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Effects of advanced life support on patients who suffered cardiac arrest outside of hospital and were defibrillated

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A B S T R A C T

Background: The effects and relative benefits of advanced airway management and epinephrine on patients with out-of-hospital cardiac arrest (OHCA) who were defibrillated are not well understood.
Methods: This was a prospective observational study. Using data of all out-of-hospital cardiac arrest cases occurring between 2005 and 2013 in Japan, hierarchical logistic regression and conditional logistic regression along with time-dependent propensity matching were performed. Outcome measures were survival and minimal neurological impairment [cerebral performance category (CPC) 1 or 2] at 1 month after the event.
Results: We analyzed 37,873 cases that met the inclusion criteria. Among propensity-matched patients, advanced airway management and/or prehospital epinephrine use was related to decreased rates of 1-month survival (adjusted odds ratio 0.88, 95% confidence interval 0.80 to 0.97) and CPC (1, 2) (adjusted odds ratio 0.56, 95% confidence interval 0.48 to 0.66). Advanced airway management was related to decreased rates of 1-month survival (adjusted odds ratio 0.89, 95% confidence interval 0.81to 0.98) and CPC (1, 2) (adjusted odds ratio 0.54, 95% confidence interval 0.46 to 0.64) in patients who did not receive epinephrine, whereas epinephrine use was not related to the outcome measures.
Conclusions: In defibrillated patients with OHCA, advanced airway management and/or epinephrine are related to reduced long-term survival, and advanced airway management is less beneficial than epinephrine. However, the proportion of patients with OHCA who responded to an initial shock was very low in the study subjects, and the external validity of our findings might be limited.

1. Introduction

Advanced life support (ALS) for patients with out-of-hospital cardiac arrest (OHCA) by emergency medical services (EMS) consists of semi-automated defibrillation, advanced airway management, and epinephrine administration. ALS by EMS has been regarded as an important element of the response to OHCA in many countries [1]. A meta-analysis of ALS and basic life support (BLS) revealed that the administration of ALS to patients with non-traumatic cardiac arrest increased survival to hospital discharge [2]. Several findings indicate that prehospital advanced airway management can be effective under certain conditions, including cases of return of spontaneous circulation (ROSC) before hospital arrival [3-5]. Some reports have indicated that prehospital epinephrine use is related to increased survival to hospital arrival and 1-month survival [6,7].

However, findings revealing the negative effects of ALS are dominant. Although one meta-analysis conducted in the 1990s to examine EMS systems including the administration of ALS to patients with OHCA showed that ALS was beneficial [8], the analysis had several limitations because of the quality and completeness of existing literature [8,9]. A robust before-and-after study conducted in Ontario, Canada, showed that ALS did not improve the rate of survival to hospital discharge [10]. Two observational studies conducted in Taiwan and the USA showed that patients with OHCA who received BLS had higher rates of survival to hospital discharge than those who received ALS [11,12]. Similarly, most studies have shown that advanced airway management has negative effects or no effect on survival and neurological outcome of patients with OHCA [13,14]. Negative effects of prehospital epinephrine use on long-term outcomes have also been reported [6,15].

Resuscitation guidelines recommend the administration of advanced airway management and epinephrine after defibrillation to patients with OHCA of presumed cardiac origin whose initial rhythms are shockable. The efficacy of early defibrillation has been established [10]. However, we know little about the effects of advanced airway management and/or epinephrine on defibrillated patients with OHCA. The optimal response intervals for advanced airway management and epinephrine administration are also less clear than that of defibrillation

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[10]. We also do not know whether advanced airway management and epinephrine interact. Thus, using national data from the whole sample of OHCAs occurring between 2005 and 2013 in Japan, we performed time-dependent propensity matching and evaluated the effects, interaction, and time modification of advanced airway management and epinephrine in patients with OHCA who were defibrillated.

2. Methods

This prospective observational study was conducted using national registry data. The study was approved by the ethics committee of Kyushu University Graduate School of Medicine. The requirement for written informed consent was waived.

2.1. Data collection

The EMS system in Japan has been described elsewhere [16]. Briefly, EMS is provided by municipal governments through about 800 fire stations with dispatch centers. The Japanese guidelines do not allow EMS providers to terminate resuscitation in the field. Thus, all patients with OHCA who are treated by EMS personnel are transported to hospitals [17]. The Fire and Disaster Management Agency (FDMA) has maintained a prospective, nationwide, population-based registry of all OHCA cases in Japan using a standardized Utstein-style template. EMS personnel, in cooperation with the physicians in charge of patients with OHCA, summarize each OHCA case in the standardized Utstein style [17,18]. Data from the 800 fire stations with dispatch centers in the 47 prefectures of Japan are then integrated into the national registry system on the FDMA database server. The data are checked electronically by the FDMA, and returned to the respective fire stations for error correction when problems are detected.

2.2. Subjects

The patients were aged 18–100 years and had OHCAs of presumed cardiac origin before the arrival of EMS personnel between 1 January 2005 and 31 December 2013 in Japan (Supplementary Fig. S1). Intervals from calls to EMS arrival at the scene and at hospital were ≤60 min and ≤120 min, respectively. OHCAs were witnessed, bystanders did not provide automated external defibrillation, no epinephrine was administered after ROSC, and EMS personnel performed defibrillation. Intervals from calls to first defibrillation by EMS personnel were ≤60 min, and patients were transported to medical institutions thereafter.

2.3. Study variables

The "ALS" group included cases in which advanced airway management and/or epinephrine was used, and the "no ALS" group included cases in which neither measure was used. Advanced airway management includes endotracheal intubation and use of supraglottic airway devices (*i.e.*, laryngeal mask airway, laryngeal tube, esophageal-tracheal twin-lumen airway device). Table 1 shows the variables used in the study by ALS status. "Advanced support by MD" is a variable that indicates if ALS was performed by MD. The origins of cardiac arrests (*i.e.*, presumed cardiac or non-cardiac) were determined clinically by physicians in charge with the aid of EMS personnel.

When patients survived cardiac arrest, they were followed for up to 1 month after the event, and information on survival and neurological function at 1 month after the event or at hospital discharge, whichever was earlier, was collected. Neurological outcomes 1 month after successful resuscitation were evaluated using the Cerebral Performance Category (CPC) scale (1: good cerebral performance, 2: moderate cerebral disability, 3: severe cerebral disability, 4: coma or vegetative state, 5: death) [17-19].

Table 1
Baseline characteristics of patients with OHCA who were defibrillated.

Variable	No ALS ($n = 14{,}621$)		ALS ($n = 23{,}252$)		*P* value
Patients with OHCA					
Cases by year, *n* (%)[a]					
2005	1906	(13.04)	2275	(9.79)	0.00
2006	1882	(12.87)	2595	(11.16)	
2007	1598	(10.93)	2430	(10.45)	
2008	1824	(12.48)	2608	(11.22)	
2009	1746	(11.94)	2721	(11.70)	
2010	1777	(12.15)	2836	(12.20)	
2011	1362	(9.32)	2357	(10.14)	
2012	1437	(9.83)	2984	(12.84)	
2013	1088	(7.44)	2441	(10.50)	
Sex (male), *n* (%)	10,919	(74.68)	18,223	(78.37)	0.00
Age (years), mean (SD)	67.80	(15.42)	66.82	(15.13)	0.00
Emergency life-saving technician in ambulance (yes), *n* (%)	13,224	(90.45)	23,137	(99.51)	0.00
Medical doctor in ambulance (yes), *n* (%)[a]	571	(3.91)	1130	(4.86)	0.00
Advanced life support by MD (yes), *n* (%)[a]	2420	(16.56)	3082	(13.26)	0.00
Relationship of bystander to patient (family member), *n* (%)	7282	(49.81)	14,053	(60.44)	0.00
CPR initiated by bystander					
Chest compression (yes), *n* (%)[a]	5674	(39.28)	10,121	(44.58)	0.00
Rescue breathing (yes), *n* (%)[a]	2000	(13.91)	3043	(13.57)	0.35
Life support by EMS personnel					
Time from call to first defibrillation (min), mean (SD)[b]	14.51	(8.25)	14.28	(8.36)	0.01
Time from call to arrival at hospital (min), mean (SD)[b]	29.78	(11.89)	35.74	(12.13)	0.00
Number of attempted defibrillations, *n* (%)					
1, 2	10,058	(68.79)	14,209	(61.11)	0.00
≥3	4563	(31.21)	9043	(38.89)	
Insertion of intravenous line (yes), *n* (%)[a]	0	(0.00)	12,948	(55.69)	0.00
ROSC (yes), *n* (%)[b]	8	(0.05)	1994	(8.58)	0.00
ALS[b]					
Epinephrine use (yes), *n* (%)	0	(0.00)	3041	(13.08)	0.00
Advanced airway management (yes), *n* (%)	0	(0.00)	14,044	(60.40)	
Epinephrine use & advanced airway management (yes), *n* (%)	0	(0.00)	6167	(26.52)	
Endpoints[b]					
1-month survival after cardiac arrest (yes), *n* (%)	1648	(11.27)	2505	(10.77)	0.13
Cerebral performance category 1 or 2 (good performance/moderate disability) 1 month after the event (yes), *n* (%)	863	(5.90)	954	(4.10)	0.00

The ALS group included cases in which advanced airway management and/or epinephrine was used, and the no ALS group included cases in which neither measure was used.
ROSC: return of spontaneous circulation before hospital arrival.
[a] Numbers do not add up to totals due to missing values.
[b] These variables were not included in the logistic regression model for the generation of the propensity score.

2.4. Endpoints

Endpoints were survival at 1 month after the event and survival with minimal neurological impairment, defined as CPC category 1 or 2 (Table 1) [17-19].

2.5. Statistical analysis

Using data for all 37,873 patients, hierarchical logistic regression models with the endpoints listed in Table 1 serving as dependent variables were fitted to examine the association between ALS and long-

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