ORIGINAL RESEARCH

Subsequent Shockable Rhythm During Out-of-Hospital Cardiac Arrest in Children With Initial Non-Shockable Rhythms: A Nationwide Population-Based Observational Study

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***Background*—**The effect of a subsequent treated shockable rhythm during cardiopulmonary resuscitation on the outcome of children who suffer out-of-hospital cardiac arrest with initial nonshockable rhythm is unclear. We hypothesized that subsequent treated shockable rhythm in children with out-of-hospital cardiac arrest would improve survival with favorable neurological outcomes (Cerebral Performance Category scale 1–2).

***Methods and Results*—**From the All-Japan Utstein Registry, we analyzed the records of 12 402 children (aged <18 years) with out-of-hospital cardiac arrest and initial nonshockable rhythms. Patients were divided into 2 cohorts: subsequent treated shockable rhythm (YES; n=239) and subsequent treated shockable rhythm (NO; n=12 163). The rate of 1-month cerebral performance category 1 to 2 in the subsequent treated shockable rhythm (YES) cohort was significantly higher when compared to the subsequent treated shockable rhythm (NO) cohort (4.6% [11 of 239] vs 1.3% [155 of 12 163]; adjusted odds ratio, 2.90; 95% CI, 1.42–5.36; all P<0.001). In the subsequent treated shockable rhythm (YES) cohort, the rate of 1-month cerebral performance category 1 to 2 decreased significantly as time to shock delivery increased (17.7% [3 of 17] for patients with shock-delivery time 0–9 minutes, 7.3% [8 of 109] for 10–19 minutes, and 0% [0 of 109] for 20–59 minutes; P<0.001 [for trend]). Age-stratified outcomes showed no significant differences between the 2 cohorts in the group aged <7 years old: 1.3% versus 1.4%, P=0.62.

***Conclusions*—**In children with out-of-hospital cardiac arrest and initial nonshockable rhythms, subsequent treated shockable rhythm was associated with improved 1-month survival with favorable neurological outcomes. In the cohort of older children (7–17 years), these outcomes worsened as time to shock delivery increased. **(*J Am Heart Assoc*. 2016;5:e003589 doi: 10.1161/JAHA.116.003589)**

Key Words: cardiopulmonary resuscitation • defibrillation • epidemiology • heart arrest • resuscitation

Out-of-hospital cardiac arrest (OHCA) in children is an uncommon event, with incidence rates between 3.0 and 9.0 per 100 000/year.[1] Recent population-based studies of children with OHCA showed survival rates ranging from 4.7% to 16%.[2–7] Children with OHCA and initial shockable rhythms (ventricular fibrillation [VF] and pulseless ventricular tachycardia) have improved outcomes when compared to patients with initial nonshockable rhythm (pulseless electrical activity [PEA] and asystole).[8–10] However, the proportion of initial shockable rhythms in children with OHCA is very low, ranging from 2.0% to 19.8%,[2–10] with the higher incidence among adolescents. Defibrillation for shockable rhythms is widely applied and has been strongly emphasized in recent guidelines for pediatric cardiopulmonary resuscitation (CPR).[11–14] In children who experienced in-hospital cardiac arrest, the survival rate with subsequent defibrillation was substantially lower than that of patients with initial shockable rhythms and in those with an initial nonshockable rhythm with no follow-up shock delivery.[15,16] However, in children with OHCA, it remains unclear as to whether shock delivery for subsequent shockable rhythm following an initial nonshockable rhythm is associated with improved outcomes.

In the present study of children with OHCA and initial nonshockable rhythms, we examined whether improved neurological outcomes are associated with shock delivery for a presumed subsequent shockable rhythm, when compared to those who did not receive shock delivery.

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Methods

Study Design

This investigation was a nation-wide population-based observational study in Japan of children with OHCA for whom resuscitation had been attempted between January 1, 2005 and December 31, 2012. Cardiac arrest was defined as the cessation of cardiac mechanical activity and was confirmed by the absence of signs of circulation. The cause of arrest was presumed to be cardiac, with the exception of those cases that showed evidence of external causes (eg, drowning, foreign body obstruction, hanging, mechanical suffocation, trauma, and accidental hypothermia), respiratory diseases, cerebrovascular diseases, malignant tumors, or any other noncardiac cause. The determination of the cause as noncardiac or cardiac was made by the physicians in charge in collaboration with the emergency medical services (EMS) personnel. This study was approved by the Ethics Committee of Kanazawa University. According to guidelines in Japan,[17] informed consent from each patient to use secondary data such as that in this anonymous database is unnecessary. Therefore, the requirement for written informed consent was waived.

Study Setting

Japan has ≈127 million residents in an area of 378 000 km^2, approximately two thirds of which is uninhabited mountainous terrain.[18] Municipal governments in Japan provide EMS through ≈800 fire stations with dispatch centers.[19] The Fire and Disaster Management Agency (FDMA) of Japan supervises the nation-wide EMS system. During the study period, all EMS providers performed CPR according to guidelines of the Japan Resuscitation Council[20,21] and the American Heart Association.[22] Emergency life-saving technicians (ELSTs), who are EMS providers, are allowed to provide several resuscitation therapies, including use of an automated external defibrillator (AED), insertion of an airway adjunct, establishment of peripheral intravenous access, and administration of Ringer's lactate solution.[19,23] However, only specially trained ELSTs receiving online physician instruction are permitted to insert a tracheal tube and administer intravenous epinephrine in the field. Because EMS personnel in Japan are legally prohibited from terminating resuscitation in the field (except in specific situations such as decapitation, incineration, decomposition, rigor mortis, or dependent cyanosis), most patients with OHCA undergo CPR by EMS providers and are subsequently transported to the hospital. When EMS providers arrived at the scene, initiation of CPR and initial rhythm assessment through AED were generally performed simultaneously. An AED delivers a shock only when it detects a shockable rhythm. When initial nonshockable rhythm was identified, rhythm analysis was performed every 2 minutes by AED during CPR.

Data Collection and Quality Control

In January 2005, the FDMA launched a prospective, population-based, observational study including all OHCA patients who received EMS in Japan.[19] EMS personnel at each center recorded OHCA patient data in cooperation with the physician in charge, using an Utstein-style template.[24] The data were transferred to their fire stations and then integrated into the registry system on the FDMA database server. All data were stored in the nation-wide database developed by the FDMA for public use. The FDMA gave permission to analyze this database and provided all anonymous data to our research group.

The main variables included in the data set were as follows: sex, age, cause of arrest, bystander witness status, bystander-witnessed category (such as a family member, a layperson other than family, or EMS personnel), initially identified cardiac rhythm, presence and type of bystander CPR (compression only or compression with ventilation), use of AED (either by the public or by EMS providers), epinephrine administration, advanced airway management, time variables (collapse, emergency call, vehicle arrival, and CPR initiation), prehospital return of spontaneous circulation (ROSC), 1-month survival, and neurological outcomes 1 month after cardiac arrest. The neurological outcome was defined using the Cerebral Performance Category (CPC) scale: category 1, good cerebral performance; category 2, moderate cerebral disability; category 3, severe cerebral disability; category 4, coma or vegetative state; and category 5, death.[24] The CPC categorization was determined by the physician in charge.

Study Endpoints

The primary study endpoint was 1-month survival with favorable neurological outcome (defined as a CPC score of 1 or 2). The secondary endpoints were prehospital ROSC and 1-month survival.

Statistical Analysis

The Wilcoxon and Kruskal–Wallis tests for continuous variables and the chi-square test for categorical variables were performed to compare the characteristics or outcomes of the cohorts. We further analyzed multivariate logistic regression models in order to clarify the relationship between subsequent shockable rhythm and outcomes. Multivariate logistic regression analyses including 7 variables were performed to assess the factors associated with increased odds of prehospital ROSC, 1-month survival, and 1-month CPC 1 or 2 for all eligible patients. The potential prehospital confounders for the analytic model were selected based on biological plausibility and data from previous studies. Independent variables included age, bystander-witnessed arrest (yes or no), initial cardiac rhythm (PEA or asystole), presumed cardiac etiology (yes or no), prehospital epinephrine administration (yes or no), use of advanced airway management (yes or no), and subsequent treated shockable rhythm (yes or no). The call-to-response time was calculated as the time from receipt of the call to the time of vehicle arrival at the scene. Shock-delivery time was defined as the time interval between initiation of CPR by EMS personnel and the first EMS-administered shock.

Outcomes of patients with subsequent treated shockable rhythm were compared according to shock-delivery time and classified into 3 groups: 0 to 9, 10 to 19, and 20 to 59 minutes. The Cochran-Armitage trend test was applied to analyze these data. Moreover, after dividing patients into 2 groups according to age (age <7 years or age 7–17 years for elementary to high school children in Japan), the outcomes in the 2 groups were compared according to the presence of subsequent treated shockable rhythm and shock-delivery time.

Continuous variables are expressed as median with interquartile range (IQR) 1 to 3. Categorical variables are expressed as percentages. As an estimate of effect size and variability, odds ratios (ORs) or proportion of outcomes with 95% CIs were used. All statistical analyses were performed using the JMP statistical package (version 11 Pro; SAS Institute Inc., Cary, NC). All tests were 2-tailed, and a value of $P<0.05$ was considered statistically significant.

Results

During the 8-year study period, 925 288 patients were documented in the database. Patients with initial shockable rhythms, those aged ≥18 years, and those with unknown initial rhythm or unknown 1-month outcome were excluded, so a total of 12 402 (1.34% of the total patients in the database) children (aged <18 years) with initial nonshockable rhythms were enrolled in this study. Figure 1 shows a flow diagram depicting the inclusion and exclusion criteria for subjects in the present study. The overall prehospital ROSC, 1-month survival, and 1-month CPC 1 or 2 rates were 3.7% (n=461), 7.7% (n=953), and 1.3% (n=166), respectively. Patients were divided into 2 cohorts: subsequent treated shockable rhythm (YES; n=239) and subsequent treated shockable rhythm (NO; n=12 163). Those patients with initial nonshockable rhythm who converted to shockable rhythms were identified by shocks delivered later in the course of resuscitation; These were assigned to the subsequent treated shockable rhythm (YES) cohort. Thus, the delivery of subsequent shocks was used as a surrogate maker for conversion to a shockable rhythm. Conversely, the subsequent treated shockable rhythm (NO) cohort was composed of those patients who did not receive any shocks during resuscitation.

Table 1 shows the baseline characteristics and results of the analyses of the 2 cohorts. Age, rates of bystander-witnessed arrest, initial PEA, presumed cardiac etiology, epinephrine administration, and advanced airway management were significantly higher in the subsequent treated shockable rhythm (YES) cohort when compared to the subsequent treated shockable rhythm (NO) cohort. The subsequent treated shockable rhythm (YES) cohort had significantly higher rates of prehospital ROSC, 1-month survival, and 1-month CPC 1 or 2 than the subsequent treated shockable rhythm (NO) cohort (13.8% vs 3.5%, 15.9% vs 7.5%, and 4.6% vs 1.3%, respectively, $P<0.001$; Figure 2).

Table 2 shows the results of multivariate logistic regression analyses to determine factors associated with outcomes in all participants. Subsequent shockable rhythm was significantly associated with increased odds of prehospital ROSC (adjusted OR, 2.77; 95% CI, 1.81–4.12), 1-month survival (adjusted OR, 2.30; 95% CI, 1.56–3.29), and 1-month CPC 1 or 2 (adjusted OR, 2.90; 95% CI, 1.42–5.36). Bystander-witnessed arrest and initial PEA were significantly associated with improved 1-month survival and 1-month CPC 1 or 2.

Figure 3 shows the outcomes stratified by shock-delivery time in the subsequent treated shockable rhythm (YES) cohort. Shock-delivery times were calculated in 98.3% (235 of 239) of those patients. Rates of 1-month survival and 1-month CPC 1 or 2 decreased significantly as time to shock delivery increased (1-month survival: 23.5% for 0–9 minutes, 22.0% for 10–19 minutes, and 9.2% for 20–59 minutes; $P=0.01$ [for trend]; 1-month CPC 1 or 2: 17.7% for 0–9 minutes, 7.3% for 10–19 minutes, and 0% for 20–59 minutes; $P<0.001$ [for trend]).

Table 3 compares the characteristics and outcomes according to age group. The proportion of male sex, bystander-witnessed arrest, initial PEA, epinephrine administration, advanced airway management, and subsequent treated shockable rhythm were significantly higher in the group aged 7 to 17 years when compared with the group aged <7 years. The group aged 7 to 17 years had a significantly higher rate of prehospital ROSC compared to the group aged <7 years (5.8% vs 2.7%; $P<0.001$). However, no significant differences were found in the rates of 1-month survival and 1-month CPC 1 or 2 between the 2 groups (1-month survival: 8.0% for those aged <7 years vs 7.1% for those aged 7–17 years; $P=0.08$; 1-month CPC 1 or 2: 1.3% for those aged <7 years vs 1.4% for those aged 7–17 years; $P=0.62$).

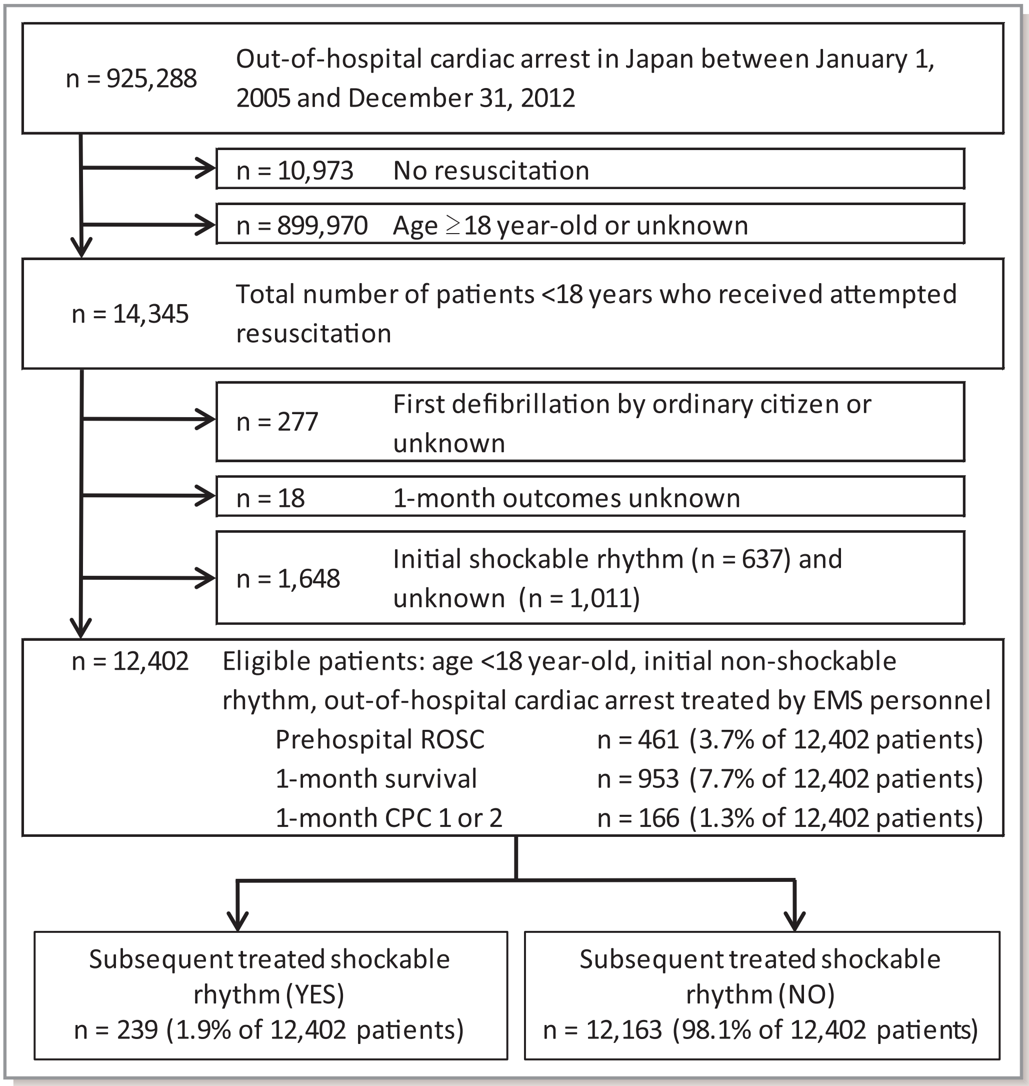

Figure 1. Design of the patient selection process. CPC indicates Cerebral Performance Category; EMS, emergency medical services; ROSC, return of spontaneous circulation.

Figure 4 shows the age-stratified outcomes according to subsequent treated shockable rhythm. In the group aged 7 to 17 years, outcomes in the subsequent treated shockable rhythm (YES) cohort were significantly better than for those in the subsequent treated shockable rhythm (NO) cohort (17.9% vs 5.3% for prehospital ROSC, 18.5% vs 6.6% for 1-month survival, and 6.0% vs 1.2% for 1-month CPC 1 or 2, respectively; $P<0.001$). However, in the group aged <7 years, no significant differences were found between the 2 cohorts.

Table 4 shows the age-stratified outcomes according to shock-delivery time in the subsequent treated shockable rhythm (YES) cohort (n=235). Rates of 1-month survival and 1-month CPC 1 or 2 in the group aged 7 to 17 years decreased significantly as time to shock delivery increased (1-month survival: 26.7% for 0–9 minutes, 26.0% for 10–19 minutes, and 9.6% for 20–59 minutes; *P* for trend=0.02; 1-month CPC 1 or 2: 20.0% for 0–9 minutes, 9.1% for 10–19 minutes, and 0% for 20–59 minutes; *P* for trend <0.01). However, significant differences were not found in the group aged <7 years.

Discussion

The present study of EMS-treated OHCA children with initial nonshockable rhythms in Japan shows that subsequent treated shockable rhythm is significantly associated with improved prehospital ROSC, 1-month survival, and 1-month survival with favorable neurological outcomes, when compared with no subsequent treated shockable rhythm. In patients with subsequent treated shockable rhythm, 1-month survival and 1-month survival with favorable neurological outcomes decreased as time to shock delivery increased. Moreover, these findings were only applicable to older children (aged 7–17 years for elementary to high school children in Japan).

Table 1. Baseline Characteristics of the Study Cohorts According to Subsequent Shockable Rhythm

Characteristics	All Patients With Initial Nonshockable Rhythm, n (%)	Subsequent Treated Shockable Rhythm (YES), n (%)	Subsequent Treated Shockable Rhythm (NO), n (%)	*P* Value
Total patients in each group	12 402 (100)	239 (1.9)	12 163 (98.1)	
Age, y, median (IQR, 1–3)	1 (0–11)	12 (5–16)	1 (0–10)	<0.001
<1 year	5154 (41.6)	26 (10.9)	5128 (42.2)	<0.001
Male	7531 (60.7)	153 (64.0)	7378 (60.7)	0.29
Bystander-witnessed arrest	3516 (28.4)	114 (47.7)	3402 (28.0)	<0.001
Bystander CPR	6302 (50.8)	111 (46.4)	6191 (50.9)	0.19
Initial cardiac rhythm				
Pulseless electrical activity	2143 (17.3)	77 (32.2)	2066 (17.0)	<0.001
Asystole	10 259 (82.7)	162 (67.8)	10 097 (83.0)	<0.001
Presumed cardiac etiology	3577 (28.8)	84 (35.2)	3493 (28.7)	0.03
Epinephrine administration	239 (1.9)	21 (8.8)	218 (1.8)	<0.001
Advanced airway management	3449 (27.8)	94 (39.3)	3355 (27.6)	<0.001
Call-to-response time, minute, median (IQR, 1–3), n=12 380	7.0 (5–9)	7.0 (5–9)	7.0 (5–9)	0.35
Shock-delivery time,* minute, median (IQR, 1–3), n=235		19 (14–26)		

Values are reported as number (%), unless indicated otherwise. CPR indicates cardiopulmonary resuscitation; IQR, interquartile range.
*Time from the initiation of CPR by emergency medical services personnel to the first shock delivery.

The present study results are inconsistent with those of a previous pediatric in-hospital cardiac arrest study.[16] In 2006, Samson et al[16] demonstrated that the proportion of survival to hospital discharge in pediatric in-hospital cardiac arrest with subsequent shockable rhythm was significantly lower than that for those who did not convert to shockable

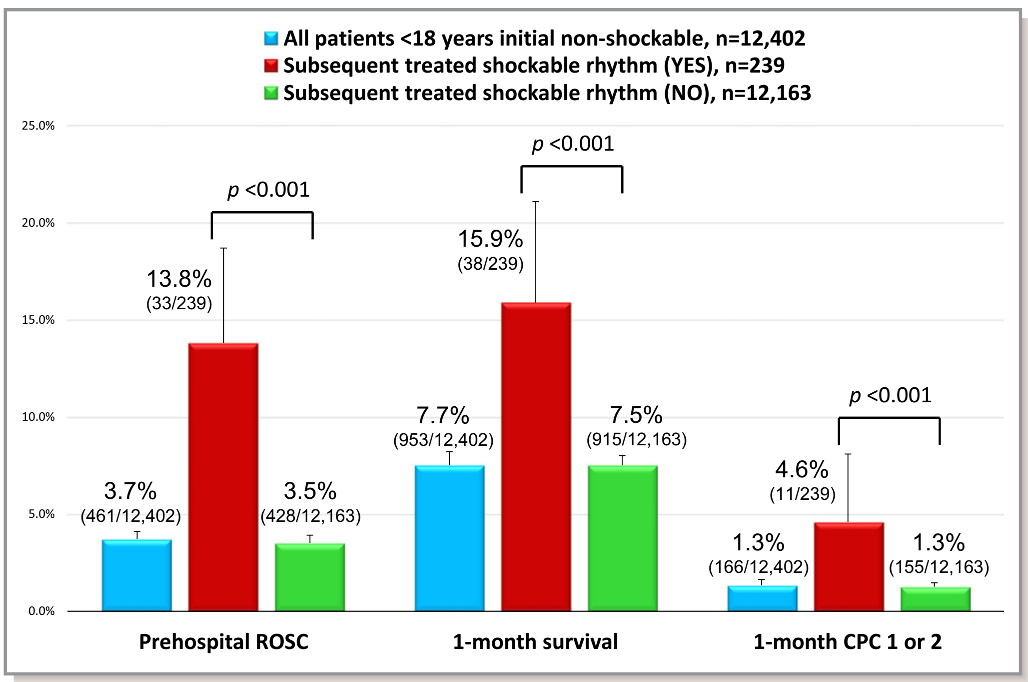

Figure 2. Outcomes stratified according to subsequent treated shockable rhythm cohort and overall study population. CPC indicates Cerebral Performance Category; ROSC, return of spontaneous circulation. Values are expressed with 95% confidence intervals.

Table 2. Results of Multivariate Logistic Regression Analyses for Variables Associated With Outcomes in All Participants

Variables	Adjusted OR (95% CI)		
	Prehospital ROSC	1-Month Survival	1-Month CPC 1 or 2
Age*	1.03 (1.02–1.05)	0.97 (0.96–0.98)	0.98 (0.95–1.00)
Bystander-witnessed arrest	1.74 (1.41–2.14)	1.60 (1.38–1.85)	2.85 (2.02–4.06)
Initial cardiac rhythm			
Pulseless electrical activity	4.87 (3.97–5.99)	2.99 (2.57–3.48)	4.62 (3.31–6.49)
Asystole	Reference	Reference	Reference
Presumed cardiac etiology	0.54 (0.42–0.70)	0.61 (0.52–0.72)	0.77 (0.53–1.10)
Epinephrine administration	4.29 (2.93–6.18)	0.49 (0.25–0.87)	0.21 (0.01–0.97)
Advanced airway management	1.07 (0.86–1.31)	0.99 (0.85–1.15)	0.99 (0.69–1.38)
Subsequent treated shockable rhythm	2.77 (1.81–4.12)	2.30 (1.56–3.29)	2.90 (1.42–5.36)

CPC indicates Cerebral Performance Category; OR, odds ratio; ROSC, return of spontaneous circulation.
*Adjusted ORs are reported for unit odds.

rhythms (11% vs 27%; adjusted OR, 3.8; 95% CI, 1.8–7.6). They surmised that a delay in diagnosis of subsequent shockable rhythm, adverse effects of resuscitative interventions, and severity of the underlying myocardial condition might have contributed to these results. Unlike in Samson et al's study, we enrolled only patients with OHCA and a subsequent shockable rhythm who were treated with shock delivery into the subsequent treated shockable rhythm (YES) cohort. Therefore, our study could both underestimate the frequency of development of subsequent shockable rhythm and overestimate favorable outcomes (survival and/or CPC 1 or 2). Moreover, most patients with in-hospital cardiac arrest are usually in a monitored setting and received shocks more quickly. Actually, the interval to first attempted defibrillation in Samson et al's study was clearly shorter than the subsequent shock-delivery time in our study (median [IQR],

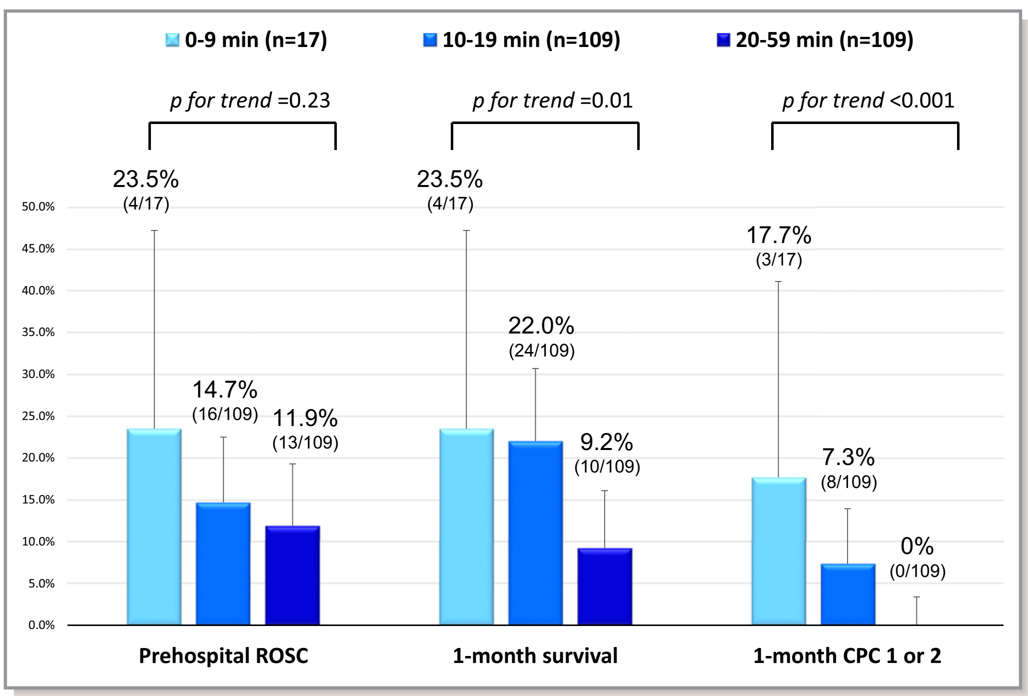

Figure 3. Outcomes stratified by shock-delivery time in the subsequent treated shockable rhythm (YES) cohort. CPC indicates Cerebral Performance Category; ROSC, return of spontaneous circulation. Values are expressed with 95% confidence intervals. Shock-delivery time (minutes) was available for 235 patients.

Table 3. Characteristics and Outcomes of Study Patients According to Age Group

	Aged <7 Years	Aged 7 to 17 Years	*P* Value
Total patients in each group, n=12 402	8309	4093	
Age, y, median (IQR, 1–3)	0 (0–1)	14 (11–16)	<0.001
Male	4878 (58.7)	2653 (64.8)	<0.001
Bystander-witnessed arrest	2034 (24.5)	1482 (36.2)	<0.001
Bystander CPR	4442 (53.5)	1860 (45.4)	<0.001
Initial cardiac rhythm			
Pulseless electrical activity	1296 (15.6)	847 (20.7)	<0.001
Asystole	7013 (84.4)	3246 (79.3)	<0.001
Presumed cardiac etiology	2828 (34.0)	749 (18.3)	<0.001
Epinephrine administration	62 (0.8)	177 (4.3)	<0.001
Advanced airway management	2035 (24.5)	1414 (34.6)	<0.001
Call-to-response time, minute, n=12 380			
Median (IQR, 1–3)	7.0 (5–8)	7.0 (5–9)	<0.001
Mean (SE)	7.1 (0.04)	7.7 (0.07)	<0.001
Subsequent treated shockable rhythm, n=239	71 (0.9)	168 (4.1)	<0.001
Shock-delivery time,* minute, n=235			
Median (IQR, 1–3)	20.0 (14–26)	18.0 (14–26)	0.39
Mean (SE)	21.6 (1.2)	20.6 (0.8)	0.39
Prehospital ROSC	223 (2.7)	238 (5.8)	<0.001
1-month survival	663 (8.0)	290 (7.1)	0.08
1-month CPC 1 or 2	108 (1.3)	58 (1.4)	0.62

Values are reported as number (%), unless indicated otherwise. CPC indicates Cerebral Performance Category; CPR, cardiopulmonary resuscitation; IQR, interquartile range; ROSC, return of spontaneous circulation.
*Time from the initiation of cardiopulmonary resuscitation by emergency medical services personnel to the first shock delivery.

0 [0–3] vs 19 minutes [14–26]; $P<0.01$). Furthermore, CPR duration for patients with subsequent shockable rhythm was significantly longer than for those with no shockable rhythm in Samson et al's study (median [IQR], 30 [15–53] vs 20 minutes [9–53]). Accordingly, the differences in outcomes between the present study of OHCA and Samson et al's study of in-hospital cardiac arrest may be explained simply by the CPR duration. However, we could not analyze CPR duration because of lack of data for in-hospital CPR time.

Samson et al's study of in-hospital cardiac arrest[16] indicated that rates of survival to hospital discharge after initial shockable rhythm were significantly higher than those after subsequent shockable rhythm: 35% versus 11%; adjusted OR (95% CI), 2.6 (1.2–5.8). Table 5 compares the outcomes in patients with initial shockable rhythm (n=637; Figure 1) and those with subsequent treated shockable rhythm (n=239) in the present study. Rates of favorable outcomes in patients with initial shockable rhythm were significantly higher than in those with subsequent treated shockable rhythm (34.9% vs 15.9% for 1-month survival, 23.4% vs 4.6% for 1-month CPC 1 or 2; $P<0.001$). Patients with initial shockable rhythm had significant positive adjusted ORs for favorable outcomes compared to those with subsequent treated shockable rhythm (1-month survival: 2.23 [95% CI, 1.49–3.39]; 1-month CPC 1 or 2: 4.30 [95% CI, 2.31–8.79]; $P<0.001$). These results were consistent with those in Samson et al's study.[16] Moreover, in the present study, the finding that patients with initial shockable rhythm had 1-month outcomes superior to those with subsequent treated shockable rhythm was also observed when analyzed by age group (aged <7 years or aged 7–17 years).

In adult patients who experienced OHCA, Hallstrom et al[25] noted a significant low adjusted OR of 0.18 for survival to hospital discharge in patients with subsequent shockable rhythms relative to those who did not receive shocks for nonshockable rhythms. Moreover, Thomas et al[26] recently reported that increased survival to hospital discharge for OHCA patients was not associated with subsequent shockable rhythm and shock delivery during EMS resuscitation

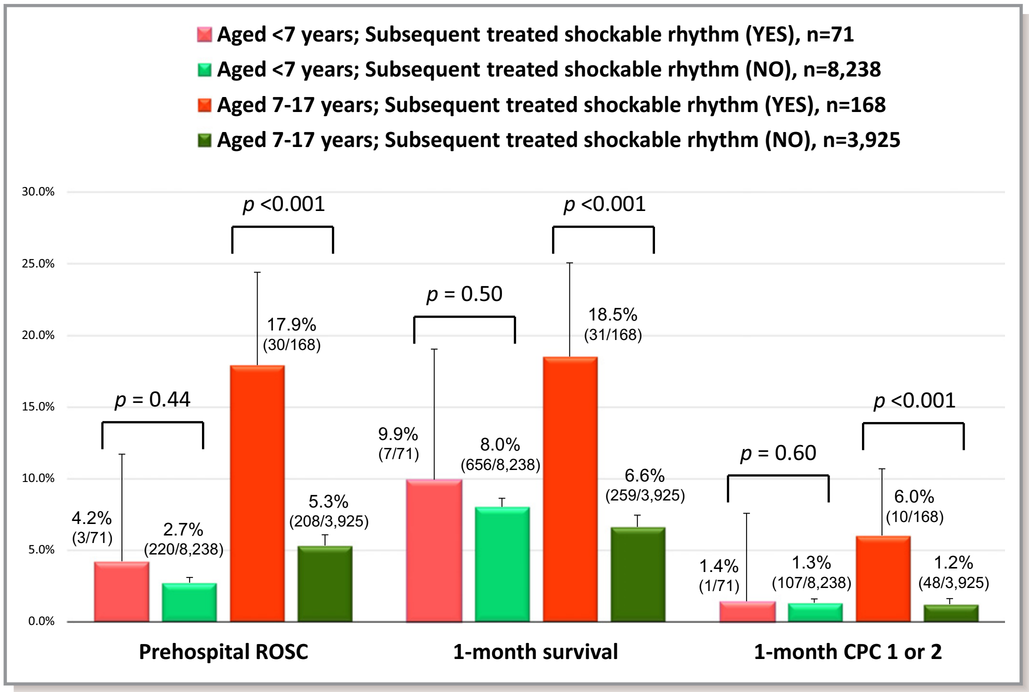

Figure 4. Age-stratified outcomes according to subsequent treated shockable rhythm. CPC indicates Cerebral Performance Category; ROSC, return of spontaneous circulation. Values are expressed with 95% confidence intervals.

efforts (adjusted OR, 0.88; 95% CI, 0.60–1.30). However, other studies of OHCA adults[27–31] demonstrated that subsequent treated shockable rhythm was associated with improved outcomes compared with no shock delivery after an initial nonshockable rhythm. Notably, Goto et al[27] showed that subsequent shockable rhythm was significantly associated with increased adjusted odds of 1-month survival with favorable neurological outcomes when the shock-delivery time was <20 minutes. The present study on children with OHCA is consistent with those adult OHCA studies (Table 2). Earlier shock delivery (shock-delivery time <20 minutes) in children with OHCA and subsequent treated shockable rhythm, particularly in patients aged 7 to 17 years, was found to be superior to later shock delivery, as demonstrated by 1-month survival with favorable neurological outcomes (Figure 3; Table 4). However, we were unable to show the

Table 4. Age-Stratified Outcomes According to Shock-Delivery Time in the Subsequent Treated Shockable Rhythm (YES) Cohort

	Shock-Delivery Time*			
	0 to 9 Minutes	10 to 19 Minutes	20 to 59 Minutes	*P* Value
Total patients in each group, n=235	17	109	109	
Aged <7 years, n=70	2	32	36	
Prehospital ROSC, n=3	0 (0.0)	3 (9.4)	0 (0.0)	0.15
1-month survival, n=7	0 (0.0)	4 (12.5)	3 (8.3)	0.75
1-month CPC 1 or 2, n=1	0 (0.0)	1 (3.1)	0 (0.0)	0.54
Aged 7 to 17 years, n=165	15	77	73	
Prehospital ROSC, n=30	4 (26.7)	13 (16.9)	13 (17.8)	0.66
1-month survival, n=31	4 (26.7)	20 (26.0)	7 (9.6)	0.02
1-month CPC 1 or 2, n=10	3 (20.0)	7 (9.1)	0 (0.0)	<0.01

Values are reported as number (%), unless indicated otherwise. CPC indicates Cerebral Performance Category; ROSC, return of spontaneous circulation.
*Time from the initiation of cardiopulmonary resuscitation by emergency medical services personnel to the first shock delivery. Shock-delivery time (minutes) was available for 235 patients.

Table 5. Outcomes in Patients With Initial Shockable Rhythm and Those With Subsequent Treated Shockable Rhythm

	No. of Patients	1-Month Survival		1-Month CPC 1 or 2	
		n (%)	Adjusted OR* (95% CI)	n (%)	Adjusted OR* (95% CI)
Total patients with prehospital shockable rhythm	876	260 (29.7)		160 (18.3)	
Initial shockable rhythm	637	222 (34.9)	2.23 (1.49–3.39)	149 (23.4)	4.30 (2.31–8.79)
Subsequent treated shockable rhythm	239	38 (15.9)	Reference	11 (4.6)	Reference
P value		<0.001	<0.001	<0.001	<0.001
Aged <7 years	290	55 (19.0)		23 (7.9)	
Initial shockable rhythm	219	48 (21.9)	2.39 (1.02–6.41)	22 (10.1)	6.60 (1.18–124.9)
Subsequent treated shockable rhythm	71	7 (9.9)	Reference	1 (1.4)	Reference
P value		0.02	0.04	0.02	0.03
Aged 7 to 17 years	586	205 (35.0)		137 (23.4)	
Initial shockable rhythm	418	174 (41.6)	2.26 (1.43–3.64)	127 (30.4)	4.17 (2.16–8.88)
Subsequent treated shockable rhythm	168	31 (18.5)	Reference	10 (6.0)	Reference
P value		<0.001	<0.001	<0.001	<0.001

Values are reported as number (%), unless indicated otherwise. CPC indicates Cerebral Performance Category; OR, odds ratio.
*Adjusted variables for potential confounders were included 7 variables: age, bystander-witnessed arrest, bystander cardiopulmonary resuscitation, initial cardiac rhythm, presumed cardiac etiology, epinephrine administration, and advanced airway management.

benefit of early shock delivery in patients with subsequent treated shockable rhythm on neurological outcomes in the multivariate logistic regression model, because an insufficient number of cases prevented further risk adjustment for outcomes.

In the present study, prehospital epinephrine administration was independently associated with increased odds of prehospital ROSC. However, it was independently associated with decreased odds of 1-month survival and 1-month CPC 1 or 2 (Table 2). Moreover, advanced airway management was not associated with prehospital ROSC, 1-month survival, or 1-month CPC 1 or 2. These results are consistent with those from previous studies on pediatric OHCAs.[32,33]

Eilevstjønn et al[34] demonstrated that cardiac rhythms before subsequent shockable rhythm were related to the outcomes (ROSC). They found that PEA before shockable rhythm had a significantly higher ROSC rate than that of asystole. Their results were consistent with our previous study for adults[27] and the present study for children. Moreover, they reported that median slope, which represents the average steepness of the VF waveform reflecting both the amplitude and frequency of the rhythm, might be a useful tool for predicting outcomes. We could not analyze subsequent VF waveforms because of lack of data. This lack of data was associated with our study design of a retrospective record review. Therefore, prospective studies are required to analyze the subsequent VF waveform and clarify the effect of subsequent shockable rhythm and shock delivery on outcomes in children with OHCA.

Study Limitations

The potential limitations of the current analysis are as follows. First, we could not exclude patients who received shocks for the wrong indication or for unrecognized initial shockable rhythms attributed to electrical misreading when an AED was used while transporting a patient[35] and/or when CPR was provided for a child with OHCA,[36] which would result in an overestimation of favorable outcomes. In addition, our study population included only those patients with initial nonshockable rhythm who had a subsequent shockable rhythm that was treated with shock delivery. If a significant number of patients who developed a subsequent shockable rhythm never received a shock, their exclusion would mean that survival in our study population is falsely high. Second, our registry database lacked detailed data to permit further risk adjustment for outcomes: for example, comorbid disease of patients, location where the OHCA occurred, years of experience as a member of EMS personnel, the degree of regional differences among EMS centers,[37,38] in-hospital medication, and the availability of specialists in emergency care (cardiologists and/or pediatric physicians). Regarding regional differences in outcomes post-OHCA in Japan, previous studies suggested there were regional disparities in prehospital care and in-hospital postresuscitation care.[37,38] Low-spending regions had significantly worse neurological outcomes post-OHCA compared to medium-spending or high-spending regions.[38] Moreover, although EMS providers delivered a shock according to guidelines during the study period,[20–22] precise energy dose, shock frequency, and defibrillation mode (monophasic or biphasic) were unknown; therefore, we could not analyze those data in the present study. Third, though a uniform data collection procedure based on the Utstein-style guidelines for reporting cardiac arrest, a large sample size, and a population-based design was used, we cannot exclude the possibility of uncontrolled confounders. Fourth, as with all epidemiological studies, the integrity, validity, and ascertainment bias of the data were potential limitations. Fifth, we should note that caution must be exercised when generalizing these results to other countries or EMS systems. Finally, because we lacked precise data on the causes of cardiac arrest, it is possible that cardiac arrest in some patients may have been caused by sudden infant death syndrome, trauma, or respiratory disease.[39]

Conclusions

In children with OHCA and initial nonshockable rhythms, subsequent treated shockable rhythm during EMS resuscitation efforts was significantly associated with improved prehospital ROSC, 1-month survival, and 1-month survival with favorable neurological outcomes. In addition, in the cohort of older children (aged 7–17 years) with subsequent treated shockable rhythm, 1-month survival and 1-month survival with favorable neurological outcomes decreased as time to shock delivery increased.

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Disclosures

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References

1. Smith CM, Colquhoun MC. Out-of-hospital cardiac arrest in schools: a systematic review. *Resuscitation*. 2015;96:296–302.
2. Herlitz J, Svensson L, Engdahl J, Gelberg J, Silfverstolpe J, Wisten A, Ängquist KA, Holmberget S. Characteristics of cardiac arrest and resuscitation by age group: an analysis from the Swedish Cardiac Arrest Registry. *Am J Emerg Med*. 2007;25:1025–1031.
3. Atkins DL, Everson-Stewart S, Sears GK, Daya M, Osmond MH, Warden CR, Berg RA; the Resuscitation Outcomes Consortium Investigators. Epidemiology and outcomes from out-of-hospital cardiac arrest in children: the Resuscitation Outcomes Consortium Epistry-Cardiac Arrest. *Circulation*. 2009;119:1484–1491.
4. Park CB, Shin SD, Suh GJ, Ahn KO, Cha WC, Song KJ, Lee EJ, Ong MEH. Pediatric out-of-hospital cardiac arrest in Korea: a nationwide population-based study. *Resuscitation*. 2010;81:512–517.
5. Deasy C, Bernard SA, Cameron P, Jaison A, Smith K, Harriss L, Walker T, Masci K, Tibballs J. Epidemiology of paediatric out-of-hospital cardiac arrest in Melbourne, Australia. *Resuscitation*. 2010;81:1095–1100.
6. Bardai A, Berdowski J, van der Werf C, Blom MT, Ceelen M, van Langen IM, Tijssen JG, Wilde AA, Koster RW, Tan HL. Incidence, causes, and outcomes of out-of-hospital cardiac arrest in children: a comprehensive, prospective, population-based study in the Netherlands. *J Am Coll Cardiol*. 2011;57:1822–1828.
7. Akahane M, Tanabe S, Ogawa T, Koike S, Horiguchi H, Yasunaga H, Imamura T. Characteristics and outcomes of pediatric out-of-hospital cardiac arrest by scholastic age category. *Pediatr Crit Care Med*. 2013;14:130–136.
8. Johnson MA, Grahan BJ, Haukoos JS, McNally B, Campbell R, Sasson C, Slattery DE. Demographics, bystander CPR, and AED use in out-of-hospital pediatric arrests. *Resuscitation*. 2014;85:920–926.
9. Topjian AA, Nadkarni VM, Berg RA. Cardiopulmonary resuscitation in children. *Curr Opin Crit Care*. 2009;15:203–208.
10. Goto Y, Maeda T, Nakatsu-Goto Y. Decision tree model for predicting long-term outcomes in children with out-of-hospital cardiac arrest: a nationwide, population-based observational study. *Crit Care*. 2014;18:R133.
11. Atkins DL, Berger S, Duff JP, Gonzales JC, Hunt EA, Joyner BL, Meaney PA, Niles DE, Samson RA, Schexnayder SM. Part 11: pediatric basic life support and cardiopulmonary resuscitation quality: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*. 2015;132:S519–S525.
12. de Caen AR, Berg MD, Chameides L, Gooden CK, Hickey RW, Scott HF, Sutton RM, Tijssen JA, Topjian A, van der Jagt ÉW, Schexnayder SM, Samson RA. Part 12: pediatric advanced life support: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*. 2015;132:S526–S542.
13. Maconochie IK, Bingham R, Eich C, López-Herce J, Rodríguez-Núñez A, Rajka T, Van de Voorde P, Zideman DA, Biarent D; Paediatric Life Support Section Collaborators. European Resuscitation Council guidelines for resuscitation 2015: section 6. Paediatric Life Support. *Resuscitation*. 2015;95:223–248.
14. Haskell SE, Atkins DL. Defibrillation in children. *J Emerg Trauma Shock*. 2010;3:261–266.
15. Rodríguez-Núñez A, López-Herce J, del Castillo J, Bellón JM; Iberian-American Paediatric Cardiac Arrest Study Network RIBEPCI. Shockable rhythms and defibrillation during in-hospital pediatric cardiac arrest. *Resuscitation*. 2014;85:387–391.
16. Samson RA, Nadkarni VM, Meaney PA, Carey SM, Berg MD, Berg RA; American Heart Association National Registry of CPR Investigators. Outcomes of in-hospital ventricular fibrillation in children. *N Engl J Med*. 2006;354:2328–2339.
17. Ministry of Education Culture, Sports, Science and Technology of Japan/ Ministry of Health, Labor and Welfare of Japan. A guideline for epidemiology studies. Available at: http://www.lifescience.mext.go.jp/files/pdf/37_139.pdf [In Japanese]. Accessed November 30, 2015.
18. Yasunaga H, Miyata H, Horiguch H, Tanabe S, Akahane M, Ogawa T, Koike S, Imamura T. Polulation density, call-response interval, and survival of out-of-hospital cardiac arrest. *Int J Health Geogr*. 2011;10:26.
19. Goto Y, Maeda T, Nakatsu-Goto Y. Neurological outcomes in patients transported to hospital without a prehospital return of spontaneous circulation after cardiac arrest. *Crit Care*. 2013;17:R274.
20. Japan Resuscitation Council and Japan Foundation for Emergency Medicine. *(Editorial Supervision) Japanese Guideline for Emergency Care and Cardiopulmonary Resuscitation*. 3rd ed. Tokyo: Health Shupansha; 2007. (in Japanese).
21. Japan Resuscitation Council CPR Guidelines Committee. *2010 Japanese Guidelines for Emergency Care and Cardiopulmonary Resuscitation*. 1st ed. Tokyo: Health Shuppansha; 2011. (in Japanese).
22. American Heart Association in collaboration with International Liaison Committee on Resuscitation. Guidelines 2000 for cardiopulmonary resuscitation and emergency cardiovascular care: international consensus on science. *Circulation*. 2000;102:I1–I384.
23. Goto Y, Maeda T, Goto YN. Effects of prehospital epinephrine during out-of-hospital cardiac arrest with initial non-shockable rhythm: an observational cohort study. *Crit Care*. 2013;17:R188.
24. Jacobs I, Nadkami V, Bahr J, Berg RA, Billi JE, Bossaert L, Cassan P, Coovadia A, D'Este K, Finn J, Halperin H, Handley A, Herlitz J, Hickey R, Idris A, Kloeck W, Larkin GL, Mancini ME, Mason P, Mears G, Monsieurs K, Montgomery W, Morley P, Nichol G, Nolan J, Okada K, Perlman J, Shuster M, Steen PA, Sterz F, Tibballs J, Timerman S, Truitt T, Zideman D. Cardiac arrest and cardiopulmonary resuscitation outcome reports: update and simplification of the Utstein templates for resuscitation registries: a statement for healthcare professionals from a task force of the International Liaison Committee on Resuscitation (American Heart Association,

European Resuscitation Council, Australian Resuscitation Council, New Zealand Resuscitation Council, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation, Resuscitation Councils of Southern Africa). *Circulation*. 2004;110:3385–3397.

25. Hallstrom A, Rea TD, Mosesso VN Jr, Cobb LA, Anton AR, Van Ottingham L, Sayre MR, Christenson J. The relationship between shocks and survival in out-of-hospital cardiac arrest patients initially found in PEA or asystole. *Resuscitation*. 2007;74:418–426.
26. Thomas AJ, Newgard CD, Fu R, Zive DM, Daya MR. Survival in out-of-hospital cardiac arrests with initial asystole or pulseless electrical activity and subsequent shockable rhythms. *Resuscitation*. 2013;84:1261–1266.
27. Goto Y, Maeda T, Nakatsu-Goto Y. Prognostic implications of conversion from nonshockable to shockable rhythms in out-of-hospital cardiac arrest. *Crit Care*. 2014;18:528.
28. Kitamura N, Nakada T, Shinozaki K, Tahara Y, Sakurai A, Yonemoto N, Nagao K, Yaguchi A, Morimura N; on behalf of the SOS-KANTO 2012 Study Group. Subsequent shock deliveries are associated with increased favorable neurological outcomes in cardiac arrest patients who had initially non-shockable rhythms. *Crit Care*. 2015;19:322.
29. Herlitz J, Svensson L, Engdahl J, Silfverstolpe J. Characteristics and outcome in out-of-hospital cardiac arrest when patients are found in a non-shockable rhythm. *Resuscitation*. 2008;76:31–36.
30. Kajino K, Iwami T, Daya M, Nishiuchi T, Hayashi Y, Ikeuchi H, Tanaka H, Shimazu T, Sugimoto H. Subsequent ventricular fibrillation and survival in out-of-hospital cardiac arrests presenting with PEA or asystole. *Resuscitation*. 2008;79:34–40.
31. Olasveengen TM, Samdal M, Steen PA, Wik L, Sunde K. Progressing from initial non-shockable rhythms to a shockable rhythm is associated with improved outcome after out-of-hospital cardiac arrest. *Resuscitation*. 2009;80:24–29.
32. Gausche M, Lewis RJ, Stratton SJ, Haynes BE, Gunter CS, Goodrich SM, Poore PD, McCollough MD, Henderson DP, Pratt FD, Seidel JS. Effect of out-of-hospital pediatric endotracheal intubation on survival and neurological outcome: a controlled clinical trial. *JAMA*. 2000;283:783–790.
33. Tijssen JA, Prince DK, Morrison LJ, Atkins DL, Austin MA, Berg R, Brown SP, Christenson J, Egan D, Fedor PJ, Fink EL, Meckler GD, Osmond MH, Sims KA, Hutchison JS; Resuscitation Outcomes Consortium. Time on the scene and interventions are associated with improved survival in pediatric out-of-hospital cardiac arrest. *Resuscitation*. 2015;94:1–7.
34. Eilevstjønn J, Kramer-Johansen J, Sunde K. Shock outcome is related to prior rhythm and duration of ventricular fibrillation. *Resuscitation*. 2007;75: 60–67.
35. Yun JG, Jeung KW, Lee BK, Ryu HH, Lee HY, Kim MJ, Heo T, Min YI, You Y. Performance of an automated external defibrillator in a moving ambulance vehicle. *Resuscitation*. 2010;81:457–462.
36. Aramendi E, de Gauna SR, Irusta U, Ruiz J, Arcocha MF, Ormaetxe JM. Detection of ventricular fibrillation in the presence of cardiopulmonary resuscitation artefacts. *Resuscitation*. 2007;72:115–123.
37. Hasegawa K, Tsugawa Y, Camargo CA Jr, Hiraide A, Brown DF. Regional variability in survival outcomes of out-of-hospital cardiac arrest: the All-Japan Utstein Registry. *Resuscitation*. 2013;84:1099–1107.
38. Tsugawa Y, Hasegawa K, Hiraide A, Jha AK. Regional health expenditure and health outcomes after out-of-hospital cardiac arrest in Japan: an observational study. *BMJ Open*. 2015;19:e008374.
39. Goto Y, Funada A, Nakatsu-Goto Y. Neurological outcomes in children dead on hospital arrival. *Crit Care*. 2015;19:410.