Shimane J. Med. Sci., Vol.38 pp.23-31, 2021

Factors Associated with Return of Spontaneous Circulation in Out-of-Hospital Cardiopulmonary Arrest Cases

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（Received March 22, 2021; Accepted April 12, 2021）

Study objective: In the present study, factors contributing to ROSC were clarified and measures to improve ROSC rates based on the Utstein style items was examined. ***Methods:*** Information from the Fire and Disaster Management Agency of japan database was analyzed. The contribution of the Utstein style items to ROSC in OHCA cases transported to medical institutions by EMT between January 01, 2010, and December 31, 2010, was assessed. ***Results:*** ventricular fibrillation（VF）and ventricular tachycardia（VT）, 7.87（7.09–8.72）; epinephrine administration, 3.09（2.84–3.35）; ambulance staffed with a physician, 3.06（2.69–3.49）were shown to be contributing factors to ROSC. ***Conclusions:*** These results showed that prompt cardiopulmonary resuscitation for VF and VT, use of an automated external defibrillator, early epinephrine administration, and development of an emergency care system in the community are important for achieving ROSC and social rehabilitation in OHCA patients.

Keywords: cardiopulmonary arrest; cardiopulmonary resuscitation; epinephrine; rehabilitation

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INTRODUCTION

More than 100,000 out-of-hospital cardiopulmonary arrests（OHCA）occur annually in Japan, and the number is expected to continue to increase as the population ages. In order to improve the social rehabilitation of OHCA patients, it is of utmost importance to achieve the return of spontaneous circulation（ROSC）at an early stage. It has been reported that the longer the time from cardiac arrest until ROSC, the worse the chance of successful social rehabilitation and that the ability to reintegrate into society substantially decreases once 25 min pass［1-7］. A report by the SOS-KANTO study group in Japan also concluded the prognosis as extremely poor if ROSC cannot be achieved before admission to the hospital［8］. The importance of ROSC for social rehabilitation of OHCA patients is gaining in recognition around the world.

The International Liaison Committee on Resuscitation proposed the “Utstein style” in 1990 for interregional and international statistical comparisons of data such as prehospital resuscitation rates［9］. The Fire and Disaster Management Agency of japan（FDMA）surveyed all OHCA cases in Japan［10］. Following this, the FDMA the Utstein style in January 2005 to collect and analyze OHCA data. However, there have been few reports on early ROSC, which is most important for the social rehabilitation of OHCA patients. In particular, there has been no detailed analysis of the effects of treatments performed by the Emergency medical technician（EMT）and bystanders who happen to be at the site and time factors. In the present study, OHCA cases were

investigated based on Utstein style items to clarify factors contributing to ROSC in Japan and the measures to improve ROSC rates were examined.

METHODS

1. Study design

This is a cross-sectional study.

2. Ethical considerations

This study was approved by the Ethics Review Committee of the Shimane University Faculty of Medicine (Shimane, Japan; approval number: 1341) in accordance with the Declaration of Helsinki.

Subjects

The FDMA database which included 30,704 out of 123,095 OHCA cases (because of internal and external factors) that were transported to medical institutions by EMT between January 01, 2010, and December 31, 2010, was analyzed. Fig. 1 shows the flowchart of subjects. Not witnessed by citizen bystanders or EMT who were present at the site were excluded. Further, 5178 cases of "Initial rhythm other" were excluded because of the possibility that these cases may include those in which ROSC had already been achieved by the arrival of an EMT. In addition, those cases with "time from witnessing until recognition" and "time from witnessing until cardiopulmonary resuscitation (CPR)" that were theoretically obvious outliers were excluded.

Survey items

Cases were divided into two groups, those in which spontaneous heartbeat was restored before being admitted to a medical institution (ROSC group) and all others (non-ROSC group). The contribution of the following Utstein style items to ROSC was analyzed: patient age, sex, an EMT-staffed ambulance, a physician-staffed ambulance, physician-performed advanced life support (ALS), CPR performed by bystanders, use of public access defibrillation (PAD), verbal instruction provided by the telecommunications services personnel, initial electrocardiogram waveforms, defibrillation by the EMT, airway management using a device by the EMT, epinephrine administration by the EMT, and cardiogenic or noncardiogenic etiology. In addition, the association between the time from witnessing until recognition

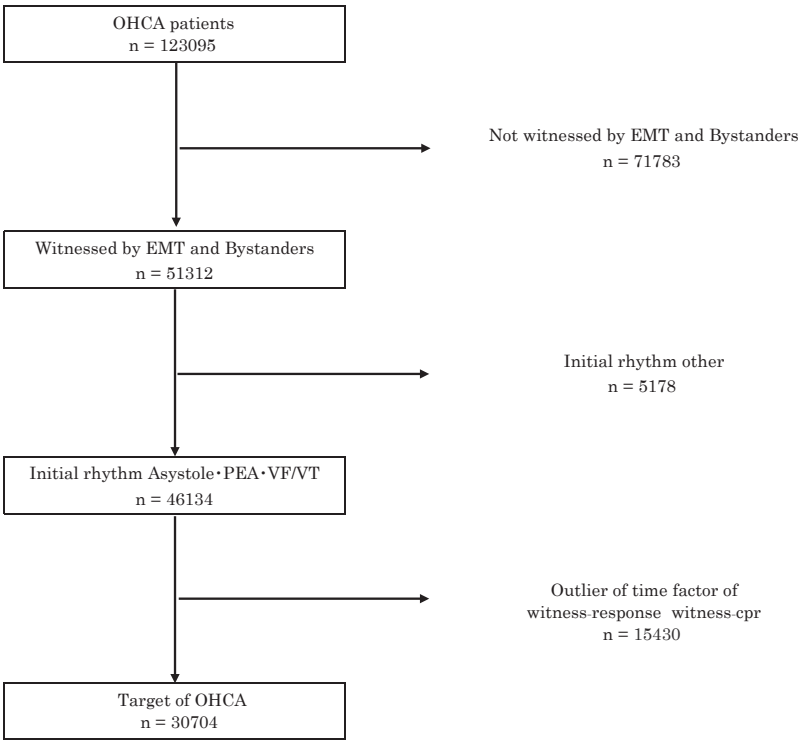

Fig. 1. Target cases of OHCA

and the time from witnessing onset until CPR were analyzed as time factors.

Statistical Analysis

Data are presented as means (standard deviations) or *n* (%), unless specified otherwise. Statistical analysis was performed with successful ROSC as the dependent variable and Utstein style items as the independent variable. First, considering multicollinearity, independent variables with a variance inflation factor of less than 10 were selected, and logistic regression analysis was performed. Then, to clarify factors contributing to ROSC, a univariate logistic analysis was performed, and the degree of contribution of the category data and continuous variables was determined by the odds ratio (95% confidence interval). Then, a multivariate analysis was performed. IBM SPSS Statistics version 24.0 (IBM Corporation, Armonk, New York,USA) was used for statistical analysis.

RESULTS

Attributes and characteristics of OHCA

In total, 30,704 cases of OHCA in Japan were examined. The overall mean age was 73.5 (17.2)

Table 1. Characteristics of out side hospital cardiac arrest. N = 30704

Variable	Category	Value	N	(%)
Age	mean ± SD	73.5 (± 17.2)		
Sex	female mean ± SD	78.3 (± 16.2)	12208	39.8
	male mean ± SD	70.3 (± 16.9)	18496	60.2
EMT-staffed ambulance	Yes		29898	97.4
Physician-staffed ambulance	Yes		1368	4.5
Advanced life support by a physician	Yes		4774	15.5
Bystander CPR	Yes		15126	49.3
Public Access defibrillation	Yes		476	1.6
Verbal instruction	Yes		14731	48.0
Initial rhythm	Asystole		16370	53.3
	PEA		9938	32.4
	VF/VT		4396	14.3
Defibrillation	Yes		5485	17.9
Airway maintenance using a device by EMT	Yes		13739	44.7
Epinephrine administration by EMT	Yes		5774	18.8
Cardiogenic etiology	Yes		16765	54.6
ROSC	Yes		3800	12.4

ROSC: return of spontaneous circulation; SD: standard deviation; EMT: emergency medical technicians; CPR: cardiopulmonary resuscitation

years; the mean age for females and males was 78.3 (16.2) and 70.3 (16.9) years, respectively, indicating that women were older on average. An EMT-staffed ambulance was used in 29,898 cases (97.4%), a physician-staffed ambulance was used in 1368 cases (4.5%), ALS was performed by a physician in 4,774 cases (15.5%), a bystander performed CPR in 15,126 cases (49.3%), and PAD was completed in 476 cases (1.6%). Command section personnel at the Fire Defense Headquarters provided verbal instruction in 14,731 cases (48.0%). Regarding the initial echocardiogram (ECG), asystole was present in the majority of cases (16,370 cases; 53.3%). This was followed by pulseless elec-

Table 2. Comparison statistics between cases with ROSC.

	ROSC		
	No (n = 26904)	Yes (n = 3800)	OR (95%CI)
Age mean±SD	74.0 (± 17.1)	70.0 (± 16.4)	0.99 (0.98-0.99)
Sex			
Female	10903 (89.3%)	1305 (10.7%)	1.30 (1.21-1.39)
male	16001 (86.5%)	2495 (13.5%)	
EMT-staffed ambulance			
No	752 (93.3%)	54 (6.7%)	1.99 (1.51-2.63)
Yes	26152 (87.5%)	3746 (12.5%)	
Physician-staffed ambulance			
No	25967 (88.5%)	3369 (11.5%)	3.54 (3.14-3.99)
Yes	937 (68.5%)	431 (31.5%)	
Advanced life support by a physician			
No	22902 (88.3%)	3028 (11.7%)	1.45 (1.33-1.59)
Yes	4002 (83.8%)	772 (16.2%)	
Bystander CPR			
No	13890 (89.2%)	1688 (10.8%)	1.33 (1.24-1.43)
Yes	13014 (86.0%)	2112 (14.0%)	
Public Access defibrillation			
No	26548 (87.8%)	3680 (12.2%)	2.43 (1.97-2.99)
Yes	356 (74.8%)	120 (25.2%)	
Verbal instruction			
No	14072 (88.1%)	1901 (11.9%)	1.09 (1.02-1.17)
Yes	12832 (87.1%)	1899 (12.9%)	
Initial rhythm			
Asystole	15403 (94.1%)	967 (5.9%)	0.25 (0.23-0.27)
PEA	8485 (85.4%)	1453 (14.6%)	1.34 (1.25-1.44)
VF/VT	3016 (68.6%)	1380 (31.4%)	4.51 (4.18-4.87)
Defibrillation			
No	22932 (90.9%)	2287 (9.1%)	3.81 (3.55-4.10)
Yes	3972 (72.4%)	1513 (27.6%)	
Airway maintenance using a devices by EMT			
No	14855 (87.6%)	2110 (12.4%)	0.98 (0.92-1.05)
Yes	12049 (87.7%)	1690 (12.3%)	
Epinephrine administration by EMT			
No	22536 (90.4%)	2394 (9.6%)	3.03 (2.81-3.26)
Yes	4368 (75.6%)	1406 (24.4%)	
Cardiogenic etiology			
No	12280 (88.1%)	1659 (11.9%)	1.08 (1.01-1.16)
Yes	14624 (87.2%)	2141 (12.8%)	
Witnessing to recognition mean (min) ± SD	5.3 ± 8.2	3.5 ± 5.7	0.95 (0.94-0.96)
Witnessing to CPR mean (min) ± SD	14.7 ± 9.9	12.1 ± 6.9	0.95 (0.94-0.95)

ROSC: return of spontaneous circulation; OR: odds ratio; CI: confidence interval; SD: standard deviation; EMT: emergency medical technicians; CPR: cardiopulmonary resuscitation; PEA: pulseless electrical activity; VF/VT: ventricular fibrillation/ventricular tachycardia

trical activity (PEA) in 9938 cases (32.4%), and ventricular fibrillation (VF) and pulseless ventricular tachycardia (VT) in 4396 cases (14.3%). As for emergency treatment performed by EMT, airway maintenance using a device occurred in 13,739 cases (44.7%), followed by epinephrine administration in 5774 cases (18.8%), and defibrillation in 5485 cases (17.9%). Next, the etiology of cardiac arrest estimated from the database was cardiogenic in 16,765 cases (54.6%), and ROSC was achieved in 3800 (12.4%) out of 30,704 cases of OHCA that were analyzed (Table 1).

Factors contributing to ROSC based on univariate analysis

Odds ratios for factors contributing to ROSC are as follows (Table 2): sex, 1.30 (1.21–1.39); an EMT-staffed ambulance, 1.99 (1.51–2.63); a physician-

Table 3. Outcome predictors using logistic regression analysis.

	ROSC		
	No (n = 26904)	Yes (n = 3800)	OR (95%CI)
Age mean ± SD	74.0 (± 17.1)	70.0 (± 16.4)	0.99 (0.99-0.99)
Sex			
Female	10903 (89.3%)	1305 (10.7%)	1.22 (1.13-1.31)
male	16001 (86.5%)	2495 (13.5%)	
EMT-staffed ambulance			
No	752 (93.3%)	54 (6.7%)	1.56 (1.17-2.09)
Yes	26152 (87.5%)	3746 (12.5%)	
Physician-staffed ambulance			
No	25967 (88.5%)	3369 (11.5%)	3.06 (2.68-3.49)
Yes	937 (68.5%)	431 (31.5%)	
Bystander CPR			
No	13890 (89.2%)	1688 (10.8%)	1.25 (1.16-1.34)
Yes	13014 (86.0%)	2112 (14.0%)	
Public Access defibrillation			
No	26548 (87.8%)	3680 (12.2%)	1.55 (1.22-1.96)
Yes	356 (74.8%)	120 (25.2%)	
Initial rhythm			
PEA	8485 (85.4%)	1453 (14.6%)	2.45 (2.24-2.68)
VF/VT	3016 (68.6%)	1380 (31.4%)	7.87 (7.09-8.72)
Airway maintenance using a device by EMT			
No	14855 (87.6%)	2110 (12.4%)	0.78 (0.73-0.85)
Yes	12049 (87.7%)	1690 (12.3%)	
Epinephrine administration by EMT			
No	22536 (90.4%)	2394 (9.6%)	3.09 (2.84-3.35)
Yes	4368 (75.6%)	1406 (24.4%)	
Cardiogenic etiology			
No	12280 (88.1%)	1659 (11.9%)	0.61 (0.56-0.66)
Yes	14624 (87.2%)	2141 (12.8%)	
Witnessing to recognition mean (min) ± SD	5.3 ± 8.2	3.5 ± 5.7	1.01 (1.00-1.02)
Witnessing to CPR mean (min) ± SD	14.7 ± 9.9	12.1 ± 6.9	0.96 (0.95-0.97)

ROSC: return of spontaneous circulation; OR: odds ratio; CI: confidence interval; SD: standard deviation; EMT: emergency medical technicians; CPR: cardiopulmonary resuscitation; PEA: pulseless electrical activity; VF/VT: ventricular fibrillation/ventricular tachycardia

staffed ambulance, 3.54 (3.14–3.99); ALS performed by a physician, 1.45 (1.33–1.59); bystander-performed CPR, 1.33 (1.24–1.43); PAD, 2.43 (1.97–2.99); verbal instruction, 1.09 (1.02–1.17); asystole, 0.25 (0.23–0.27); PEA, 1.34 (1.25–1.44); VF and VT, 4.51 (4.18–4.87); defibrillation, 3.81 (3.55–4.10); airway maintenance using a device, 0.98 (0.92–1.05); epinephrine administration, 3.03 (2.81–3.26); and etiology of cardiac arrest, 1.08 (1.01–1.16). The odds ratios for VF and VT, defibrillation, a physician-staffed ambulance, epinephrine administration, and PAD were especially high, indicating that these factors contributed to ROSC. Regarding age and time course, odds ratios were 0.99 (0.98–0.99) for age, 0.95 (0.94–0.95) for time from witnessing until recognition, and 0.95 (0.94–0.95) for time from witnessing onset until CPR, indicating that younger age and a shorter time from witnessing onset until CPR had a significant correlation. Asystole, in contrast, had the lowest odds ratio (Table 2).

Factors contributing to ROSC based on multivariable analysis

Odds ratios obtained from multivariate analysis were as follows: age, 0.99 (0.99–0.99); sex, 1.22 (1.13–1.31); an EMT-staffed ambulance, 1.56 (1.17–2.09); a physician-staffed ambulance, 3.06 (2.68–3.49); bystander-performed CPR, 1.25 (1.16–1.34); PAD, 1.55 (1.22–1.96); PEA, 2.45 (2.24–2.68); VF and VT, 7.87 (7.09–8.72); airway maintenance using a device, 0.78 (0.73–0.85); administration of epinephrine, 3.09 (2.84–3.35); and etiology of cardiac arrest, 0.61 (0.56–0.66). These results indicated that VF and VT, epinephrine administration, a physician-staffed ambulance, and PEA were contributing factors to ROSC, showing a similar trend as those obtained from the univariate analysis. Furthermore, the time from witnessing until recognition of the ROSC group was shorter by 1.8 min compared with that of the non-ROSC group, and the time from witnessing until CPR of the ROSC group was also shorter by 2.6 min (Table 3).

DISCUSSION

In order to improve the social rehabilitation of OHCA patients, it is important to achieve ROSC at an early stage. The present study analyzed factors of OHCA cases that achieved ROSC using logistic regression based on FDMA Utstein style data. The following three items strongly contributed to ROSC: "VF and VT by the initial ECG," "epinephrine administration," and "an ambulance staffed with a physician." First, it was shown that VF and VT contribute to ROSC. As with the current results, many previous studies have reported that VF and VT cases have a better social rehabilitation outcome compared with asystole and PEA cases [11, 12]. However, the percentage of VF and VT in the initial ECG was 13.6% herein, which was lower than those in studies conducted in the US and Europe [13, 14]. This suggests that there were more cases of asystole and PEA when cardiac arrest was witnessed in Japan, which may be one of the reasons why it is challenging to increase the possibility of ROSC. In addition, it is desirable to increase the probability of VF and VT detection. The only treatment method for VF and VT is defibrillation, which also contributed to ROSC in the present study. The use of AED has now been approved not only for physicians and EMTs but also for the general public in Japan, and it is expected to lead to early ROSC and improvement of successful social rehabilitation rates. The lifesaving rate is closely correlated with the number of AEDs installed [15]. While there are more than 420,000 AEDs installed in Japan, and numbers are increasing [16], the percentage of AED use among the general public is as low as 1.6%. In most cases, defibrillation is considered to be performed when the EMT arrives at the site; therefore, establishment of the PAD system is an urgent issue. Among the witnessed OHCA cases, the lifesaving rate is said to be higher in public places [17]. However, three-quarters of OHCA occur at home, many of which are not witnessed, and it is too late when discovered [18-21]. Therefore, the question of whether CPR is promptly performed and an AED used is a pressing issue for OHCA cases that occur at home. An increase in VF and VT can be expected if community residents could quickly bring an AED to the home of the OHCA patient and use it on them. Suzukawa *et al*. conducted a survey/study on introduction of first responder sys-

tems in Japan and reported that their introduction in some remote locations on a trial basis was useful, and 86.6% of citizens were hoping the PAD system is established [22].

International comparison of the prevalence of myocardial infarction shows it is the highest in Western countries and the lowest in Japan, among all regions that were surveyed [23, 24]. The low incidence of VF and VT in Japan result from differences in the disease structure mentioned above. The present findings are most consistent with those reported by Czapla *et al*. [25] because they showed that VF and VT had a higher chance of ROSC in Poland. Despite the variety of styles of prehospital emergency in different countries, the contributing factors to ROSC were examined by the international Utstein styles. Therefore, a detailed epidemiological survey is warranted in future.

Second, epinephrine administration was shown to contribute to ROSC in the present study. In Japan, epinephrine administration by an EMT was approved in 2006. Like the current study, epinephrine administration at an early stage has been reported to contribute to ROSC [26]. Thus, seamless cooperation between prehospital emergency care and hospitals in each regional area is essential for the prompt administration of epinephrine.

Third, the present results revealed a physician-staffed ambulance contributes to ROSC—in this case, physicians riding in a fire department ambulance to the scene. In Japan, this generally means a system in which not only an ambulance and EMTs are stationed in an emergency room but also physicians and EMTs dispatched by an ambulance upon request. This system may have contributed to ROSC by increasing the types of medical activities, such as prompt basic life support and epinephrine administration at the site. There have also been many reports on the usefulness of a nontransporting EMS vehicle system [27, 28], which was introduced in various areas in Japan beginning in 1991. However, a physician is not necessarily onboard all such vehicles, with figures indicating that a physician is only onboard in 4.2% of cases. This system should lead to improvement of EMT performance and the quality of medical control; thus, nationwide development of this system is desired.

LIMITATIONS

In the present study, cardiac arrest cases of both cardiogenic and noncardiogenic etiology were included in the analysis, which affected results related to initial ECG and defibrillation. Also, “other cases of ECG” that were measured by EMTs were excluded from the analysis. This group included cases in which a normal sinus rhythm had resumed before the arrival of EMTs. This, therefore, included PAD cases, which may have lowered the performance rate of PAD. Furthermore, multiple medical activities, such as epinephrine administration, defibrillation, and airway maintenance using a device, may have been performed in the same case, and the contribution of each medical activity could not be analyzed independently.

CONCLUSIONS

The present study analyzed factors related to ROSC in OHCA cases. The results showed that “VF/VT”, “epinephrine administration” and “doctor-staffed ambulance” contributed to ROSC, which is a prerequisite of successful social rehabilitation. The importance of promptly performing CPR for VF and VT cases, the early administration of epinephrine, and the preparation of an emergency system in the community were shown to be essential to achieve ROSC in OHCA patients in a timely manner and subsequent social rehabilitation.

Conflict of interest

The authors declare no conflicts of interest associated with this manuscript.

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