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Association between ambulance response time and neurologic outcome in patients with cardiac arrest

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ABSTRACT

Purpose: Emergency medical services (EMS) response time is one of prehospital factors associated with survival rate of patients with out-of-hospital cardiac arrest (OHCA). The objective of this study was to determine whether short EMS response time was associated with improved neurologic outcome of patients with OHCA through prospective analysis.
Methods: We performed a prospective observational analysis of collected data from KoCARC registry between October 2015 and December 2016. OHCA patients aged 18 years or older with presumed cardiac etiology by emergency physicians in emergency department were included in this study.
Results: Of 3187 cardiac arrest patients enrolled in the KoCARC registry, 2309 patients were included in the final analysis. Response time threshold was 11.5 min for prehospital return of spontaneous circulation and 7.5 min for survival to discharge and favorable neurologic outcome. Patients in the ≤7.5 min response time group showed increased odds of survival to discharge (OR: 1.54, 95% CI: 1.13–2.10, $p = .006$) and favorable neurologic recovery (OR: 2.01, 95% CI: 1.36–2.99, $p = .001$). When response time was decreased by 1 min, all outcomes were improved (survival to discharge, OR: 1.08; 95% CI: 1.04–1.12, $p < .001$; favorable neurological outcome, OR: 1.14, 95% CI: 1.07–1.21, $p < .001$).
Conclusion: We found that shorter EMS response time could lead to favorable neurologic outcome in patients with OHCA of presumed cardiac origin. EMS response time threshold associated with improved favorable outcome was ≤7.5 min.

1. Introduction

Emergency medical services (EMS) response time, the period of time from when a call is made to the EMS to the point when the EMS arrive at the scene, is one of prehospital factors associated with survival rate of patients with out-of-hospital cardiac arrest (OHCA) [1]. Response time has attracted a lot of attention lately as it is a factor that could be changed sufficiently with policy and support of EMS.

Recently, several reports have shown that shorter EMS response time can improve survival rate of patients with OHCA [1-8]. Ono et al. [1] have reported that response time is closely associated with favorable neurological outcomes in bystander-witnessed patients with OHCA. However, no study has reported the relationship between response time and favorable neurologic outcomes in all patients with OHCA of cardiac origin. Therefore, the objective of this study was to determine whether short EMS response time was associated with improved neurologic outcomes of patients with OHCA through prospective analysis.

2. Methods

2.1. Study design and data collection

The Korean Cardiac Arrest Research Consortium (KoCARC) is a Korean collaborative research network developed to conceive various researches conducted in the field of out-of-hospital cardiac arrest [9]. A total of 62 secondary or tertiary hospitals in Republic of Korea participated in this consortium. All OHCA patients who were transported to participated hospitals by emergency medical technician (EMT) were enrolled in the KoCARC registry initiated in October 2015. The KoCARC registry was designed to include patients with OHCA who had a medical etiology identified by emergency physicians in each emergency department. The registry excluded OHCA patients with a terminal illness documented by medical records, patients under hospice care, pregnant patients, and patients with a previously documented 'Do Not Resuscitate' card. Patients who suffered cardiac arrest due to non-medical etiology, including trauma, drowning, poisoning, burn, asphyxia, or hanging, were also excluded from the registry [9].

Each principal investigator of participating hospital reviewed hospital records of OHCA patients and filled out their baseline

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characteristics, prehospital environmental factors, and emergency medical service (EMS) factors including time intervals, hospital interventions, and clinical outcomes. Characteristics of EMS factors were investigated based on ambulance run sheets entered by EMT. Data Safety and Monitoring Board Committee in KoCARC monitored and qualified these data periodically. Neurological recovery outcomes were measured at discharge. Cerebral performance category (CPC) score was used to measure the recovery rate. CPC scores of 1 (good performance) and 2 (moderate disability) were defined as favorable neurological outcome while a score of 3 (severe cerebral disability), 4 (vegetative state), or 5 (death) was defined as unfavorable neurologic outcome [10,11].

2.2. Study setting

This study performed prospective observational analysis of collected data from KoCARC registry between October 2015 and December 2016. Additionally, OHCA patients aged 18 years or younger were excluded in this study. Patients with missing or incomplete medical record data (especially time interval) and those whose OHCA episode had been witnessed by EMS personnel were also excluded. This study was approved by the Institutional Review Board of Soonchunhyang University.

2.3. Korean EMS system

The Korean EMS system is operated directly by the government. A basic-to-intermediate service level of ambulance is operated by 16 provincial headquarters of the national fire department, covering a population of approximately 50 million [12]. Korean EMS has recently established a centrally based, two-tiered system for OHCA patients in which an ambulance is dispatched with two or three EMTs, including at least one level 1 EMT. Level 1 EMT can execute care that is comparable to EMT-I (intermediate EMT) level in the US, including administering intravenous fluids, endotracheal intubation, and laryngeal mask airway insertion under direct medical oversight. However, they can only use medications for advanced cardiac life support (e.g., epinephrine, amiodarone) under direct medical control in limited areas. EMTs dispatched to the field can perform conventional BLS and transfer the patient to the nearest hospital. EMTs cannot declare death or stop CPR on scene or during transport. All patients with OHCA should be transported to the emergency department unless emergency physician instructed EMTs to stop CPR by direct medical instruction [13].

EMS response time was defined by the time interval from the time of call receipt to EMS dispatcher center to arrival of vehicle at the scene. The time of call receipt was automatically stored in the EMS headquarters, printed in the ambulance run sheet. The time to arrival was electronically stored based on Global Positioning System (GPS) location and time of the ambulance, whereas if there is a problem with the GPS, EMT could modified it with the correct time.

2.4. Statistical analysis

Statistical analysis was performed using SPSS version 21.0 for Windows (SPSS Inc., Chicago, IL, USA). Nominal variables are expressed as counts and percentages of total numbers. Continuous variables are expressed as mean and standard deviation (SD). χ^2-test (Fisher's exact test) and Student's *t*-test (for continuous variables) at a significance level of $p < .05$ were used to test differences of observed characteristics and outcomes of patients. Receiver operating characteristic (ROC) curve analysis with Youden Index were performed to calculate optimal cut-off values for the response time that predicted prehospital ROSC, survival to discharge, and favorable neurological outcomes. We also executed ROC curve analysis for patients with OHCA who received bystander CPR and witnessed by bystander.

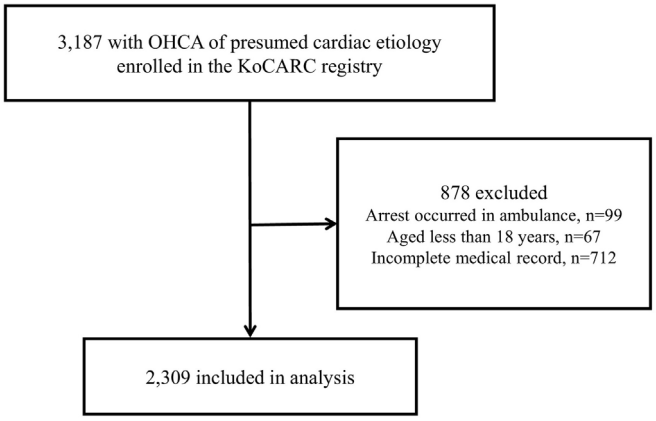

Fig. 1. Flow charts of the inclusion of patients.

Using logistic regression analysis including seven independent variables (sex, age, witnessed, bystander CPR, place, cardiac rhythm, and drug administration on scene), we assessed the adjusted odds ratios (ORs) and 95% confidence intervals for prehospital ROSC, survival to discharge, and favorable neurological outcome.

3. Results

3.1. Patient collection

Of 3187 cardiac arrest patients enrolled in the KoCARC registry, 2309 were included in the final analysis during the study period

Table 1
Characteristics of all patients with OHCA.

Characteristics	Total
	(*N* = 2309)
Age, years	67.1 ± 15.3
Male sex	1519 (65.8%)
Witnessed arrest	1274 (55.2%)
Occurrence place	
Housing facility	1560 (67.6%)
Industrial facility	98 (4.2%)
Sports/leisure facility	123 (5.3%)
Road/motorway	212 (9.2%)
Public facility/restaurants	166 (7.2%)
Hospital/nursing facility	131 (5.7%)
Educational facility	6 (0.3%)
Unknown	13 (0.6%)
Bystander CPR	
Chest compression only	1225 (53.1%)
Chest compression and rescue breathing	60 (2.6%)
No CPR	1024 (44.3%)
AED by bystander	58 (2.5%)
Initial cardiac rhythm	
Ventricular fibrillation or tachycardia	481 (20.8%)
Pulseless electrical activity	423 (18.3%)
Asystole	1405 (60.8%)
EMS response time, minutes	9.28 ± 8.27
Life support by EMT	
Defibrillation	623 (27.0%)
Airway management	1934 (83.8%)
Drug administration	337 (14.6%)
Outcome	
Prehospital ROSC	301 (13.0%)
Survival to discharge	258 (11.2%)
Favorable neurological outcome	174 (7.5%)

Data was reported as mean ± standard deviation for continuous variables and frequency (percentage) for categorical variables.
OHCA, out-of-hospital cardiac arrest; CPR, cardiopulmonary resuscitation; AED, automated external defibrillator; EMS, emergency medical services; EMT, emergency medical technician; ROSC, return of spontaneous circulation.

(Fig. 1). A total of 878 patients, including 99 patients whose OHCA episode occurred in ambulance, 67 patients aged <18 years, and 712 patients with missing or incomplete medical record were excluded from final analysis.

Table 1 displays patient characteristics, EMS factor, time interval, post resuscitation care, and outcome for all OHCA patients. During the study period, the average response time of EMT was 9.28 ± 8.27 min. Rates of prehospital ROSC, survival to discharge, and favorable neurologic outcome were 13.0%, 11.2%, and 7.5%, respectively.

3.2. Cumulative rates for patients' outcome

Cumulative rates drawn with line graph for prehospital ROSC, survival to discharge, favorable neurologic outcome, and cumulative number drawn with bar charts of all OHCA patients are shown in Fig. 2. Cumulative numbers of patients with OHCA receiving bystander CPR and witnessed OHCA patients are also displayed. Cumulative rates for all outcomes in patients with OHCA receiving bystander CPR and witnessed OHCA patients were always higher than those for all OHCA patients. With increasing response time, cumulative rates for all outcomes decreased and plateaued after 10 min.

3.3. Response time threshold measured by ROC curve analysis

ROC curve analysis was performed to determine the optimal response time threshold to predict prehospital ROSC, survival discharge, and favorable neurological outcome. Response time threshold for prehospital ROSC was 11.5 min. It was 7.5 min for survival to discharge and favorable neurologic outcome (Table 2). In patients with OHCA receiving bystander CPR and witnessed OHCA patients, the response time threshold was the same as the threshold for all OHCA patients.

Characteristics of patients with response time of 7.5 min and 11.5 min are shown in Tables A and B. There was no significant difference in any variable between the two groups except for the administration of epinephrine.

3.4. Adjusted odds ratios for patients' outcome

Table 3 displays adjusted ORs for prehospital ROSC, survival to discharge, and favorable neurologic outcome in OHCA patients with response time ≤ 7.5 min or ≤ 11.5 min per min shorter. Patients in the $\leq$7.5 min response time group showed increased odds of survival to discharge (OR: 1.54, 95% CI: 1.13–2.10, $p = .006$) and favorable neurologic recovery (OR: 2.01, 95% CI: 1.36–2.99, $p = .001$) than patients in the >7.5 min response time group. Patients in the $\leq$11.5 min response time group showed increased odds of all outcomes than patients in the >11.5 min response time group (survival to discharge, OR: 1.91, 95% CI: 1.20–3.04, $p = .007$; favorable neurological outcome, OR: 3.94, 95% CI: 2.01–7.74, $p < .001$). When response time was decreased by 1 min, all outcomes were improved (survival to discharge, OR: 1.08, 95% CI: 1.04–1.12, $p < .001$; favorable neurological outcome, OR: 1.14, 95% CI: 1.07–1.21, $p < .001$).

4. Discussion

This was a prospective observational study that evaluated the relationship between EMS response time and neurologic outcomes among OHCA patients regardless of bystander-witness. We found that shorter EMS response time was associated with favorable neurologic outcome in patients with OHCA of cardiac origin. The response time threshold for favorable neurologic outcome was 7.5 min. This study showed that the optimal response time threshold to predict outcome of all OHCA patients, OHCA patients receiving bystander CPR, or witnessed OHCA patients was not different.

BLS is the corner stone for saving lives after cardiac arrest. Fundamental aspects of BLS include immediate recognition of sudden cardiac arrest and rapid activation of the EMS, early CPR, and rapid defibrillation with an automated external defibrillator (AED) [14-16]. If the bystander can recognize cardiac arrest and start CPR and EMT arrives quickly, survival rate and neurologic recovery rate are expected to increase. Eisenberg et al. [17] have assessed the relationship between response time and survival of OHCA patients. They originally reported a response time threshold of 4 min in 1979. Several recent studies have concluded decrease in EMS response time is associated with improved survival of OHCA. However, these reports did not show the optimal threshold for survival of OHCA or neurological outcome. To demonstrate the efficacy of pure response time, the study should be directed to bystander-witnessed cardiac arrest patients. Ono et al. [1] have shown evidence to support the hypothesis that a shorter response time is closely associated with favorable neurological outcomes in witnessed patients with OHCA in a retrospective study. They also demonstrated that the response time threshold associated with favorable neurologic outcomes was 6.5 min for all patients with witnessed OHCA and 7.5 min for patients who received bystander CPR. We theorize that a shorter response time is associated with improved neurological outcomes of all OHCA patients of cardiac origin regardless of witness. This study is the first attempt to assess this response time threshold in a prospective fashion.

The response time threshold associated with favorable neurological outcome in our study was 7.5 min, which was the same as that in a previous study [6]. Nevertheless, whether the threshold

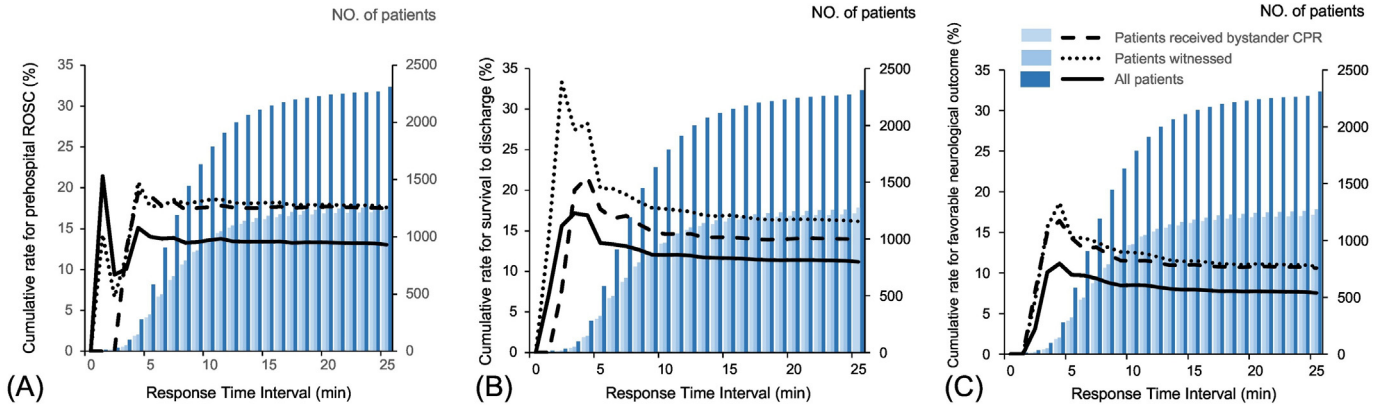

Fig. 2. Cumulative rates of all patients, witnessed patients and patients receiving bystander CPR for (A) prehospital ROSC, (B) survival to discharge and (C) favorable neurological outcome. The cumulative rates (line graphs) for prehospital ROSC, survival to discharge, favorable neurologic outcome, and the cumulative number (bar charts) of all OHCA patients are shown. The cumulative rates of all patients for prognosis decreases over time. CPR, cardiopulmonary resuscitation; ROSC, return of spontaneous circulation.

Table 2
Diagnostic performance of good outcome.

Outcome	THR†	SEN	SPE	ACC	PPV	NPV	AUC (95% CI)
All patients							
Prehospital ROSC	11.5	263/301 (87.4%)	363/2008 (18.1%)	626/2309 (27.1%)	263/1908 (13.8%)	363/401 (90.5%)	0.524 (0.490–0.558)
Survival to discharge	7.5	156/258 (60.5%)	1017/2051 (49.6%)	1173/2309 (50.8%)	156/1190 (13.1%)	1017/1119 (90.9%)	0.567 (0.531–0.604)
Favorable neurological outcome	7.5	111/174 (63.8%)	1056/2135 (49.5%)	1167/2309 (50.5%)	111/1190 (9.3%)	1056/1119 (94.4%)	0.587 (0.545–0.629)
Patients received bystander CPR							
Prehospital ROSC	11.5	191/221 (86.4%)	174/1064 (16.4%)	365/1285 (28.4%)	191/1081 (17.7%)	174/204 (85.3%)	0.512 (0.471–0.554)
Survival to discharge	7.5	107/179 (59.8%)	559/1106 (50.5%)	666/1285 (51.8%)	107/654 (16.4%)	559/631 (88.6%)	0.559 (0.513–0.604)
Favorable neurological outcome	7.5	84/136 (61.8%)	579/1149 (50.4%)	663/1285 (51.6%)	84/654 (12.8%)	579/631 (91.8%)	0.576 (0.526–0.626)
Patients witnessed							
Prehospital ROSC	11.5	195/224 (87.1%)	196/1050 (18.7%)	391/1274 (30.7%)	195/1049 (18.6%)	196/225 (87.1%)	0.521 (0.481–0.562)
Survival to discharge	7.5	128/206 (62.1%)	538/1068 (50.4%)	666/1274 (52.3%)	128/658 (19.5%)	538/616 (87.3%)	0.585 (0.543–0.627)
Favorable neurological outcome	7.5	91/138 (65.9%)	569/1136 (50.1%)	660/1274 (51.8%)	91/658 (13.8%)	569/616 (92.4%)	0.607 (0.56–0.654)

† Threshold was computed by Youden's index.
Sensitivity, specificity, accuracy, PPV and NPV were calculated from the threshold and the 95% CI of AUC was computed by Delong's method. AUC of the splenic factor was compared to the AUC of splenic volume by Delong's method and the *p*-values were corrected by Bonferroni's method.
THR, threshold; SEN, sensitivity; SPE, specificity; ACC, accuracy; PPV, positive predictive value; NPV, negative predictive value; CI, confidence interval.

Table 3
Adjusted odd ratios for outcomes in all patients.

Outcome	Response time interval (min)					
	Per min shorter		≤7.5		≤11.5	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Prehospital ROSC	0.97 (0.94–1.01)	0.10	1.14 (0.86–1.52)	0.36	1.59 (1.05–2.40)	0.03
Survival to discharge	0.93 (0.89–0.97)	<0.001	1.54 (1.13–2.10)	0.006	1.91 (1.20–3.04)	0.007
Favorable neurological outcome	0.88 (0.83–0.93)	<0.001	2.01 (1.36–2.99)	0.001	3.94 (2.01–7.74)	<0.001

OR, odds ratio; CI, confidence interval; ROSC, return of spontaneous circulation.

for response time that predicts survival to discharge, favorable neurological outcomes in patients with OHCA receiving bystander CPR, and witnessed OHCA patients is the same as that for all OHCA patients remains unclear. This might be due to the fact that the number of patients was not enough to address the relationship between bystander-CPR witnessed and response time. Recent studies of OHCA have reported that bystander CPR with a shorter EMS response time is associated with improved survival and neurological outcome [1,5,18]. Bystander-witness and bystander CPR were independently associated with clinical outcomes in our study. Although there was no statistical significance, adjusted ORs were higher in bystander witness and bystander CPR for clinical outcomes. Another possibility is that differences might have occurred due to prehospital characteristics of OHCA. Lay rescuer AED use is rare in South Korea [19]. The bystander CPR rate was increased by dispatcher assisted bystander CPR using a simplified protocol based on compression only CPR [20]. Although CPR training and education have been implemented every year, the quality of bystander CPR performance and dispatcher CPR instruction remain variable. Further research on the quality of bystander CPR and response time is needed.

This study has several limitations. First, although prospectively collected data were used, 712 patients (22.3%) with incomplete or missing important variables were excluded in the analysis. This might have resulted in some selection bias. Second, we could not analyze the relationship between bystander CPR witnessed and response time. Further study including more OHCA patients is needed. Third, 1 or 6-month outcome after cardiac arrest was not included in the analysis. Thus, more accurate clinical outcomes were not evaluated in this investigation.

5. Conclusions

Shorter EMS response time can lead to favorable neurologic outcome in patients with OHCA of presumed cardiac origin. EMS response time threshold associated with improved favorable outcome was ≤7.5 min.

Conflicts of interest

The authors have no conflict of interest to report.

Source(s) of support

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Appendix A

Table A

Characteristics of all patients according to response time interval 11.5 min

Response time interval	≤11.5 (N = 1908)	>11.5 (N = 401)	p-value
Age, years	67.2 ± 15.1	66.7 ± 16.0	0.707
Male sex	1252 (65.6%)	267 (66.6%)	0.755
Witnessed arrest	1049 (55.0%)	225 (56.1%)	0.72
Occurrence place			0.125
Housing facility	1303 (68.3%)	257 (64.1%)	
Industrial facility	80 (4.2%)	18 (4.5%)	
Sports/leisure facility	92 (4.8%)	31 (7.7%)	
Road/motorway	174 (9.1%)	38 (9.5%)	
Public facility/restaurants	143 (7.5%)	23 (5.7%)	
Hospital/nursing facility	100 (5.2%)	31 (7.7%)	
Educational facility	5 (0.3%)	1 (0.2%)	
Unknown	11 (0.6%)	2 (0.5%)	
Bystander CPR			0.073
Chest compression only	1033 (54.1%)	192 (47.9%)	
Chest compression and rescue breathing	48 (2.5%)	12 (3.0%)	
No CPR	827 (43.3%)	197 (49.1%)	
AED by bystander	49 (2.6%)	9 (2.2%)	0.841
Initial cardiac rhythm			0.16
Ventricular fibrillation or tachycardia	405 (20.2%)	76 (18.9%)	
Pulseless electrical activity	360 (18.9%)	63 (15.7%)	
Asystole	1143 (59.9%)	262 (65.3%)	
Life support by EMT			
Defibrillation	521 (27.3%)	102 (25.4%)	0.481
Airway management	1598 (83.8%)	336 (83.8%)	1
Drug administration	256 (13.4%)	81 (20.2%)	0.001
Outcome			
Prehospital ROSC	263 (13.8%)	38 (9.5%)	0.025
Survival discharge	230 (12.1%)	28 (7.0%)	0.004
Favorable neurological outcome	162 (8.5%)	12 (3.0%)	<0.001

Data was reported as mean ± standard deviation for continuous variables and frequency (percentage) for categorical variables.
OHCA, out-of-hospital cardiac arrest; CPR, cardiopulmonary resuscitation; AED, automated external defibrillator; EMS, emergency medical services; EMT, emergency medical technician; ROSC, return of spontaneous circulation.

Table B

Characteristics of all patients according to response time interval 7.5 min

Response time interval	≤7.5 (N = 1190)	>7.5 (N = 1119)	p-value
Age, years	67.4 ± 15.2	66.9 ± 15.4	0.41
Male sex	782 (65.7%)	737 (65.9%)	0.975
Witnessed arrest	658 (55.3%)	616 (55.0%)	0.939
Occurrence place			0.006
Housing facility	805 (67.6%)	755 (67.5%)	
Industrial facility	49 (4.1%)	49 (4.4%)	
Sports/leisure facility	48 (4.0%)	75 (6.7%)	
Road/motorway	117 (9.8%)	95 (8.5%)	
Public facility/restaurants	101 (8.5%)	65 (5.8%)	
Hospital/nursing facility	60 (5.0%)	71 (6.3%)	
Educational facility	5 (0.4%)	1 (0.1%)	
Unknown	5 (0.4%)	8 (0.7%)	
Bystander CPR			0.73
Chest compression only	622 (52.3%)	603 (53.9%)	
Chest compression and rescue breathing	32 (2.7%)	28 (2.5%)	
No CPR	536 (45.0%)	488 (43.6%)	
AED by bystander	30 (2.5%)	28 (2.5%)	1
Initial cardiac rhythm			0.538
Ventricular fibrillation or tachycardia	263 (22.1%)	218 (19.5%)	
Pulseless electrical activity	217 (18.2%)	206 (18.4%)	
Asystole	710 (59.7%)	695 (62.1%)	
Life support by EMT			
Defibrillation	331 (27.8%)	292 (26.1%)	0.377
Airway management	1000 (84.0%)	934 (83.5%)	0.755
Drug administration	149 (12.5%)	188 (16.8%)	0.004
Outcome			
Prehospital ROSC	165 (13.9%)	136 (12.2%)	0.246
Survival discharge	156 (13.1%)	102 (9.1%)	0.003
Favorable neurological outcome	111 (9.3%)	63 (5.6%)	0.001

Data was reported as mean ± standard deviation for continuous variables and frequency (percentage) for categorical variables.
OHCA, out-of-hospital cardiac arrest; CPR, cardiopulmonary resuscitation; AED, automated external defibrillator; EMS, emergency medical services; EMT, emergency medical technician; ROSC, return of spontaneous circulation.

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