 min, range from 1 min to 142 min. The Cochran-Armitage trend test showed that the rate of successful discharge was significantly decreased with the increase of accumulated on-site rescue time (P<0.001).

*The dose of adrenaline (**Table 7**)*

The average dose of adrenaline in 351 patients was 5.4 ± 4.1 mg, range from 0 to 20 mg. There was no epinephrine used in 37 cases. The Cochran-Armitage trend test showed that the rate of successful discharge was significantly decreased with the increased dose of adrenaline given (P<0.001).

Table 3. ECG before and after resuscitation

ECG	Successful CPR (n=351)	Died without discharge (n=312)	Survived to discharge (n=39)	Discharge rate (%)
ECG before resuscitation				
Pulseless ventricular tachycardia (VT)	72	67	5	6.94
Ventricular fibrillation (VF)	74	52	22	29.73
Ventricular arrest (VA)	205	193	12	5.85
ECG after resuscitation				
Sinus rhythm	162	137	25	15.43
Others	189	175	14	7.41

Table 4. First-aid response time of the total 351 cases

First-aid response time (min)	Successful CPR (n=351)	Died without discharge (n=312)	Survived to discharge (n=39)	Discharge rate (%)
0-3	50	47	3	6.00
3-5	18	16	2	11.11
5-10	130	113	17	13.08
10-15	120	107	13	10.83
>15	23	19	4	17.39

Table 5. Transfusion time of the total 351 cases

Transfusion time (min)	Successful CPR (n=351)	Died without discharge (n=312)	Survived to discharge (n=39)	Discharge rate (%)
0-3	23	20	3	13.04
3-5	33	26	7	21.21
5-10	51	43	8	15.69
10-15	123	112	11	8.94
15-30	108	99	9	8.33
>30	13	12	1	7.69

Table 6. On-site rescue time of the total 351 cases

On-site rescue time (min)	Successful CPR (n=351)	Died without discharge (n=312)	Survived to discharge (n=39)	Discharge rate (%)
0-3	5	2	3	60.00
3-5	6	3	3	50.00
5-10	9	5	4	44.44
10-15	14	9	5	35.71
15-30	87	79	8	9.20
30-60	207	192	15	7.25
>60	23	22	1	4.35

*Number ofe times of defibrillation (**Table 8**)*

The average number of defibrillation given in 351 patients was 2.9 ± 2.8 times, including the maximum of 12 times. The Cochran-Armitage trend test showed no statistical difference between the number of defibrillation given and the rate of successful discharge (P=0.465).

*Floor distribution (**Table 9**)*

According to the floor distribution, the rate of successful discharge was highest in public places (21.74%). The Cochran-Armitage trend test showed that with the rise of living floor, the rate of successful discharge decreased. However, the difference was not statistically significant (P=0.075).

Table 7. The dose of adrenaline used in the total 351 cases

The dose of adrenaline (mg)	Successful CPR (n=351)	Died without discharge (n=312)	Survived to discharge (n=39)	Discharge rate (%)
0	37	16	21	56.76
1	17	12	5	29.41
2-3	56	48	8	14.29
4-5	53	50	3	5.66
6-10	103	102	1	0.10
≥10	79	77	1	1.27

Table 8. The number of defibrillation times in the total 351 cases

The times of defibrillation	Successful CPR (n=351)	Died without discharge (n=312)	Survived to discharge (n=39)	Discharge rate (%)
0	239	214	25	10.46
1	36	32	4	11.11
2	26	22	4	15.38
3-4	34	31	3	8.82
4-6	8	7	1	12.50
≥6	8	6	2	25.00

Table 9. Floor distribution of the total 351 cases

Floor distribution	Successful CPR (n=351)	Died without discharge (n=312)	Survived to discharge (n=39)	Discharge rate (%)
0 (public places)	69	54	15	21.74
1	79	73	6	7.59
2	44	40	4	9.09
3	43	37	6	13.95
4	25	23	2	8.00
5	28	24	4	10.71
6	20	19	1	5.00
≥7	43	42	1	0.00

Table 10. The qualifications of doctors (working years)

Qualifications of doctor (working years)	Successful CPR (n=351)	Died without discharge (n=312)	Survived to discharge (n=39)	Discharge rate (%)
1	5	4	1	20.00
2-5	171	155	16	9.36
5-10	103	94	9	8.74
≥10	72	59	13	18.06

*The qualifications of doctors (working years) (**Table 10**)*

There was no significant difference between the rate of successful discharge and the physicians' working years (P=0.281). There is no significant difference between high-grade senior physicians and low-grade junior physicians.

*Comparison of clinical parameters between survival-to-discharge group and death group (**Table 11**)*

In the survival-to-discharge group, the proportion of patients older than 60 years, the first-aid response time, the dose of epinephrine and the proportion of tracheal intubations were signifi-

Table 11. Comparison of clinical parameters between 37 cases of survival discharge and 314 cases of death after successful out-of-hospital CPR

Variable	Successful CPR (n=351)	Survived to discharge (n=39)	Died without discharge (n=312)	*P* value
Age (year)				0.022
≤60	104	19	95	
>60	237	20	217	
Gender				0.877
Male	212	24	188	
Female	139	15	124	
Disease spectrum				0.005
Circulatory system	124	22	102	
Trauma and accident	43	6	37	
Others	184	11	173	
ECG before resuscitation				<0.001
VF	74	22	52	
VA	205	12	193	
VT	72	5	67	
ECG after resuscitation				0.017
Sinus rhythm	162	25	137	
Others	189	14	175	
First-aid response time (min)				0.727
≤5 min	68	5	63	
>5 min	283	34	249	
Transfusion time (min)				0.218
≤15 min	230	29	201	
>15 min	121	10	111	
On-site rescue time (min)				<0.001
≤30 min	177	23	154	
>30 min	174	16	158	
The amount of adrenaline (mg)				<0.001
0	37	21	16	
≤3 mg	73	13	60	
>3 mg	241	5	236	
Endotracheal intubation				<0.001
Yes	297	18	279	
No	54	21	33	
The times of defibrillation				0.400
0	239	25	214	
≤2	62	8	54	
>2	50	6	44	
Qualifications of doctor (working years)				0.711
≤5	176	17	159	
>5	175	19	156	
Floor distribution				0.078
≤3	235	31	204	
>3	116	8	108	

cantly lower than that in the death group. ECG before and after resuscitation were both statistically different between two groups (P<0.05). Among the relevant etiology, cardiac arrest

Table 12. Results of Logistic multivariate regression analysis

Variable	OR	95% CI	P
Age (year)	1.412	0.505-3.953	0.511
≤60			
>60			
Gender	1.284	0.473-3.489	0.624
Male			
Female			
Disease spectrum	1.398	0.786-2.486	0.255
Circulatory system			
Others			
ECG before resuscitation	13.120	4.403-39.098	<0.001
VF			
Others			
ECG after resuscitation	0.835	0.294-2.368	0.734
Sinus rhythm			
Others			
First aid response time	0.316	0.062-1.607	0.165
≤5 min			
>5 min			
Transfusion time	0.635	0.192-2.093	0.455
≤15 min			
>15 min			
On-site rescue time	5.054	1.774-14.395	0.002
≤30 min			
>30 min			
The amount of adrenaline			
0	57.611	11.929-278.236	<0.001
≤3 mg	5.797	1.707-19.681	0.005
>3 mg			
Endotracheal intubation	2.424	0.739-7.952	0.144
Yes			
No			
Defibrillation	0.325	0.097-1.093	0.069
Yes			
No			
Qualifications of doctor (working years)	1.643	0.614-4.395	0.323
≤5			
>5			
Floor distribution	1.752	0.581-5.286	0.319
≤3			
>3			

caused by circulatory system had a significantly higher rate of successful discharge. In contrast, gender, qualifications of doctors (working years) and floor distribution had no statistical significance (P>0.05).

*Logistic multivariate regression analysis of the total 351 cases (**Table 12**)*

Logistic multivariate regression analysis showed that ECG before resuscitation showing ventricular fibrillation (OR=13.120; 95% CI: 4.403-39.098; P<0.001), the on-site rescue time more than 30 min (OR=5.054; 95% CI: 1.774-14.395; P=0.002) and less use of adrenaline (no adrenaline/adrenaline >3 mg: OR=57.611; 95% CI: 11.929-278.236; P<0.001; adrenaline ≤3 mg/adrenaline >3 mg: OR=5.797; 95% CI: 1.707-19.681; P=0.005) were independently associated with the survival discharge after successful out-of-hospital CPR.

Discussion

Among the 351 patients of successful out-of-hospital CPR, the majority were concentrated in the age group of more than 70 years, accounting for 50.7%. Shanghai is one of the most developed cities in China, and the aging problem is also serious. The decline in physical function and the underlying diseases are high risk factors for out-of-hospital cardiac arrest (OHCA) in older people [14]. In this study, it can be seen that the successful discharge rate decreased with increased age. However, the difference was not statistically significant (P=0.123). The successful discharge rate in patients over 80 years old accounted for 14.29% in the study, which suggested that advanced age was not an independent influencing factor of resuscitation failure.

As a result, we should not lose confidence of CPR in older people.

The quality of pre-hospital first aid is an important factor of reducing mortality in OHCA patients. A large amount of studies have indicated that the first-aid response time was an independent factor for the survival in pre-hospital first-aid [15, 16]. In this study, there was no direct relationship between the successful discharge rate and the first-aid response time (P=0.340). The reason may be attributed to the first-aid response time not being completely present during the duration of cardiac arrest. At times, the patient's family calls for emergency help when the patient begins to have symptoms, but without cardiac arrest. As a result, the first-aid response time in OHCA cannot exactly reflected the interval from cardiac arrest to receiving emergency treatment. The average first-aid response time of patients who were successfully discharged from the hospital was 11.19 ± 7.83 min. There was no successful discharge in patients that the first-aid response time was more than 30 min. Perhaps the successful discharge rate was significantly affected when the first-aid response time exceeded a certain range (such as more than 30 min). However, we found that the rate of successful discharge decreased significantly with the increase of accumulated on-site rescue time (P<0.001). It was suggested that the shorter the accumulated on-site rescue time was, the higher the successful discharge rate was. Perhaps the accumulated on-site rescue time may have more value in practice.

In a qualitative study of paramedics' attitudes to pre-hospital first aid, the government goal is that emergency calls should receive a timely response within a "golden hour"; this emerged as a key factor influencing attitudes of staff morale and attitudes on the job as a whole [17, 18]. The relationship between ambulance response times and patient outcome is conflicting [19, 20]. A Swiss study found that cardiac arrest patients defibrillated in the hospital for an average of 15.6 minutes after cardiac arrest were more likely to survive to hospital discharge, and be alive at the 1 year follow up, and to survive without any neurological impairment, than those defibrillated in the community for 5.7 minutes [21]. In any case, cardiac arrest represents a very small proportion of emergency calls. The suggestion that reduced response times may improve survival "remains speculative and unreported" [20]. There is a clear need for targets to be based on rigorous systematic review of the evidence, and where evidence is absent or inconclusive, for a well-designed definitive investigation to be undertaken.

The successful discharge rate in OHCA was significantly associated with the dose of adrenaline use. Adrenaline can increase myocardial function and reduce perfusion of the sub-endocardial myocardium [22]. One ME had found there was no significant difference in survival admission rates and survival discharge rates between the two groups with and without adrenaline [23]. In the study, we found that the rate of successful discharge decreased significantly with the increased dose of adrenaline use (P<0.001). As a result, we recommend that the moderate use of adrenaline may be beneficial to further survival in patients with successful out-of-hospital CPR. The number of defibrillations was an independent factor affecting the recovery of spontaneous circulation in a previous study [24]. However, there was no statistical relationship between the rate of successful discharge and the number of defibrillations in this study. The reason may be the small sample size and the multiple defibrillations in refractory ventricular fibrillation. During the on-site rescue process, the multiple defibrillations were still effective for refractory ventricular fibrillation. In this study, there was one case of survival discharge who received 12-times of defibrillation. The relationship between the number of defibrillations and the rate of discharge requires a large sample of data for further research.

Previous studies have shown that the successful discharge rate after the initial CPR is still low [6-8]. The survival to discharge from the hospital was the objective measure of out-of-hospital CPR. In this paper, the successful discharge rate was 11.11%, which was consistent with previous reports [8, 10]. Multi-factors should be solved to improve the successful discharge rate. The first-aid level and the tactical understanding of the out-of-hospital emergency team also have a direct impact [25]. It was concluded that the lack of confidence in medical staff, irregular operation, poor coordination and traffic jams were the negative factors for the survival rate [26].

The "seamless connection" between the hospital and first-aid staff was very important. Colquhoun described the results of 555 self-reported resuscitation attempts that had been trained and equipped with defibrillators, reporting that 27% of patients were discharged alive from the hospital [27]. In a five-year cross-sectional study (n=272) also using self-reporting, Bury reported that 18.7% of patients survived to discharge [28]. One potential source of variation may be the impact of medical staff in pre-hospital resuscitation. The data does not fully explain the positive association between first-aid personnel quality and survival, but rapid response, good quality CPR and prompt defibrillation are known predictors of survival from OHCA, while the value of more advanced techniques such as epinephrine administration and advanced airway management are not conclusive [29]. The reality is that internationally, ambulance services struggle to achieve adequate response times and the need for skilled, competent responders in the community remains [30]. Masterson S has shown an association between general practitioner participation and positive OHCA outcomes [31]. However, in this study, there is no significant difference in the rate of successful discharge between high-grade senior physicians and low-grade junior physicians. This may be related to the disease itself and relatively small samples. The more important reason was that all emergency doctors in Shanghai have received standardized high-quality CPR training before first-aid practice.

In conclusion, improving survival to discharge rate from OHCA is a continuing challenge. This challenge is emphasized by the fact that reported survival is still unsatisfactory. Patients with ECG presenting ventricular fibrillation before resuscitation and the on-site rescue time of less than 30 min had higher discharge rates. The moderate use of adrenaline may be beneficial to further survival in patients with successful out-of-hospital CPR. In addition, we should not lose confidence in out-of-hospital CPR in older people. Standardized high-quality CPR training before first-aid practice is very important for improving the rate of successful discharge.

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Disclosure of conflict of interest

None.

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