Immediate Defibrillation or Defibrillation After Cardiopulmonary Resuscitation

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Abstract

Objectives. This study aimed to determine whether short cardiopulmonary resuscitation (CPR) by emergency medical services before defibrillation (*CPR first*) has a better outcome than immediate defibrillation followed by CPR (*shock first*) in patients with ventricular fibrillation/pulseless ventricular tachycardia (VF/pulseless VT) out-of-hospital cardiac arrest. **Methods.** We analyzed a national database between 2006 and 2008, and included patients aged 18 years or more who had witnessed cardiac arrests and whose first recorded rhythm was VF/pulseless VT. Those study subjects were divided into five groups in accordance with the CPR/defibrillation intervention sequence. Each group was subdivided into call-to-response intervals of <5 minutes and ≥5 minutes. We identified 267 patients in the shock-first group and 6,407 patients in the CPR-first group. One-month survival and neurologically favorable one-month survival rates were used for outcome measures. The association of intervention type on outcomes (one-month survival or neurologically favorable one-month survival) was analyzed using multivariate logistic regression analyses by adjusting potential confounding factors such as survey year, gender, age (years), bystander CPR, intubation, and call-to-response interval (min). **Results.** The overall one-month survival rate was 26.2% (3,125/11,941) and the neurologically favorable one-month survival rate was 16.6% (1,983/11,934). The CPR-first group had a one-month survival rate of 27.8% (1,780/6,407) and a neurologically favorable one-month survival rate of 17.8% (1,140/6,404), and the shock-first group had survival rates of 24.7% (66/267) and 18.4% (49/267), respectively. There were no significant differences in one-month survival and neurologically favorable one-month survival in these two primary comparison groups (odds ratio [95% confidence interval], 0.85 [0.64–1.13] and 1.04 [0.76–1.42], respectively). Logistic regression analysis showed that neither CPR first nor shock first was associated with the rate of one-month survival or neurologically favorable one-month survival, after adjusting for potential confounders. **Conclusions.** In our study, CPR prior to attempted defibrillation did not present a better outcome compared with shock first as measured by either one-month survival or neurologically favorable one-month survival, after adjusting for potential confounders. Further studies are required to determine whether CPR first has an advantage over shock first. **Key words:** cardiopulmonary resuscitation; electric defibrillation; emergency medical services; ventricular fibrillation; survival; cardiac arrest.

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Introduction

Current cardiopulmonary resuscitation (CPR) guidelines recommend that emergency medical services (EMS) system directors consider implementing a protocol that would allow EMS responders to provide approximately five cycles (approximately 2 minutes) of CPR before defibrillation of patients found by EMS personnel to be in ventricular fibrillation (VF), particularly when the EMS system call-to-response interval is greater than 4 to 5 minutes.[1]

These guidelines are supported by some evidence from animal and human studies. Myocardial metabolic degradation may be slowed or partially reversed by increased blood flow generated by CPR.[2] In a study on dogs, after 7.5 minutes of VF, CPR and high-dose epinephrine were given followed by defibrillation, and it was found that there was a higher rate of return of spontaneous circulation than with defibrillation only.[3] In humans, Cobb et al.[4] carried out a population-based study using 42 months of preintervention analysis and 36 months of postintervention analysis, and they showed that 90 seconds of CPR prior to defibrillation improved survival. This improvement was predominantly in the subgroup of a later (≥4 min) response interval. In a randomized study, Wik et al.[5] showed that

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3 minutes of CPR before defibrillation did not show overall improvement compared with shock first, but there was better survival in the subgroup of a later (≥5 min) response. In other randomized trials, Jacobs et al.[6] showed that 90 seconds of CPR before defibrillation does not improve overall survival, and Baker et al.[7] showed that 3 minutes of CPR before defibrillation also does not improve overall survival. The optimal CPR duration prior to defibrillation is unknown. Bradley et al.[8] demonstrated that 46–195 seconds of EMS CPR before defibrillation was weakly associated with a higher survival rate compared with that for ≤45 seconds.

It is still debatable whether shock first or CPR first has the best outcome. The purpose of this study was to determine whether EMS CPR first has a better outcome compared with immediate defibrillation (shock first) in patients with VF/pulseless ventricular tachycardia (pulseless VT) out-of-hospital cardiac arrest (OHCA).

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METHODS

Study Design

The present study was a nonrandomized, nationwide, retrospective observational study that analyzed the national OHCA registry of the Fire and Disaster Management Agency between 2006 and 2008. We obtained permission from the Agency to use the data in this study. The national guidelines for epidemiology studies issued by the Ministry of Education, Culture, Sports, Science and Technology and the Ministry of Health, Labour and Welfare state that obtaining individual informed consent from each patient is not required if the study is an analysis of secondary data from a preexisting data set. Therefore, we did not obtain individual consent from the study participants. This study was approved by the Institutional Review Board of Nara Medical University.

Study Setting and Population

In Japan, the emergency network covers the whole country. The universal emergency access number, 1-1-9, is directly connected to a dispatch center located in the regional fire defense headquarters. Upon receiving a call, the nearest available ambulance is dispatched to the site. The OHCA registry of the Fire and Disaster Management Agency comprises almost all cases of OHCA in Japan. The national CPR guidelines are based on the International Liaison Committee on Resuscitation (ILCOR) 2005 guidance. The national guidelines implemented during study period were revised in June 2006 for Basic Life Support (BLS)[9] and in August 2006 for Advanced Life Support (ALS) and published in July 2006 and February 2007,[10] respectively.

Study Subjects

Regional fire defense headquarters identified OHCA patients according to the modified Utstein-style format.[11] Parameters analyzed in the study included survey year, gender, age, estimated time of collapse (the time that sudden falling into unconsciousness was either seen or heard by a bystander), time of the call, bystander CPR, public automated external defibrillator (AED) use, time of arrival of EMS personnel, the first documented cardiac rhythm, presumed etiology, EMS CPR start time, first defibrillation time, intubation, epinephrine, time of return of spontaneous circulation, time of hospital admission, one-month survival rate, and one-month cerebral performance category (CPC) score. Emergency medical services personnel recorded the presumed etiology, one-month survival, and neurologically favorable one-month survival in cooperation with attending physicians at medical institutions.[12]

Out of 329,230 OHCA patients between 2006 and 2008, we included those who were aged 18 years or more, whose arrests were witnessed (but not witnessed by paramedics) and had a presumed cardiac origin, whose first recorded rhythm was VF/pulseless VT, and whose call-to-response interval (interval from call to EMS arrival on site) was shorter than 60 minutes. In this study, *call* time was defined as the time the 1–1-9 call was connected to the dispatch center, and *EMS arrival on site* time was defined as the time when EMS personnel arrived at the building or nearest available location and stopped their vehicle. Those who had public AED use ($n = 745$) were excluded from this study because the time of defibrillation was not recorded in the database. A call-to-response interval longer than 60 minutes ($n = 49$) was excluded to avoid potential outliers. The 11,941 study subjects were divided into five groups in accordance with the CPR/defibrillation intervention sequence. These five groups were also subdivided into call-to-response intervals of <5 minutes and ≥5 minutes. We identified 267 patients in the *shock-first* group (call-to-response interval <5 min, $n = 54$; ≥5 min, $n = 213$) and 6,407 patients in the *CPR-first* group (call-to-response interval <5 min, $n = 1{,}488$; ≥5 min, $n = 4{,}919$) (Fig. 1). Because no data were obtained for neurologically favorable outcome in seven patients (0.06%), these patients were excluded from the analysis of neurologically favorable outcomes.

Measurements

Our primary outcome measure was the one-month survival rate. Our secondary outcome measure was the neurologically favorable one-month survival rate, which was defined as the rate of CPC 1 (good performance) and CPC 2 (moderate disability) over all CPC categories.[13]

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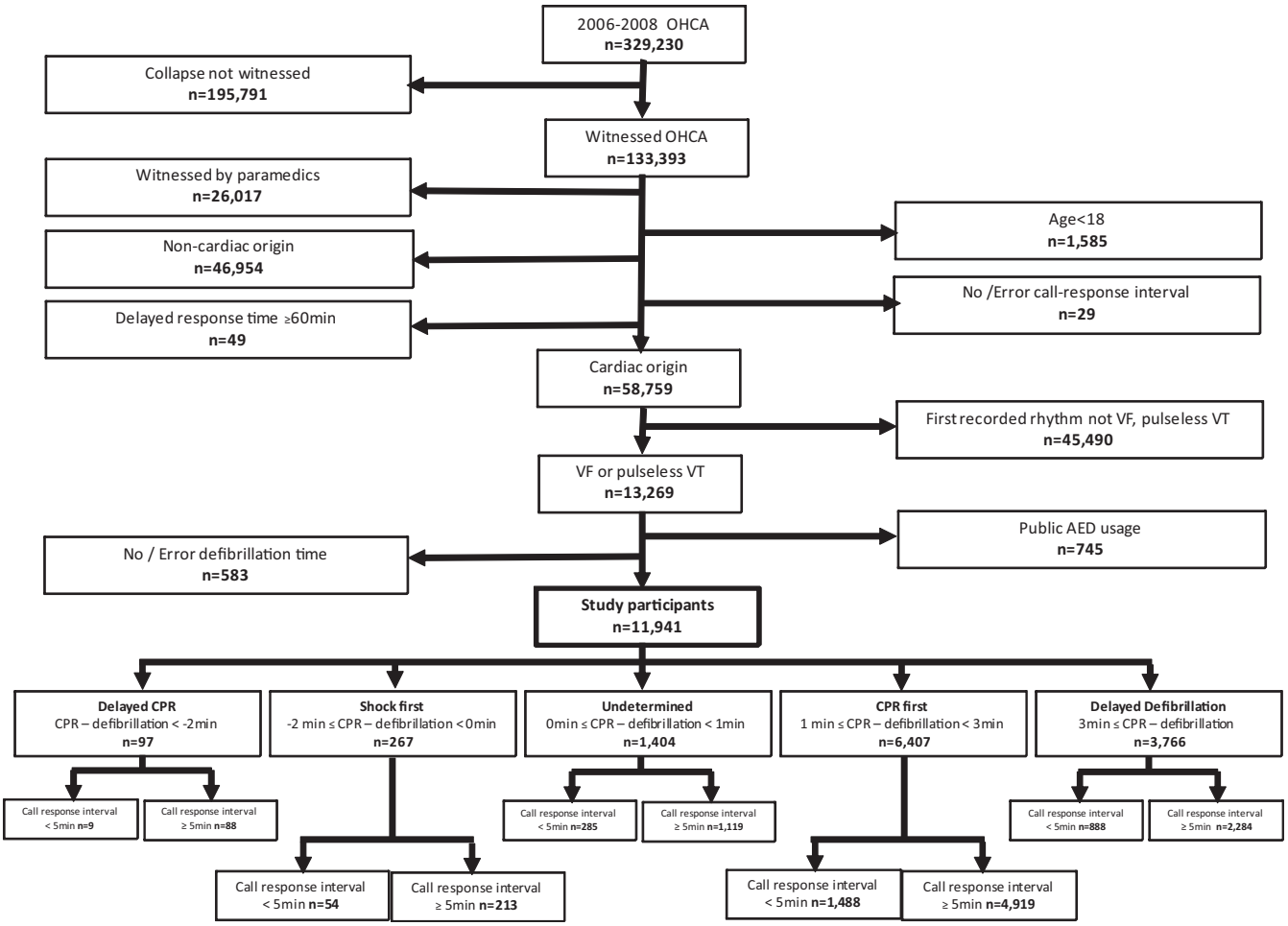

FIGURE 1. Flow diagram of the study participants from 2006 to 2008 from the national out-of-hospital cardiac arrest (OHCA) registry. AED = automated external defibrillator; CPR = cardiopulmonary resuscitation; VF = ventricular fibrillation; VT = ventricular tachycardia.

Data Analysis

We used descriptive statistics to assess characteristics according to the five CPR–defibrillation interval groups. Overall outcome in each intervention group is presented as odds ratios and 95% confidence intervals (CIs). The association of intervention type on outcomes (one-month survival or neurologically favorable one-month survival) was determined using multivariate logistic regression analyses adjusting for potential confounding factors, such as survey year, gender, age (years), bystander CPR, intubation, and call-to-response interval (min). A p-value < 0.05 was considered statistically significant. All statistical analyses were conducted using SPSS 16.0J (SPSS Japan Inc., Tokyo, Japan).

RESULTS

The characteristics of the study subjects, including survey year, gender, age, bystander CPR, intubation, epinephrine, call-to-response interval, and amounts of time defibrillation was attempted, are presented in Table 1.

Call-to-Response Interval and Outcomes

Outcomes, i.e., one-month survival and neurologically favorable one-month survival, were measured for the call-to-response intervals (Fig. 2). The longer the call-to-response interval was, the lower the outcome result was.

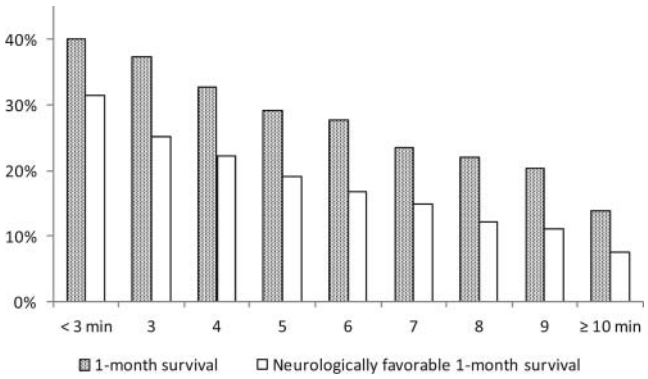

FIGURE 2. One-month survival and neurologically favorable one-month survival rates, presented by the call-to-response time interval.

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TABLE 1. Characteristics of the Study Participants

	Total $n = 11,941$		CPR First (≥1 min and <3 min) $n = 6,407$		Shock First (≥1 min and <3 min) $n = 267$		Undetermined (<1 min) $n = 1,404$		Delayed (≥3 min) Defibrillation) $n = 3,766$		Delayed (≥3 min) CPR) $n = 97$	
Survey year												
2006	4,089	(34.2%)	2,226	(34.7%)	156	(58.4%)	642	(45.7%)	1,033	(27.4%)	32	(33.0%)
2007	3,539	(29.6%)	1,898	(29.6%)	54	(20.2%)	331	(23.6%)	1,224	(32.5%)	32	(33.0%)
2008	4,313	(36.1%)	2,283	(35.6%)	57	(21.3%)	431	(30.7%)	1,509	(40.1%)	33	(34.0%)
Gender—male (%)	9,522	(79.7%)	5,152	(80.4%)	232	(86.9%)	1,146	(81.6%)	2,915	(77.4%)	77	(79.4%)
Age—mean (±SD), years	64.6	(±15.0)	64.4	(±14.9)	62.7	(±15.7)	63.8	(±14.6)	65.4	(±15.3)	67.1	(±14.1)
Bystander CPR	6,078	(50.9%)	3,347	(52.2%)	159	(59.6%)	837	(59.6%)	1,674	(44.5%)	61	(62.9%)
Intubation	5,855	(49.1%)	3,220	(50.3%)	138	(51.7%)	674	(48.0%)	1,784	(47.4%)	39	(40.2%)
Epinephrine	1,205	(10.1%)	625	(9.8%)	18	(6.7%)	122	(8.7%)	432	(11.5%)	8	(8.2%)
Call-to-response interval—mean (±SD), min	6.6	(±3.0)	6.5	(±2.9)	7.0	(±3.3)	6.9	(±3.5)	6.6	(±3.0)	8.7	(±4.0)
Time during which defibrillation was attempted—mean (±SD), min	2.4	(±1.7)	2.4	(±1.7)	2.6	(±1.9)	2.5	(±1.8)	2.3	(±1.6)	2.6	(±1.8)

CPR = cardiopulmonary resuscitation; SD = standard deviation.

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Overall Outcomes by Intervention Sequence

Overall comparison of the outcomes by CPR/defibrillation sequence and odds ratios with CPR first as a reference value are shown in Table 2. Without adjusting for potential confounders, there were no significant differences in outcome between CPR first and shock first in all call-to-response interval subcategories (≥5 min, <5 min, and total response interval). There was no significant difference between CPR first and the undetermined category in outcome. However, a delayed (CPR/defibrillation interval ≥3 min) defibrillation showed a lower outcome than short CPR followed by defibrillation (CPR first; CPR/defibrillation interval ≥1 min and <3 min).

Cardiopulmonary Resuscitation First versus Shock First by Logistic Regression Analysis

Logistic regression analyses showed that a survey year of 2007 or 2008, being female, a younger age, having bystander CPR, and no intubation were associated with a higher rate of one-month survival (all response time categories). There was no significant difference in the rate of one-month survival between shock first and CPR first ($p = 0.26$ for a call-to-response interval <5 min; $p = 0.84$ for ≥5 min; and $p = 0.68$ for total call-to-response interval) (Table 3).

Regression analysis also showed that in the survey year of 2007 or 2008, a younger age, having bystander CPR, no intubation, and a shorter call-to-response interval were associated with a higher rate of neurologically favorable one-month survival (all response time categories). Being female was associated with a higher neurologically favorable one-month survival in the call-to-response interval total and ≥5 minutes. Shock first was not associated with a higher rate of neurologically favorable one-month survival than CPR first ($p = 0.99$ for a call-to-response interval <5 min; $p = 0.15$ for ≥5 min; and $p = 0.24$ for total call-to-response interval) (Table 4).

DISCUSSION

Call-to-Response Interval and Outcome

Previous studies have shown that with successful defibrillation, survival rates following VF are decreased by approximately 7–10% with every minute that defibrillation is delayed.[14] Survival after sudden cardiac arrest varies as a function of the delay before the onset of critical prehospital interventions such as CPR, defibrillation, and Advanced Cardiac Life Support.[15] Another study reported that the effect of defibrillation response intervals on survival showed a steep decrease in the first 5 minutes, and then leveled off gradually at longer intervals.[16] A study of VF patients proposed that an increasing time interval may decrease survival reciprocally as time proceeds.[17]

In the current study, the shorter the call-to-response interval was, the better the one-month survival and neurologically favorable outcome were. This result reiterates the prognostic importance of early defibrillation, but further studies are required to determine the relationship between response time and outcome of patients with VF/pulseless VT.

Cardiopulmonary Resuscitation First versus Shock First

In the present study, we did not detect any significant difference in either one-month survival or neurologically favorable one-month survival in OHCA patients

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TABLE 2. Overall Outcomes by Intervention Sequence

	Call-to-Response Interval, Total				Call-to-Response Interval <5 min				Call-to-Response Interval ≥5 min			
	No. / Total	(%)	OR	(95% CI)	No. / Total	(%)	OR	(95% CI)	No. / Total	%	OR	(95% CI)
One-month survival	3,125 / 11,941	(26.2%)			959 / 2,724	(35.2%)			2,166 / 9,217	(23.5%)		
CPR first (≥1 min and <3 min)	1,780 / 6,407	(27.8%)	*Reference*		555 / 1,488	(37.3%)	*Reference*		1,225 / 4,919	(24.9%)	*Reference*	
Shock first (≥1 min and <3 min)	66 / 267	(24.7%)	0.85	(0.64–1.13)	16 / 54	(29.6%)	0.71	(0.39–1.28)	50 / 213	(23.5%)	0.93	(0.67–1.28)
Undetermined (<1 min)	390 / 1,404	(27.8%)	1.00	(0.88–1.14)	111 / 285	(38.9%)	1.07	(0.83–1.39)	279 / 1,119	(24.9%)	1.00	(0.86–1.16)
Delayed (≥3 min) defibrillation	868 / 3,766	(23.0%)	0.78	(0.71–0.85)	274 / 888	(30.9%)	0.75	(0.63–0.90)	594 / 2,878	(20.6%)	0.78	(0.70–0.88)
Delayed (≥ 3 min) CPR	21 / 97	(21.6%)	0.72	(0.44–1.17)	3 / 9	(33.3%)	0.84	(0.21–3.37)	18 / 88	(20.5%)	0.78	(0.46–1.31)
Neurologically favorable one-month survival	1,983 / 11,934	(16.6%)			666 / 2,724	(24.4%)			1,317 / 9,210	(14.3%)		
CPR first (≥1 min and <3 min)	1,140 / 6,404	(17.8%)	*Reference*		388 / 1,488	(26.1%)	*Reference*		752 / 4,916	(15.3%)	*Reference*	
Shock first (≥1 min and <3 min)	49 / 267	(18.4%)	1.04	(0.76–1.42)	14 / 54	(25.9%)	0.99	(0.53–1.84)	35 / 213	(16.4%)	1.09	(0.75–1.58)
Undetermined (<1 min)	272 / 1,402	(19.4%)	1.11	(0.96–1.29)	85 / 285	(29.8%)	1.20	(0.91–1.59)	187 / 1,117	(16.7%)	1.11	(0.93–1.33)
Delayed (≥ 3 min) defibrillation	512 / 3,764	(13.6%)	0.73	(0.65–0.81)	177 / 888	(19.9%)	0.71	(0.58–0.86)	335 / 2,876	(11.6%)	0.73	(0.64–0.84)
Delayed (≥ 3 min) CPR	10 / 97	(10.3%)	0.53	(0.27–1.02)	2 / 9	(22.2%)	0.81	(0.17–3.92)	8 / 88	(9.1%)	0.55	(0.27–1.15)

CI = confidence interval; CPR = cardiopulmonary resuscitation; OR = odds ratio (unadjusted).

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TABLE 3. Logistic Regression Model on One-Month Survival

	Call-to-Response Interval, Total			Call-to-Response Interval <5 min			Call-to-Response Interval ≥5 min		
	OR	(95% CI)	p-Value	OR	(95% CI)	p-Value	OR	(95% CI)	p-Value
Survey year									
2006		*Reference*			*Reference*			*Reference*	
2007	1.24	(1.11-1.38)	<0.001	1.26	(1.03-1.54)	0.02	1.23	(1.08-1.40)	<0.001
2008	1.31	(1.18-1.45)	<0.001	1.37	(1.12-1.67)	<0.001	1.29	(1.14-1.45)	<0.001
Gender									
Male		*Reference*			*Reference*			*Reference*	
Female	1.24	(1.11-1.37)	<0.001	1.25	(1.01-1.53)	0.04	1.23	(1.09-1.40)	<0.001
Age	0.98	(0.98-0.98)	<0.001	0.98	(0.98-0.99)	<0.001	0.98	(0.98-0.98)	<0.001
Bystander CPR									
Without bystander CPR		*Reference*			*Reference*			*Reference*	
With bystander CPR	1.36	(1.25-1.49)	<0.001	1.26	(1.06-1.48)	0.01	1.40	(1.26-1.55)	<0.001
Intubation									
No intubation		*Reference*			*Reference*			*Reference*	
Intubation	0.53	(0.49-0.58)	<001	0.40	(0.34-0.47)	<0.001	0.59	(0.53-0.65)	<0.001
Call-to-response interval	0.87	(0.85-0.88)	<001	0.91	(0.82-0.99)	0.04	0.87	(0.85-0.89)	<0.001
CPR/defibrillation									
CPR first (≥1 min and <3 min)		*Reference*			*Reference*			*Reference*	
Shock first (≥1 min and <3 min)	0.94	(0.70-1.26)	0.68	0.70	(0.38-1.30)	0.26	1.04	(0.74-1.44)	0.84
Undetermined (<1 min)	1.03	(0.90-1.18)	0.63	0.99	(0.76-1.30)	0.96	1.04	(0.89-1.22)	0.60
Delayed (≥ 3 min) defibrillation	0.77	(0.70-0.85)	<0.001	0.73	(0.61-0.88)	<0.001	0.79	(0.71-0.89)	<0.001
Delayed (≥ 3 min) CPR	0.88	(0.53-1.46)	0.63	0.81	(0.19-3.34)	0.77	0.91	(0.53-1.57)	0.74

CI = confidence interval; CPR = cardiopulmonary resuscitation; OR = odds ratio (adjusted).

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who received CPR prior to defibrillation. For the total response interval, our results are consistent with the studies of Wik et al.,[5] Jacobs et al.,[6] and Baker et al.[7] In a subgroup analysis, the lack of difference in subgroups was not consistent with Cobb et al.[4] and Wik et al.,[5] who found a better outcome with CPR before defibrillation with response intervals of ≥4 minutes and ≥5 minutes, respectively.

Jacobs et al.[6] pointed out that the study by Cobb et al.[4] had changes in clinical protocol and guidelines that might have influenced their results, and the nonrandomized study design might have overestimated the treatment effect.[18] Jacobs et al.[6] also found that the subgroup analysis by Cobb et al.[4] had wide confidence intervals and no adjustment for three interim analyses. Baker et al.[7] mentioned that in the studies of Cobb

TABLE 4. Logistic Regression Model on Neurologically Favorable One-Month Survival

	Call-to-Response Interval, Total			Call-to-Response Interval <5 min			Call-to-Response Interval ≥5 min		
	OR	(95% CI)	p-Value	OR	(95% CI)	p-Value	OR	(95% CI)	p-Value
Survey year									
2006		*Reference*			*Reference*			*Reference*	
2007	1.51	(1.33-1.73)	< 0.001	1.50	(1.19-1.89)	< 0.001	1.52	(1.30-1.79)	< 0.001
2008	1.60	(1.41-1.82)	< 0.001	1.64	(1.31-2.06)	< 0.001	1.59	(1.37-1.86)	< 0.001
Gender									
Male		*Reference*			*Reference*			*Reference*	
Female	1.22	(1.07-1.38)	< 0.001	1.16	(0.92-1.47)	0.21	1.24	(1.06-1.45)	0.01
Age	0.97	(0.97-0.98)	< 0.001	0.98	(0.97-0.98)	< 0.001	0.97	(0.97-0.98)	< 0.001
Bystander CPR									
Without bystander CPR		*Reference*			*Reference*			*Reference*	
With bystander CPR	1.78	(1.60-1.98)	< 0.001	1.54	(1.28-1.86)	<.001	1.91	(1.68-2.17)	< 0.001
Intubation									
No intubation		*Reference*			*Reference*			*Reference*	
Intubation	0.38	(0.34-0.42)	< 0.001	0.36	(0.30-0.44)	< 0.001	0.38	(0.34-0.44)	< 0.001
Call-to-response interval	0.83	(0.82-0.85)	< 0.001	0.83	(0.75-0.92)	< 0.001	0.84	(0.81-0.86)	< 0.001
CPR/defibrillation									
CPR first (≥1 min and <3 min)		*Reference*			*Reference*			*Reference*	
Shock first (≥1 min and <3 min)	1.22	(0.87-1.71)	0.24	0.99	(0.52-1.92)	0.99	1.33	(0.90-1.95)	0.15
Undetermined (<1 min)	1.15	(0.99-1.35)	0.07	1.11	(0.82-1.48)	0.51	1.17	(0.97-1.41)	0.10
Delayed (≥3 min) defibrillation	0.72	(0.64-0.81)	< 0.001	0.68	(0.55-0.84)	< 0.001	0.74	(0.64-0.85)	< 0.001
Delayed (≥3 min) CPR	0.64	(0.33-1.27)	0.20	0.78	(0.15-3.94)	0.76	0.62	(0.29-1.33)	0.22

CI = confidence interval; CPR = cardiopulmonary resuscitation; OR = odds ratio (adjusted).

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et al.[4] and Wik et al.,[5] an extended period of CPR before subsequent defibrillation had the greatest impact on survival. These factors discussed above may have affected the results of our study.

LIMITATIONS AND FUTURE RESEARCH

Our study has several limitations. First, this study was nonrandomized for intervention. In addition, the distribution of the participants receiving CPR first and shock first was not balanced. The allocation criteria were not very clear as to why certain patients received particular interventions (CPR first or shock first). Therefore, even after adjusting for potential confounders in a logistic regression analysis, unpredicted confounding factors may have affected the outcome of the patients. In contrast to the guidelines, 31.5% (3,766/11,941) of the study participants had delayed (>3 min) defibrillation and their prognosis was significantly poorer, which could be an indication of poor compliance with protocol or potential conditions that prevented defibrillation or whatever unknown unpredictable confounders. Second, the database contained no information on the hospitals to which the patients were transferred. Transportation to critical care medical centers results in a better outcome for OHCA patients in Japan[19]; therefore, this may have affected the outcome.

Third, recording an accurate time in the EMS system is still a challenge.[20] In Japan, the proportion of EMS teams whose clocks (control center, emergency medical technician's watch, and emergency transport care and defibrillator) were synchronized every day increased from 39% in December 2005 to 43% in July 2007.[21] In addition, as time is recorded in units of minutes, we could not identify the sequence of CPR and defibrillation in the "undetermined" category, which comprised 11.8% (1,404/11,941) of the study participants. Although an improvement in clock synchronization has been achieved, the quality of the time was still a limitation of this study.

Further studies are required to determine whether CPR prior to attempted defibrillation has a positive outcome. However, the present study, which was a three-year, multicentered, large-scale study, has provided additional evidence regarding effective intervention for shockable OHCA patients.

CONCLUSIONS

In our study, CPR prior to attempted defibrillation did not present a significantly different outcome compared with shock first in either one-month survival or neurologically favorable one-month survival after adjusting for potential confounders. Further studies are needed before consideration is given to revision of the current guidelines, and for evaluation of the advantage of shock first over CPR first.

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