Mechanical Cardiopulmonary Resuscitation and Hospital Survival Among Adult Patients With Nontraumatic Out-of-Hospital Cardiac Arrest Attending the Emergency Department: A Prospective, Multicenter, Observational Study in Japan (SOS-KANTO [Survey of Survivors after Out-of-Hospital Cardiac Arrest in Kanto Area] 2012 Study)

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Background—Mechanical cardiopulmonary resuscitation (mCPR) for patients with out-of-hospital cardiac arrest attending the emergency department has become more widespread in Japan. The objective of this study is to determine the association between the mCPR in the emergency department and clinical outcomes.

Methods and Results—In a prospective, multicenter, observational study, adult patients with out-of-hospital cardiac arrest with sustained circulatory arrest on hospital arrival were identified. The primary outcome was survival to hospital discharge. The secondary outcomes included a return of spontaneous circulation and successful hospital admission. Multivariate analyses adjusted for potential confounders and within-institution clustering effects using a generalized estimation equation were used to analyze the association of the mCPR with outcomes. Between January 1, 2012 and March 31, 2013, 6537 patients with out-of-hospital cardiac arrest were eligible; this included 5619 patients (86.0%) in the manual CPR group and 918 patients (14.0%) in the mCPR group. Of those patients, 28.1% (1801/6419) showed return of spontaneous circulation in the emergency department, 20.4% (1175/5754) had hospital admission, 2.6% (168/6504) survived to hospital discharge, and 1.2% (75/6419) showed a favorable neurological outcome at 1 month after admission. Multivariate analyses revealed that mCPR was associated with a decreased likelihood of survival to hospital discharge (adjusted odds ratio, 0.40; 95% confidence interval, 0.20–0.78; *P*=0.005), return of spontaneous circulation (adjusted odds ratio, 0.71; 95% confidence interval, 0.53–0.94; *P*=0.018), and hospital admission (adjusted odds ratio, 0.57; 95% confidence interval, 0.40–0.80; *P*=0.001).

Conclusions—After accounting for potential confounders, the mCPR in the emergency department was associated with decreased likelihoods of good clinical outcomes after adult nontraumatic out-of-hospital cardiac arrest. Further studies are needed to clarify circumstances in which mCPR may benefit these patients. (***J Am Heart Assoc***. 2017;6:e007420. DOI: 10.1161/JAHA.117.007420.)

Key Words: cardiopulmonary resuscitation • emergency department • mechanical chest compression device

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Clinical Perspective

What Is New?

- In a large, multicenter, prospective cohort study of out-of-hospital cardiac arrest in Japan, the mechanical cardiopulmonary resuscitation for adult patients with out-of-hospital cardiac arrest attending the emergency department was associated with a decreased likelihood of survival to hospital discharge, successful return of spontaneous circulation, and hospital admission, after accounting for potential confounders and the within-institution clustering effect.

What Are the Clinical Implications?

- Our data do not support the routine use of mechanical cardiopulmonary resuscitation devices for patients with out-of-hospital cardiac arrest in the emergency department.
- Attending physicians and medical teams treating patients with out-of-hospital cardiac arrest in the emergency department should be aware that the introduction of mechanical cardiopulmonary resuscitation devices is likely to have a negative effect on patient outcomes.

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Out-of-hospital cardiac arrest (OHCA) is a leading cause of death.[1] There are almost 424 000 cases of emergency medical service (EMS)–assessed OHCA each year in the United States,[1] 300 000 in Europe,[2] 100 000 in Japan,[3] and upwards of 3.7 million worldwide.[4] The achievement of a successful return of spontaneous circulation (ROSC) depends on a chain of survival, including the recognition of early signs of cardiac arrest and the provision of early and high-quality cardiopulmonary resuscitation (CPR).[5] Several studies have shown that the high-quality CPR improves the survival rate and the neurological outcome of patients experiencing nontraumatic OHCA.[6–8]

Most mechanical CPR (mCPR) devices have been proposed to provide compressions of an appropriate depth and frequency for long periods without interruption or fatigue. The use of mCPR devices during CPR has become more widespread and allows for constant chest compressions to be performed during transportation from the scene of cardiac arrest to the hospital.[9] However, the evidence to support or refute the use of mCPR devices during the transfer of patients with OHCA to the hospital is insufficient to support that it achieves high-quality CPR.[9,10]

Besides the mCPR in the prehospital setting, the use of mCPR for patients with OHCA attending the emergency department (ED) has also become more widespread in Japan. Although there is no randomized clinical trial or large-cohort study to determine the effectiveness of mCPR in the ED on the clinical outcomes of patients with OHCA in comparison to manual CPR, it is conceivable that the shortcomings of manual CPR can be overcome by mCPR devices, which can help minimize interruptions in chest compressions during CPR and reduce the demands on medical staff in the ED. However, the frequency of real-world use and the beneficial effect of mCPR in the ED on clinical outcomes in cases of adult nontraumatic OHCA are still unknown.

The objective of this study was to determine the association between the mCPR for the resuscitation of adult patients with nontraumatic OHCA in the ED and the clinical outcomes using the database from a large, prospective, multicenter cohort of patients with OHCA in the Kanto area of Japan.

Methods

The data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure.

Study Design and Settings

The SOS-KANTO (Survey of Survivors after Out-of-Hospital Cardiac Arrest in Kanto Area) 2012 study was a survey of OHCA survivors in the Kanto area, including Tokyo Prefecture, of Japan between January 1, 2012 and March 31, 2013. A total of 16 452 patients with OHCA who were transported to 67 emergency hospitals by EMS personnel were included in this prospective, multicenter, observational study.[11–16] In this study, patients treated with mCPR devices during advanced cardiovascular life support in the ED were compared with patients who received manual CPR alone. The attempt to use an mCPR device was decided by the physicians who were caring for the patient, according to each institutional protocol or their own decision making. The commercially available devices, which included a load-distributing band-type device (AutoPulse, ZOLL Medical Corporation, Chelmsford, MA), piston-compression devices (LUCAS or LUCAS2 Chest Compression System, Physio-Control Inc., Redmond, WA), or others, were used for mCPR at each participating medical institution. The study protocol was approved by the institutional review board or ethics committee of each participating medical institution, and the requirement for informed patient consent was waived to ensure participant anonymity.

Emergency Medical System in Japan

In Japan, emergency services are provided 24 hours every day, anywhere. Most ambulance crews have 3 EMS personnel, including at least 1 emergency life-saving technician who is allowed to provide extensive emergency care. EMS providers perform CPR according to the current CPR

guidelines. They are permitted to perform tracheal intubation and administer intravenous epinephrine, but not to terminate CPR in the field; thus, most patients with OHCA are transported to hospitals.

Patient Selection

In this study, a predefined subcohort of patients with OHCA was investigated. On the basis of the previous studies,[10,17–24] we selected adult patients with nontraumatic OHCA who had sustained circulatory arrest on hospital arrival (thus, all eligible patients who attended the ED received ongoing CPR by EMS). The inclusion criteria were as follows: (1) age ≥18 years, (2) patients with undetectable blood pressure on hospital arrival, (3) patients who received advanced cardiovascular life support after hospital arrival, and (4) patients who were transferred to hospitals that had an mCPR device. The exclusion criteria were as follows: (1) traumatic OHCA and (2) patients with missing data on the type of CPR (manual CPR or mCPR) in the ED.

Data Collection and Definition of the Outcome Measures

The data collection of this study has been reported previously.[11–16] The prehospital information was collected by EMS providers. The cause of CA was determined by the physician caring for the patient. The in-hospital information was collected by institutional researchers. The Cerebral Performance Category (CPC) scale was used to categorize the neurological outcomes, as follows: CPC 1, good performance; CPC 2, moderate disability; CPC 3, severe disability; CPC 4, comatose or persistent vegetative status; and CPC 5, brain death or death. CPC 1 and 2 were defined as good neurological recovery. The CPC scores were further dichotomized into good (CPC 1 or 2) and poor (CPC 3, 4, or 5) outcomes.[25,26] If the patients were discharged from the hospital or transferred out to rehabilitation hospitals, the institutional researchers collected the information by telephone.[11,16]

The primary outcome was survival to hospital discharge.[10,19–21,23,24] The secondary outcomes included ROSC[10,17–21] and successful hospital admission.[10,18–22]

Laboratory Data on ED Arrival

Previous articles reported that an increased blood ammonia level is independently associated with poor clinical outcome of OHCA,[27,28] and the predictive accuracy of ammonia is higher than that of most other traditional risk factors of OHCA.[28] $Paco_2$ on ED arrival can be a surrogate biomarker that reflects adequate ventilatory management during transportation, which is one of the main components of the CPR

procedure by EMS personnel. Thus, we reported laboratory data, including blood ammonia (µmol/L), pH, and $Paco_2$ (mm Hg), on ED arrival.

Statistical Analyses

Categorical variables are presented as the number (frequency), and continuous variables are presented as the median (interquartile range) because the duration of all continuous variables in our data showed nonnormal distribution. The distribution of the continuous variables was compared using the Mann-Whitney U test. The χ^2 test or Fisher exact test was used for the comparison of binary variables.

To address the missing data, all missing nonoutcome data were appropriately imputed by multiple imputation using the assumption that data were missing at random.[11,29] Then, we compared outcomes between manual CPR and mCPR in the ED for all adult nontraumatic OHCAs. We used a generalized estimating equation model with an independence correlation structure to account for within-institution clustering. With the full cohort, 3 generalized estimating equation models (univariate, adjusted for selected variables, and adjusted for all covariates) were fit using each of the 3 end points as a dependent variable. A set of potential confounders was chosen a priori based on biological plausibility and a priori knowledge.[12,15,24,30–38] These selected variables included the following: age, sex, hospital category (to adjust for the difference in the frequency of mCPR device use between each institution, hospitals were categorized on the basis of the numbers of patients on whom mCPR devices were used: low volume, <20 per year; moderate volume, 20–100 per year; and high volume, >100 per year), witnessed status, bystander CPR, first documented rhythm, presumed cardiac cause, airway management by EMS, prehospital administration of epinephrine by EMS, tracheal intubation during advanced cardiovascular life support, administration of epinephrine, defibrillation attempt, extracorporeal CPR performed in the ED, and time from call to EMS arrival at scene, time from EMS arrival at scene to EMS arrival at the patient's side, time from EMS arrival at the patient's side to CPR initiation, and time from CPR initiation to hospital arrival (while also adjusting for within-institution clustering effects using a generalized estimating equation,[36–39] because several articles have suggested the existence of hospital-related differences in survival after OHCA).[40–44] All covariates included the selected variables above and location at which the cardiac arrest occurred, observational period, time of cardiac arrest, prehospital mCPR by EMS, number of defibrillations by EMS, time from call to the first epinephrine dose, and laboratory data, including blood ammonia, pH, and $Paco_2$ on ED arrival (while also adjusting for within-

institutional clustering effects). The odds ratios for all outcomes were reported, along with *P* values and Wald 95% confidence intervals.

For further sensitivity analyses, we performed the multi-variate analyses with adjustment for the above-mentioned selected variables to evaluate the association between mCPR and survival to hospital discharge in the subgroup of patients who were divided into the following categories: sex, age (18–75 versus >75 years; the patients were divided on the basis of the median age), cause (cardiac versus noncardiac), time of day (8:00 AM to 9:59 PM versus 10:00 PM to 7:59 AM), witness status (yes versus no), bystander CPR (yes versus no), initial rhythm (shockable versus nonshockable), and the transfer time interval from call to hospital arrival (<35 versus ≥35 minutes; the patients were divided on the basis of the median transfer time interval).

P<0.05 indicated statistical significance. All analyses were conducted using the SPSS software program (version 23.0).

Results

General Characteristics

A total of 16 452 adults with OHCA were consecutively enrolled in the SOS-KANTO 2012 study. After the exclusion of 9945 patients according to the predetermined criteria, 6537 patients with OHCA were eligible for inclusion in this study; this included 5619 patients (86.0%) in the manual CPR group and 918 patients (14.0%) in the mCPR group (Figure 1). The characteristics of the patients in the manual CPR and mCPR groups are shown in Table 1. There were no significant differences in the age, observation period, time of cardiac arrest, time from call to EMS arrival at scene, time from EMS arrival at the patient's side to CPR initiation, number of defibrillations by EMS, airway management by EMS, or administration of epinephrine by EMS. The mCPR group had a faster time from CPR initiation to hospital arrival and time from call to the first epinephrine dose. The mCPR group had higher frequencies of male sex, witnessed status, received
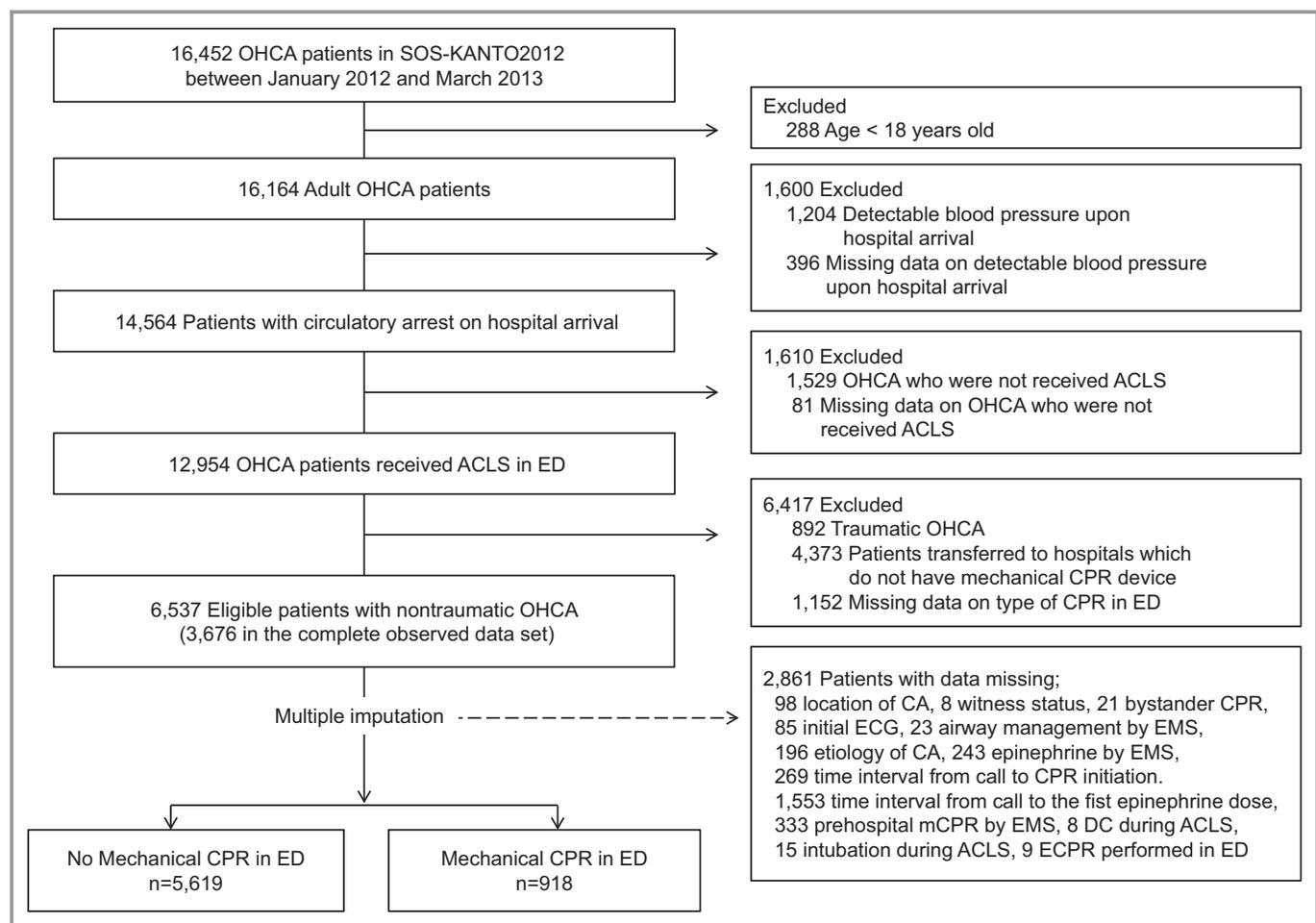
Figure 1. Patient selection. ACLS indicates advanced cardiovascular life support; CA, cardiac arrest; CPR, cardiopulmonary resuscitation; DC, direct current defibrillation; ECPR, extracorporeal CPR; ED, emergency department; EMS, emergency medical service; mCPR, mechanical CPR; OHCA, out-of-hospital CA; and SOS-KANTO, Survey of Survivors after Out-of-Hospital Cardiac Arrest in Kanto Area.

Table 1. Patient, Hospital, and Event Characteristics and Laboratory Data Among Study Patients With Manual CPR vs mCPR

Variable	Manual CPR (n=5619)	mCPR (n=918)	P Value
Age, median (IQR), y	75 (63–83)	75 (63–83)	0.523
Male sex	3375 (60.1)	583 (63.5)	0.048
Missing	0 (0)	0 (0)	
Location of cardiac arrest			0.057
Home	3989 (71.0)	619 (67.4)	
Public building	1012 (18.0)	174 (19.0)	
Others	536 (9.6)	109 (11.9)	
Missing	82 (1.5)	16 (1.7)	
No. of institutional use for mCPR device per y			<0.001
<20	4603 (81.9)	110 (12.0)	
20–100	879 (15.6)	224 (24.4)	
>100	137 (2.4)	584 (63.6)	
Observation period			0.552
January–September 2012	3136 (55.8)	522 (56.9)	
October 2012–March 2013	2483 (44.2)	396 (43.1)	
Time of cardiac arrest			0.193
8:00 AM to 9:59 PM	1736 (30.9)	264 (28.8)	
10:00 PM to 7:59 AM	3883 (69.1)	654 (71.2)	
Witnessed status	2653 (47.2)	498 (54.2)	<0.001
Missing	5 (0.1)	3 (0.3)	
Bystander CPR	1870 (33.3)	389 (42.4)	<0.001
Missing	21 (0.4)	0 (0)	
First documented rhythm			<0.001
VF/pulseless VT	397 (7.1)	77 (8.4)	
Asystole/PEA	4855 (86.4)	768 (83.7)	
Others	303 (5.4)	47 (5.1)	
Missing	64 (1.1)	26 (2.8)	
Time interval, median (IQR), min			
Time from call to EMS arrival at scene	7 (6–10)	7 (6–9)	0.202
Missing	1 (0.0)	0 (0.0)	
Time from EMS arrival at scene to EMS arrival at the patient's side	1 (1–2)	1 (1–2)	0.009
Missing	18 (0.3)	2 (0.2)	
Time from EMS arrival at the patient's side to CPR initiation	0 (0–1)	0 (0–1)	0.730
Missing	524 (9.3)	87 (9.5)	
Time from CPR initiation to hospital arrival	25 (19–31)	23 (18–29)	<0.001
Missing	273 (4.9)	52 (5.7)	
Prehospital mCPR by EMS	81 (1.4)	40 (4.4)	<0.001
Missing	545 (9.7)	107 (11.7)	
No. of defibrillations by EMS, median (IQR)	0 (0–0)	0 (0–0)	0.106
Missing	79 (1.4)	22 (2.4)	

Table 1. Continued

Variable	Manual CPR (n=5619)	mCPR (n=918)	P Value
Airway management by EMS	5371 (95.6)	869 (94.7)	0.421
Missing	21 (0.4)	5 (0.5)	
Epinephrine use by EMS	1135 (20.2)	175 (19.1)	0.439
Missing	243 (4.3)	47 (5.1)	
Presumed cardiac cause	3142 (55.9)	386 (42.0)	<0.001
Missing	172 (3.1)	38 (4.1)	
Time from call to the first epinephrine dose, median (IQR), min	36 (27−44)	34 (26−42)	0.006
Missing	1587 (28.2)	299 (32.6)	
Defibrillation attempt during ACLS	652 (11.6)	140 (15.3)	<0.001
Missing	9 (0.2)	11 (1.2)	
No. of defibrillations in ED, median (IQR)	0 (0−0)	0 (0−0)	<0.001
Missing	28 (0.5)	16 (1.7)	
Tracheal intubation in ED	5000 (89.0)	832 (90.6)	<0.001
Missing	19 (0.3)	14 (1.5)	
Epinephrine use in ED	4952 (88.1)	890 (96.9)	<0.001
Missing	2 (0)	1 (0.1)	
ECPR performed in ED	138 (2.5)	47 (5.1)	<0.001
Missing	28 (0.5)	10 (1.1)	
Type of mCPR device			
AutoPulse	…	93 (10.1)	
LUCAS or LUCAS2	…	172 (18.7)	
Others	…	570 (62.1)	
Missing	…	83 (9.0)	
Laboratory data on ED arrival, median (IQR)			
Blood ammonia level, μmol/L	282 (151−468)	280 (141−500)	0.982
Missing	3326 (59.2)	292 (31.8)	
Blood pH	6.86 (6.74−6.98)	6.87 (6.73−7.00)	0.442
Missing	703 (12.5)	72 (7.8)	
Blood $PaCO_2$, mm Hg	90 (66−116)	91 (68−113)	0.769
Missing	639 (11.7)	65 (7.1)	

Data are number (percentage) unless otherwise indicated. ACLS indicates advanced cardiovascular life support; CPR, cardiopulmonary resuscitation; ECPR, extracorporeal CPR; ED, emergency department; EMS, emergency medical service; IQR, interquartile range; mCPR, mechanical CPR; PEA, pulseless electrical activity; VF, ventricular fibrillation; and VT, ventricular tachycardia.

bystander CPR, initial shockable rhythm, presumed cardiac cause, prehospital mCPR by EMS, defibrillation attempt, tracheal intubation, epinephrine use, and received extracorporeal CPR in the ED (Table 1).

Among the 918 patients in the mCPR group, other devices were used for 570 (62.1%) and accounted for most mCPR devices. Load-distributing band-type and piston-compression devices were used 93 times (10.1%) and 172 times (18.7%), respectively. In the remaining 83 cases (9.0%), the type of mCPR device was unknown (Table 1).

The overall ROSC rate was 28.1% (1801/6419), the admission rate was 20.4% (1175/5754), the rate of survival to hospital discharge was 2.6% (168/6504), and a good neurological outcome at 1 month was observed in 1.2% of the patients (75/6494).

Primary Outcome

Table 2 shows the association between mCPR in the ED and primary outcome among all patients. The unadjusted model

Table 2. Association Between mCPR and Primary Outcome

Outcome	Total No. of Patients	Manual CPR, No. (%)	mCPR			
			No. (%)	OR	95% CI	P Value
Total	6537	5619 (86.0)	918 (14.0)			
Survival to hospital discharge	6504					
Crude		145 (2.6)	23 (2.5)	0.97	0.62–1.51	0.887
Adjusted for selected variables*				0.43	0.22–0.83	0.012
Adjusted for all variables†				0.40	0.20–0.78	0.005

CI indicates confidence interval; CPR, cardiopulmonary resuscitation; mCPR, mechanical CPR; and OR, odds ratio.
*Generalized estimating equation (GEE) models were used with adjustment for age, sex, hospital category, witnessed status, bystander CPR, first documented rhythm, presumed cardiac cause, airway management by emergency medical service (EMS), prehospital administration of epinephrine by EMS, tracheal intubation during advanced cardiovascular life support, administration of epinephrine, defibrillation attempt, extracorporeal CPR performed in the emergency department, and time from call to EMS arrival at scene, time from EMS arrival at scene to EMS arrival at the patient's side, time from EMS arrival at the patient's side to CPR initiation, and time from CPR initiation to hospital arrival (while also adjusting for within-institution clustering effects).
†Adjustment for all variables and within-institution clustering effects by a GEE model.

demonstrated that there was not significant association between mCPR in the ED and survival to hospital discharge (*P*=0.887). In the adjusted model using the selected variables, mCPR in the ED was an independent negative predictor of survival to hospital discharge (adjusted odds ratio, 0.43; 95% confidence interval, 0.22–0.83; *P*=0.012). Similarly, in the adjusted model using all variables, mCPR was associated with a decreased likelihood of survival to hospital discharge (adjusted odds ratio, 0.40; 95% confidence interval, 0.20–0.78; *P*=0.005).

Secondary Outcomes

Table 3 summarizes secondary outcomes for each group among all patients. The unadjusted model showed that there

was not a significant association between mCPR and the secondary outcomes (Table 3). In the adjusted models using the selected variables and all variables, mCPR was significantly associated with a decreased likelihood of ROSC (*P*=0.027 for the model with the selected variables, and *P*=0.018 for the model with all variables) and successful hospital admission (*P*=0.001 for each model).
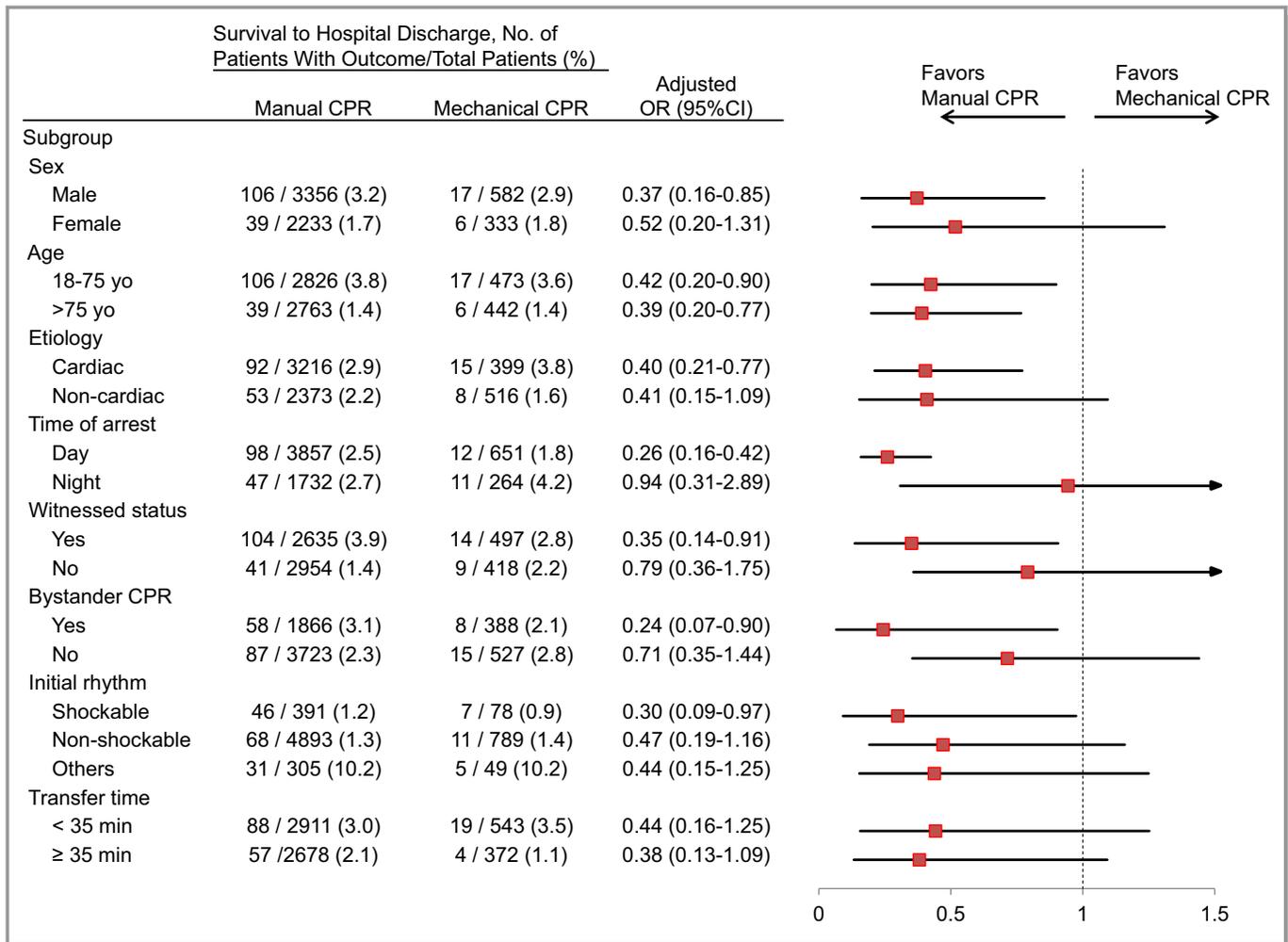
Subgroup Analyses

To assess the robustness of the results, we performed a series of sensitivity analyses. The results of the subgroup analyses of the factors associated with survival to hospital discharge are presented in Figure 2. mCPR was significantly associated with a decreased likelihood of survival in the

Table 3. Associations Between mCPR and Secondary Outcomes

Outcome	Total No. of Patients	Manual CPR, No. (%)	mCPR			
			No. (%)	OR	95% CI	P Value
Total	6537	5619 (86.0)	918 (14.0)			
ROSC in the ED	6419					
Crude		1561 (28.3)	240 (26.3)	0.90	0.77–1.06	0.214
Adjusted for selected variables*				0.72	0.54–0.96	0.027
Adjusted for all variables†				0.71	0.53–0.94	0.018
Hospital admission	5754					
Crude		1019 (20.6)	156 (19.3)	0.92	0.76–1.11	0.377
Adjusted for selected variables*				0.57	0.40–0.80	0.001
Adjusted for all variables†				0.57	0.40–0.80	0.001

CI indicates confidence interval; CPR, cardiopulmonary resuscitation; ED, emergency department; mCPR, mechanical CPR; OR, odds ratio; and ROSC, return of spontaneous circulation.
*Generalized estimating equation (GEE) models were used with adjustment for age, sex, hospital category, witnessed status, bystander CPR, first documented rhythm, presumed cardiac cause, airway management by emergency medical service (EMS), prehospital administration of epinephrine by EMS, tracheal intubation during advanced cardiovascular life support, administration of epinephrine, defibrillation attempt, extracorporeal CPR performed in the ED, and time from call to EMS arrival at scene, time from EMS arrival at scene to EMS arrival at the patient's side, time from EMS arrival at the patient's side to CPR initiation, and time from CPR initiation to hospital arrival (while also adjusting for within-institution clustering effects).
†Adjustment for all variables and within-institution clustering effects by a GEE model.

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	Survival to Hospital Discharge, No. of Patients With Outcome/Total Patients (%)				
	Manual CPR	Mechanical CPR	Adjusted OR (95%CI)	Favors Manual CPR	Favors Mechanical CPR
Subgroup					
Sex					
Male	106 / 3356 (3.2)	17 / 582 (2.9)	0.37 (0.16-0.85)		
Female	39 / 2233 (1.7)	6 / 333 (1.8)	0.52 (0.20-1.31)		
Age					
18-75 yo	106 / 2826 (3.8)	17 / 473 (3.6)	0.42 (0.20-0.90)		
>75 yo	39 / 2763 (1.4)	6 / 442 (1.4)	0.39 (0.20-0.77)		
Etiology					
Cardiac	92 / 3216 (2.9)	15 / 399 (3.8)	0.40 (0.21-0.77)		
Non-cardiac	53 / 2373 (2.2)	8 / 516 (1.6)	0.41 (0.15-1.09)		
Time of arrest					
Day	98 / 3857 (2.5)	12 / 651 (1.8)	0.26 (0.16-0.42)		
Night	47 / 1732 (2.7)	11 / 264 (4.2)	0.94 (0.31-2.89)		
Witnessed status					
Yes	104 / 2635 (3.9)	14 / 497 (2.8)	0.35 (0.14-0.91)		
No	41 / 2954 (1.4)	9 / 418 (2.2)	0.79 (0.36-1.75)		
Bystander CPR					
Yes	58 / 1866 (3.1)	8 / 388 (2.1)	0.24 (0.07-0.90)		
No	87 / 3723 (2.3)	15 / 527 (2.8)	0.71 (0.35-1.44)		
Initial rhythm					
Shockable	46 / 391 (1.2)	7 / 78 (0.9)	0.30 (0.09-0.97)		
Non-shockable	68 / 4893 (1.3)	11 / 789 (1.4)	0.47 (0.19-1.16)		
Others	31 / 305 (10.2)	5 / 49 (10.2)	0.44 (0.15-1.25)		
Transfer time					
< 35 min	88 / 2911 (3.0)	19 / 543 (3.5)	0.44 (0.16-1.25)		
≥ 35 min	57 /2678 (2.1)	4 / 372 (1.1)	0.38 (0.13-1.09)		

(x-axis: 0   0.5   1   1.5)

Figure 2. Forest plot of subgroup analyses of survival to hospital discharge. The dotted vertical line represents a risk ratio of 1.0. CI indicates confidence interval; CPR, cardiopulmonary resuscitation; mCPR, mechanical CPR; and OR, odds ratio.

following subgroups: male sex (*P*=0.020), both young and old patients (*P*=0.025 in younger patients, and *P*=0.006 in older patients), cardiac cause (*P*=0.006), day time (*P*<0.001), witnessed status (*P*=0.031), received bystander CPR (*P*=0.035), and initial shockable rhythm (*P*=0.045).

Discussion

To the best of our knowledge, this is the first study to demonstrate an association between mCPR in the ED and the clinical outcomes after adult nontraumatic OHCA using data from a large, multicenter, prospective cohort study of OHCA in Japan. None of the previous studies accounted for the within-institution clustering effect and potential confounders, as was done in the current study. We found that, although the use of mCPR devices in the ED has become widespread in Japan, most CPR efforts were performed without them in the ED. When adjusted for potential confounders and within-institution clustering effects, mCPR in the ED was significantly

associated with decreased likelihoods of favorable clinical outcomes in those patients.

Previous studies failed to demonstrate an improved clinical outcome in comparison to manual CPR when mCPR devices were used in the prehospital setting. The PARAMEDIC (Prehospital Randomized Assessment of a Mechanical Compression Device in Cardiac Arrest) trial,[45] CIRC (Circulation Improving Resuscitation Care) trial,[19] and LINC (LUCAS in Cardiac Arrest) study[46] reported that the superiority of prehospital mCPR in comparison to manual CPR had not been demonstrated. Thus, there is insufficient evidence to suggest the superiority of prehospital mCPR devices, which is reflected by a class IIb recommendation (Usefulness is less well established by evidence.) and a level of evidence of C (consensus opinion of experts) in the American Heart Association guidelines.[47] However, although the results from clinical trials have been conflicting, the use of mCPR devices is currently established and they are widely used not only in the prehospital setting but also in the ED in Japan.

Recently, Buckler et al reported the adverse effect of prehospital mCPR provided by EMS personnel on adult patients with nontraumatic OHCA.[10] They demonstrated that survival to hospital discharge with a favorable neurological function was more likely among patients who were treated with manual CPR in comparison to those who received mCPR. Consistent with these observations, Youngquist et al demonstrated that prehospital mCPR was associated with poor neurological outcomes among surviving patients by propensity score analyses using the database from the CARES (Cardiac Arrest Registry to Enhance Survival) in Utah.[24] Although these findings were in contrast to the results of randomized controlled trials that showed no benefit, but also no harm, from mCPR use, these recent studies suggest that the real-world implementation of mCPR is different from the environment of a well-designed randomized controlled trial.[10] Given the potential benefits of mCPR devices, we had hypothesized that the use of mCPR in the ED to treat adult patients with nontraumatic OHCA may be associated with improved or equivalent survival from OHCA. However, we found that mCPR was associated with significantly worse outcomes after OHCA. Collectively, these observations suggest that the use of mCPR devices could be associated with poor clinical outcomes among adult patients with OHCA resuscitated in the in-hospital setting and the out-of-hospital setting. Therefore, it is conceivable that attending physicians and medical teams treating patients with OHCA in the ED should be aware that the introduction of mCPR devices is likely to have a negative effect on patient outcomes, at least for the time being.

There are some potential explanations as to why the use of mCPR in the ED was associated with significantly worse outcomes in this study. First, the application of the device on hospital arrival may lead to more prolonged pauses in compressions at the beginning of CPR in comparison to manual CPR. Ong et al measured the no-flow time and no-flow ratio before and after the ED switched from manual CPR to a load-distributing band mCPR device.[48] They reported that application of a load-distributing band in the ED was associated with a higher no-flow ratio in comparison to manual CPR in the first 5 minutes of resuscitation.[48] It is conceivable that attention to team training and the rapid application of the device would contribute to minimizing the interruption of chest compression and improving performance in resuscitation. Second, rescuers performing manual CPR can be aware whether the ongoing chest compressions are being performed appropriately (eg, compression depth, compression rate, recoil, and duty cycle) in real time, whereas the mCPR device does not provide real-time CPR feedback. A randomized, crossover mannequin study demonstrated a remarkably poor quality of compressions with the use of the mechanical device in simulated CPR.[49] In addition, in human

case reports, it was observed that switching from mCPR to manual compressions enabled increasing chest compression depth, resulting in hemodynamic improvement, which highlighted the usefulness of physiological monitoring during CPR.[50] There is clinical evidence to support that the assessment of CPR quality has revealed significant increases in survival and a favorable neurological function after cardiac arrest.[51,52] Thus, it is possible that the use of mCPR with an assessment of CPR quality may be useful to improve the resuscitation performance. Human or mechanical error during the use of mCPR devices is another possibility. A single human case report in which transthoracic echocardiography was performed during CPR noted that an mCPR device was ineffective in generating blood flow.[53] Thus, rescuers should consider checking the pulse during mCPR and constantly assessing the efficacy of the device.

We note a large decrease in the number of people admitted to the hospital relative to ROSC in the ED. We considered the possibility that the decision to use the mCPR device may be influenced by anticipation of prolonged resuscitation that potentially has poor prognosis. To address this issue, we investigated the difference in the proportion of hospital admissions among the patients with successful ROSC between each group. Of the 1801 patients who achieved successful ROSC, 75 had data missing on hospital admission. Of the remaining 1726 patients, there was no significant difference in the admission rate between each group (manual CPR group versus mCPR group, 924/1497 [61.7%] versus 149/229 [65.1%]; $P=0.331$). Second, we analyzed the time interval from EMS call to ROSC among the patients who had successful ROSC. Notably, there was no difference in the time interval from EMS call to ROSC in the ED between each group (median [interquartile range] for manual CPR group versus mCPR group, 44 [36–51] versus 46 [35–51] minutes; $P=0.506$). These observations suggest that patients in the mCPR group could not be considered to have a poorer prognosis and require prolonged resuscitation, as anticipated by the treating physician, compared with patients in the manual CPR group.

The low survival rate in our data set is best understood as being attributable, in part, to the fact that Japan EMS is not allowed to terminate resuscitation efforts in the field. Furthermore, patients with prehospital ROSC were excluded from the present analyses (Figure 1). Several articles have shown that prehospital ROSC is significantly associated with a better survival rate after OHCA. Thus, the low survival rate in this study should be because of exclusion of the patients with prehospital ROSC from the overall number of adult patients with nontraumatic OHCA.

There are several limitations in the current study. First, this was not a randomized controlled trial but rather a multicenter, observational study with all of the limitations inherent to such

a study design. As with any observational study, the association between the mCPR and patient outcomes does not necessarily prove causality and might be confounded by unmeasured factors. Furthermore, this study might have been affected by confounding indications. However, given that the patients who received mCPR in the ED had a higher proportion of patients with witnessed arrests and who received bystander CPR, a shorter time interval from CPR initiation to hospital arrival and from call to the first epinephrine dose, and a similar blood ammonia level compared with the manual CPR group (Table 1), the patients with a good prognosis on ED arrival likely underwent appropriate resuscitation efforts, which would have included the use of mCPR. The mCPR was associated with worse survival in patients who had better prognostic factors (Figure 2).[54] Second, we were not able to analyze the association between mCPR and neurological outcome after OHCA because of the few events. Thus, the role of mCPR in the ED on neurocognitive function after OHCA remains undetermined. Third, the in-hospital procedures or protocols for the implementation of the devices among each hospital were unknown in this study. To account for the institutional and regional factors associated with an improved outcome, we performed multivariate analyses with adjustment for within-institution clustering effects using a generalized estimating equation. Nevertheless, selection biases pertaining to the decision to use mCPR by the treating physician cannot be accounted for in this study. Finally, most mCPR use (60.7%) was with "other" devices rather than the AutoPulse, LUCAS, or LUCAS2, which are recommended as class IIb in the current guidelines. To our best knowledge, some piston-style electromechanical devices are approved and commercially available for prehospital and in-hospital CPR in Japan. Generally, these piston devices with an arm are designed to be placed in the center of the chest, push the sternum down, and return to the neutral position automatically. Compression depth and frequency are easily adjustable to meet the recommendations of the International Liaison Committee on Resuscitation guidelines. However, as this study is an observational registry of OHCA, we were not able to collect details on the other devices. Recently, new devices have been developed with design and setup modifications to improve the quality of CPR and overcome the disadvantages associated with other devices. Thus, the role of mCPR could be limited to patients who were transported to the hospitals participating in this study.

Conclusion

The current study suggested that the mCPR for adult patients with OHCA attending the ED was associated with a decreased likelihood of survival to hospital discharge, successful ROSC, and hospital admission, after accounting for potential confounders and the within-institution clustering effect. Further studies are warranted to clarify the circumstances in which mCPR may benefit patients with nontraumatic OHCA; however, our data do not support the routine use of mCPR devices for patients with OHCA in the ED.

Appendix

SOS-KANTO 2012 Steering Council

Naoto Morimura, Atsushi Sakurai, Yoshio Tahara, Arino Yaguchi, Ken Nagao, Takashi Tagami, Yosuke Homma, Tomoko Ogasawara, Kei Hayashida, Masaru Suzuki; Mari Amino, Nobuya Kitamura, Tomohisa Nomura, Naoki Shimizu, Akiko Akashi, Naohiro Yonemoto.

SOS-KANTO 2012 Study Group

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Disclosures

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Mechanical Cardiopulmonary Resuscitation and Hospital Survival Among Adult Patients With Nontraumatic Out −of−Hospital Cardiac Arrest Attending the Emergency Department: A Prospective, Multicenter, Observational Study in Japan (SOS−KANTO [Survey of Survivors after Out−of−Hospital Cardiac Arrest in Kanto Area] 2012 Study)

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