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Association Between Immediate Defibrillation and Outcomes in Shockable Out-of-Hospital Cardiac Arrest: A Propensity Score Analysis

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ABSTRACT

Objectives: This study aimed to examine the association between the timing of defibrillation by emergency medical service (EMS) and out-of-hospital cardiac arrest (OHCA) patient prognosis using a nationwide database.

Methods: We included patients with non-traumatic OHCA aged ≥15 years from 2010 to 2019, with an initial shockable rhythm, who received EMS defibrillation. Patients were divided into 2 groups: defibrillation within 2 min of cardiopulmonary resuscitation (CPR; immediate defibrillation) or after 2 min (delayed defibrillation). The primary outcome was 1-month survival. We set the primary exposure to immediate defibrillation and employed a 1:1 propensity score matching. Multiple logistic regression analysis estimated the adjusted odds ratio (AOR) and 95% confidence interval (CI) for exposure and outcomes.

Results: After propensity score matching, 16,970 patients were included in each group. The 1-month survival were 32.5% and 29.1% for immediate defibrillation and delayed defibrillation, respectively. Immediate defibrillation was significantly associated with 1-month survival compared to delayed defibrillation (AOR [95% CI], 1.18 [1.12, 1.24]).

Conclusions: Defibrillation within 2 min of starting CPR was associated with 1-month survival, emphasizing the importance of immediate defibrillation.

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Introduction

In Japan, approximately 130,000 out-of-hospital cardiac arrest (OHCA) cases occur annually, making it a serious public health concern. In OHCA cases where the initial rhythm is shockable (ventricular fibrillation [VF] or pulseless ventricular tachycardia [pVT]), a relatively favorable prognosis is expected. However, the 1-month survival remains around 30%, indicating the potential for improvement (1). To achieve a favorable prognosis after OHCA with a shockable rhythm, high-quality bystander cardiopulmonary resuscitation (CPR) and timely defibrillation by emergency medical services (EMS) are important, and more effective defibrillation strategies for EMS are needed (2,3).

Current EMS protocols prioritize immediate rhythm analysis and timely defibrillation after patient contact (4–6). Once EMS recognizes cardiac arrest, they perform chest compressions until the defibrillator is ready, promptly analyze the initial rhythm, and perform defibrillation. This protocol has been recommended by the International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations (CoSTR) 2020 review and has been adopted in Japan (4). In line with this, several studies have explored the effectiveness of performing 90–180 s of CPR prior to rhythm analysis and defibrillation, aiming to improve coronary perfusion pressure and enhance the likelihood of successful defibrillation (7,8). This approach may also contribute to improved defibrillation outcomes by facilitating right heart decompression, thereby reducing transthoracic impedance (9). While this strategy is supported by physiological rationale and observational data, optimal timing for defibrillation in the prehospital setting remains an active area of investigation (10,11). The CoSTRc2020 and the Japan Resuscitation Council (JRC) Resuscitation Guideline 2020 raise a clinical question regarding whether shorter duration of chest compression before defibrillation improves patient outcomes compared to longer durations (4,5).

Additionally, the guidelines state that further evidence is needed on the appropriate duration of CPR before defibrillation by EMS (4,5). Prehospital systems reported in previous studies vary across countries, complicating the generalization of findings, and the results differ accordingly (4). Although some randomized trials have provided supporting data, their applicability to different EMS contexts remains limited. In Japan, existing reports are based on specific regions or small sample sizes (5,11–16), highlighting the need for large-scale nationwide investigations. By leveraging a comprehensive

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national registry, this observational study aimed to provide meaningful insights into the relationship between the timing of EMS defibrillation and outcomes in patients with shockable rhythms (VF/pVT) OHCA, thereby contributing to evidence improvements in resuscitation strategies.

Methods

Study Design

This retrospective cohort study used data from the nationwide Utstein data in Japan. The study was approved by the Ethics Committee of Kokushikan University (No. 23029).

Study Setting

In 2019, Japan had a population of 126.16 million and a land area of 378,000 km2. EMS in Japan is provided by fire departments 24 h a day, 365 days a year. An ambulance crew consists of 3 emergency medical technicians (EMTs), 1 of whom is an emergency life-saving technician (17).

The protocols for basic life support and advanced life support are established in accordance with the JRC Resuscitation Guidelines, based on the consensus of the International Liaison Committee on Resuscitation (ILCoR). In April 2017, the 2015 JRC Resuscitation Guidelines were used as the basis for issuing EMS operational protocols across all prefectures. As part of the defibrillation protocol in Japan, EMTs perform continuous chest compression until the defibrillator is ready for rhythm analysis. Semi-automatic external defibrillator (AED) is commonly used in the prehospital setting which have a brief delay during rhythm analysis and charging before defibrillation can be delivered. To minimize hands-off time, CPR is typically continued during AED charging whenever operationally feasible (4,18)

No protocol intentionally delays defibrillation after rhythm analysis (19). All defibrillation is performed using semi-automatic defibrillators under the comprehensive direction of the medical director; and manual defibrillation is not permitted in the EMS system in Japan.

Under the medical director's online supervision, the emergency life-saving technician is authorized to establish intravenous access, administer adrenaline, and perform advanced airway management, including supraglottic airway and endotracheal intubation, for OHCA. The medical director is not present on scene but gives explicit direction *via* phone for each procedure (17). In Japan, EMTs are not allowed to terminate resuscitation at the scene, and all patients undergoing resuscitation attempts are transported to hospitals. However, resuscitation procedures are not initiated if death is obvious, such as in cases of a severed trunk, traumatic brain injury with severe cerebral prolapse, or when the body shows signs of advanced decomposition, including partial or complete skeletonization (ie, exposure of the skeletal remains due to soft tissue decay).

Study Participants

Among OHCA cases occurring between January 1, 2010, and December 31, 2019, those with an initial shockable rhythm in which defibrillation was performed by EMS were included in this study. Exclusion criteria were: (1) age <15 years or >94 years (the 99th percentile or higher), (2) traumatic cases, (3) witnessed by EMS cases, and (4) outliers or negative values in time data regarding EMS activity (emergency call to EMS arrival [response time] > 22 min, CPR to defibrillation >4 min, and defibrillation to hospital arrival <3 min or >87 min). Outliers for time data were defined as the 99th percentile or higher.

Definition of Immediate Defibrillation and Delayed Defibrillation

For the purpose of this study, we classified cases according to the time from the initiation of EMS-performed CPR to the first defibrillation. Cases in which defibrillation was performed less than 2 min after CPR initiation were categorized as "immediate defibrillation," while those receiving defibrillation at 2 to 4 min were categorized as "delayed defibrillation."

This classification was based on clinical discussions in the CoSTR 2020 and the JRC Resuscitation Guideline 2020, as well as prior studies that examined defibrillation timing in OHCA (4,11–16).

There are 2 key reasons for using a 2-min cutoff. First, the Utstein-style dataset records time variables in 1-min increments, which limits the precision of time-based thresholds and precludes the use of second-level granularity, as adopted in some previous studies. Second, while previous studies have used cutoffs ranging from 90 to 180 s to our knowledge, no prior research has used an exact 2-min threshold, despite its clinical relevance. Nevertheless, 2 min is considered a clinically relevant and pragmatic threshold that aligns with the time frames discussed in the CoSTR 2020 and JRC 2020 guidelines for delayed defibrillation strategies.

Data Collection and Quality Control

In January 2005, the Fire and Disaster Management Agency began recording nationwide Utstein data from all fire departments in Japan according to the international Utstein style, an OHCA registry. The variables included in the Utstein data have been detailed in previous studies conducted in Japan. Patient data, including demographic information, such as age and prehospital EMS activities, were documented using EMS records (17,20). Time data were recorded by the EMS based on ambulance activity logs. The Utstein data used in this study recorded time variables based on ambulance activity logs maintained by EMS. The recorded prognostic items included return of spontaneous circulation (ROSC), 1-month survival, and cerebral function prognosis. Return of spontaneous circulation was assessed by EMTs and defined as prehospital ROSC when a pulse was palpable in the carotid artery, in accordance with the JRC resuscitation guideline (4). 1-month survival and cerebral function categories were assessed by the treating physician in the hospital, and cerebral performance was classified using the cerebral performance category (CPC): (1) good cerebral performance; (2) moderate cerebral disability; (3) severe cerebral disability; (4) coma or vegetative state; (5) death. The database did not record the exact time of patient discharge or death; if the patient was discharged within 1 month, the cerebral performance category at discharge was recorded. Although previous studies have often evaluated CPR duration as a continuous variable, we used a 2-min cutoff in this study to allow for categorical comparison that may be more applicable in practical EMS settings. We acknowledge that dichotomizing continuous variables may reduce analytical granularity, and we discuss this as a potential limitation of our approach.

Outcomes

The primary outcome was 1-month survival, and the secondary outcomes were prehospital ROSC and favorable cerebral function. Favorable cerebral function was defined as CPC 1 or 2 (CPC 1–2).

Statistical Analysis

We used propensity score matching (PSM) to adjust for confounders and estimate the average treatment effect on treatment. Patient characteristics were described using frequency and percentage for categorical variables and mean and standard deviation for continuous variables. Standardized mean differences (SMD) were calculated to confirm differences in patient characteristics between the 2 groups. The propensity score was calculated using multiple logistic regression, with immediate defibrillation as the primary exposure. The logistic model included year, season, day (weekday; weekend), sex, age (<65 years; ≥65 years), public access defibrillation, time of awareness (daytime: 9:00 to 16:59; nighttime: 17:00 to 8:59), witness status (unwitnessed; witnessed by family; witnessed by non-family member), bystander CPR type (chest compressions only; chest compressions with ventilation; no bystander CPR), online instructions, etiology (cardiogenic; noncardiogenic), and response time (<5 min; ≥5 min). We dichotomized age at 65 years as the assumption of linearity with immediate defibrillation was not met, and 65 years is a common threshold for defining older adults in clinical settings. A 1:1 nearest-neighbor propensity score matching without replacement was performed using a caliper of 0.1. To confirm the applicability of PSM, the area under the curve of the logistic model was calculated. The area under the curve was 0.67; therefore, PSM was deemed appropriate (21).

After matching, the balance between the 2 groups was evaluated using the probability density distribution of the propensity score and the SMD. An SMD < 0.1 was defined as no imbalance.

Multiple logistic regression analysis, including post-exposure variables, was performed to estimate the adjusted odds ratios (AOR) and 95% confidence intervals (CI) for exposure and outcome. We assessed collinearity among EMS witness status, PAD, and EMS response time using the variance inflation factor. All values ranged within 1 to 2, indicating that multicollinearity was not a concern. Covariates for patient prognosis included propensity score (increments of 0.2), timing of defibrillation (immediate defibrillation; delayed defibrillation), adrenaline (yes or no), advanced airway management (yes or no), time from initial defibrillation by EMS to hospital arrival (minutes/continuous variable), and number of defibrillations (≤3; >3). By including the propensity score as a covariate in post-matching logistic regression, previous research has suggested improved adjustment for residual confounding, especially when dealing with a limited number of events or when balancing high-dimensional confounders (22,23). Since this possibility has been suggested, we incorporated the propensity score into the logistic model to further refine the balance between groups and provide more robust estimates of the treatment effect.

As a subgroup analysis using the post-PSM dataset, patients were classified into groups based on response time: less than 5 min and 5 min or more. The impact of defibrillation timing by EMS on patient outcomes was then examined. As suggested by previous studies, defibrillation effectiveness may vary depending on response time; hence, a 5-min cutoff was used for analysis (5,11–13,15). In addition, to examine whether the association between defibrillation timing and patient outcomes was influenced by changes in JRC resuscitation guideline, we performed a subgroup analysis by classifying the dataset into 2 temporal periods: 2010–2014 and 2015–2019. This division aligns with the approximate 5-year revision cycle of the JRC resuscitation guideline revision. Statistical analyses were conducted using JMP Pro ver 17.0.0 (SAS Institute Inc., Cary, NC, USA), and SMD was calculated using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan)(24).

Results

Patient Data Extraction Flow

The flow of patient data extraction is shown in Figure 1. A total of 1,257,127 OHCA cases occurred during the study period, of which 60,662 met the eligibility criteria and were included in the study (immediate defibrillation: $n = 30{,}851$ [50.9%]; delayed defibrillation: $n = 29{,}811$ [49.1%]).

Participant Characteristics

Table 1 shows the patient characteristics before and after PSM. Until 2013, delayed defibrillation became more prevalent, but immediate defibrillation became more prevalent from 2014 onwards, and this trend continued. With respect to witness status, the percentage of unwitnessed patients was higher in the delayed defibrillation group (immediate defibrillation vs. delayed defibrillation: 25.1% vs. 29.9%). In the bystander CPR, CPR was not performed as frequently in the immediate defibrillation group as in the delayed defibrillation group (immediate defibrillation vs. delayed defibrillation: 34.3% vs. 48.2%), and only chest compressions were more frequently performed in the immediate defibrillation group (immediate defibrillation vs. delayed defibrillation: 58.1% vs. 47.0%). Online instruction was more common in immediate defibrillation cases (immediate defibrillation vs. delayed defibrillation: 58.6% vs. 50.1%). After PSM, 16,970 patients were included. Patient characteristics after

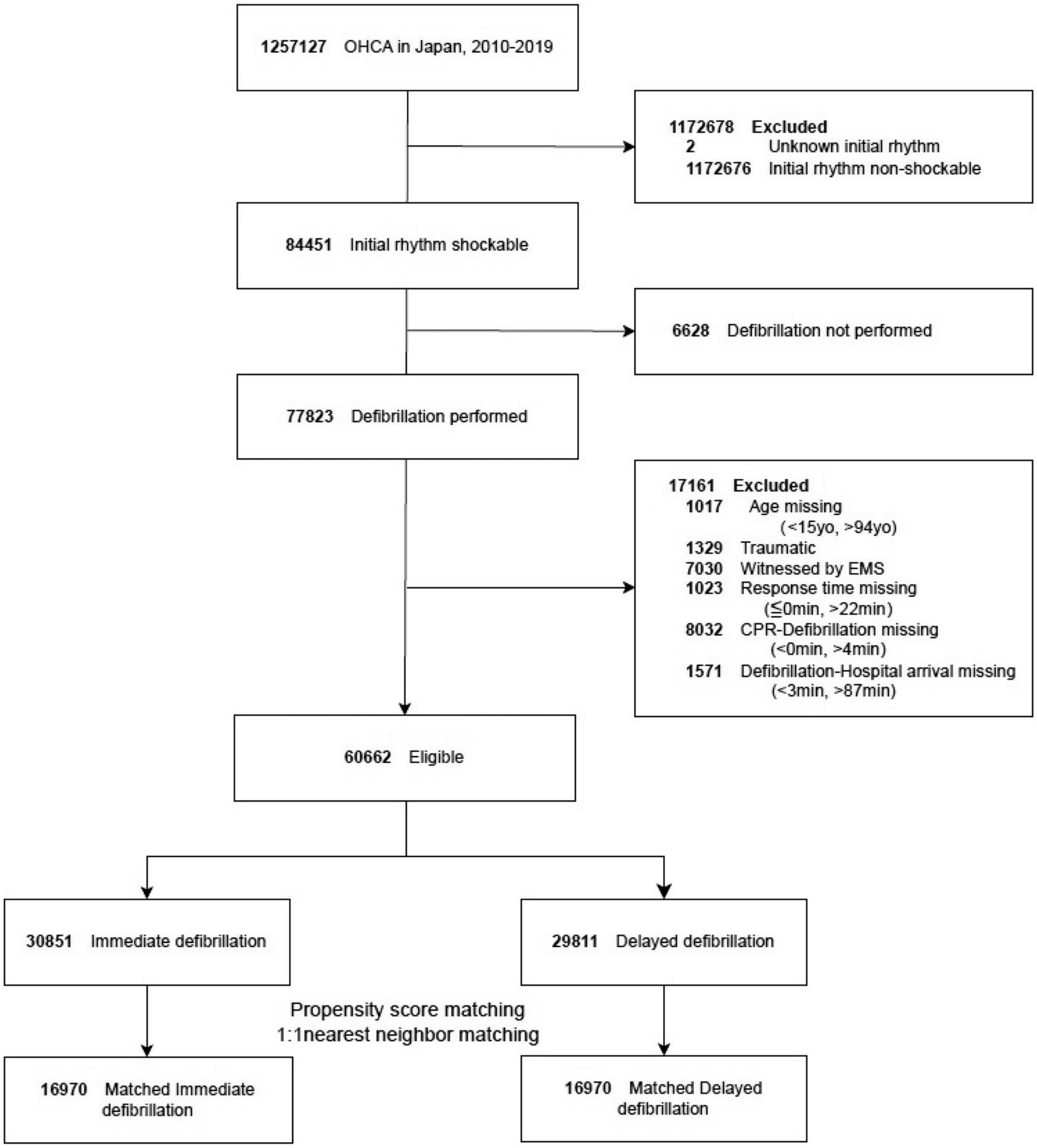

Figure 1. Flowchart for selection of eligible patients.
OHCA = out-of-hospital cardiac arrest; shockable = ventricular fibrillation or pulseless ventricular tachycardia; yo = years old; CPR = cardiopulmonary resuscitation; immediate defibrillation = 0 min ≤ CPR–defibrillation ≤ 1 min; delayed defibrillation = 2 min ≤ CPR–defibrillation ≤ 4 min

PSM are shown in Table 1. The probability density distributions of the propensity scores before and after matching are shown in Online Supplemental File Appendix Figure S1. The SMD for all variables was below 0.1, indicating that the probability density distributions of the propensity scores of both groups were similar, and the balance between the 2 groups was achieved.

Primary Analysis

Figure 2 shows 1-month survival by time between CPR and first shock. The 1-month survival decreased as the time from CPR to defibrillation increased. A comparison of the outcomes based on the timing of initial defibrillation by EMS is shown in Table 2. Immediate defibrillation was significantly associated with 1-month survival compared to delayed defibrillation (AOR [95% CI], 1.18 [1.12, 1.24]). Return of spontaneous circulation and CPC 1–2 also showed a significant association with immediate defibrillation (AOR [95% CI], 1.21 [1.16, 1.27] and 1.27 [1.20, 1.34] for ROSC and CPC1-2, respectively).

Subgroup Analysis

The results of the subgroup analyses based on response time are presented in Online Supplemental File Appendix Table S1. In the group with a response time of <5 min, the immediate defibrillation treatment group showed a significant association with ROSC, and CPC 1–2 compared with the delayed defibrillation treatment group, but the association with 1-month survival did not reach statistical significance (AOR [95% CI], 1.22 [0.98, 1.51]; 1.35 [1.09, 1.68]; 1.36 [1.10, 1.72] for 1-month survival, ROSC and CPC 1–2,

Table 1. Patient characteristics before and after propensity score matching.

Characteristics	Before matching			After matching		
	Immediate defibrillation	Delayed defibrillation	SMD	Immediate defibrillation	Delayed defibrillation	SMD
n(%)	30851	29811		16970	16970	
Pre exposure variable						
Year						
2010	2047 (6.6)	3963 (13.3)	0.48	2044 (12.0)	1997 (11.8)	0.03
2011	2054 (6.7)	3920 (13.1)		2054 (12.1)	2026 (11.9)	
2012	2249 (7.3)	3826 (12.8)		2240 (13.2)	2251 (13.3)	
2013	2683 (8.7)	3136 (10.5)		1558 (9.2)	1622 (9.6)	
2014	3185 (10.3)	2984 (10.0)		1645 (9.7)	1750 (10.3)	
2015	3367 (10.9)	2619 (8.8)		1601 (9.4)	1632 (9.6)	
2016	3530 (11.4)	2590 (8.7)		1580 (9.3)	1551 (9.1)	
2017	3825 (12.4)	2497 (8.4)		1479 (8.7)	1445 (8.5)	
2018	3907 (12.7)	2237 (7.5)		1436 (8.5)	1420 (8.4)	
2019	4004 (13.0)	2039 (6.8)		1333 (7.9)	1276 (7.5)	
Season						
Spring (Mar–May)	7417 (24.0)	7370 (24.7)	0.07	4103 (24.2)	4060 (23.9)	0.01
Summer (Jun–Aug)	7417 (24.0)	6545 (22.0)		3958 (23.3)	3949 (23.3)	
Autumn (Sep–Nov)	7597 (24.6)	6941 (23.3)		4095 (24.1)	4049 (23.9)	
Winter (Dec–Feb)	8420 (27.3)	8955 (30.0)		4814 (28.4)	4912 (28.9)	
Day						
Weekday (Mon–Fri)	21678 (70.3)	21203 (71.1)	0.02	11954 (70.4)	11991 (70.7)	<0.01
Weekend (Sat–Sun)	9173 (29.7)	8608 (28.9)		5016 (29.6)	4979 (29.3)	
Time of awareness						
Daytime (9:00 to 16:59)	15095 (48.9)	13966 (46.8)	0.04	8135 (47.9)	8107 (47.8)	<0.01
Nighttime (17:00 to 8:59)	15756 (51.1)	15845 (53.2)		8835 (52.1)	8863 (52.2)	
Age, ≥65yo	17707 (57.4)	17850 (59.9)	0.05	9683 (57.1)	9764 (57.5)	0.01
Sex, male	24696 (80.0)	23199 (77.8)	0.06	13434 (79.2)	13465 (79.3)	<0.01
Etiology, cardiogenic	28640 (92.8)	27313 (91.6)	0.05	15640 (92.2)	15714 (92.6)	0.02
Witness status						
Unwitnessed	7758 (25.1)	8925 (29.9)	0.13	4461 (26.3)	4548 (26.8)	0.01
Witnessed by family member	13150 (42.6)	12714 (42.6)		7107 (41.9)	7098 (41.8)	
Witnessed by non-family member	9943 (32.2)	8172 (27.4)		5402 (31.8)	5324 (31.4)	
Bystander CPR type						
No bystander CPR	7637 (34.3)	10968 (48.2)	0.29	6734 (39.7)	6623 (39.0)	0.02
Chest compression only	12942 (58.1)	10704 (47.0)		9164 (54.0)	9320 (54.9)	
Chest compression with ventilation	1682 (7.6)	1100 (4.8)		1072 (6.3)	1027 (6.1)	
PAD	1737 (5.6)	1155 (3.9)	0.08	1106 (6.5)	1061 (6.3)	0.01
Online instruction	18063 (58.6)	14941 (50.1)	0.17	9226 (54.4)	9182 (54.1)	<0.01
Time interval between emergency call and EMS contact with patient						
<5 min	1076 (3.5)	1593 (5.3)	0.09	757 (4.5)	765 (4.5)	<0.01
≥5 min	29775 (96.5)	28218 (94.7)		16213 (95.5)	16205 (95.5)	
Post exposure variable						
AAM	12754 (41.3)	12711 (42.6)	0.03	6965 (41.0)	7042 (41.5)	0.01
Adrenaline	9658 (31.3)	8887 (29.8)	0.03	5010 (29.5)	5062 (29.8)	<0.01
Number of defibrillations, >3	7329 (23.8)	6731 (22.6)	0.03	3925 (23.1)	3907 (23.0)	<0.01
Time interval between initial defibrillation by the EMS and arrival hospital, mean (SD)	22.53 (10.50)	22.28 (10.96)	0.02	22.6 (10.2)	22.3 (10.7)	0.02

Immediate defibrillation = 0 min ≤ CPR–defibrillation ≤ 1 min; delayed defibrillation = 2 min ≤ CPR–defibrillation ≤ 4 min; SMD = standardized mean difference; yo = years old; EMS = emergency medical services; CPR = cardiopulmonary resuscitation; PAD = public access defibrillation; AAM = advanced airway management; SD = standard deviation.

respectively). A similar significant association was shown in the response time ≥5 min group (AOR [95% CI], 1.18 [1.12, 1.24]; 1.21 [1.15, 1.27]; 1.26 [1.19, 1.33] for 1-month survival, ROSC and CPC 1–2, respectively). Additionally, using the matched dataset, the trends in immediate defibrillation and 1-month survival over time are shown in Online Supplemental File Appendix Figure S2. From 2010 to 2019, the immediate defibrillation remained at approximately 50%, and the 1-month survival for patients who received immediate defibrillation remained consistently in the 30% range. The results of the subgroup analyses based on time period are presented in Online Supplemental File Appendix Table S2. In both the 2010–2014 and 2015–2019 groups, immediate defibrillation was significantly associated with 1-month survival, ROSC, and CPC 1–2 (AOR [95% CI]; 2010–2014; 1.18 [1.11, 1.26]; 1.19 [1.12, 1.26]; 1.29 [1.20, 1.39], 2015–2019; 1.18 [1.10, 1.26]; 1.26 [1.17, 1.35]; 1.24 [1.14, 1.35], for 1-month survival, ROSC and CPC 1–2, respectively).

Discussion

We analyzed the relationship between the timing of EMS defibrillation and outcomes in patients with an initial shockable rhythm. The results showed that the immediate defibrillation group was significantly associated with 1-month survival, ROSC, and CPC 1–2 compared to the delayed defibrillation group. This study used OHCA data from all of Japan and was based on an analysis of a sufficient number

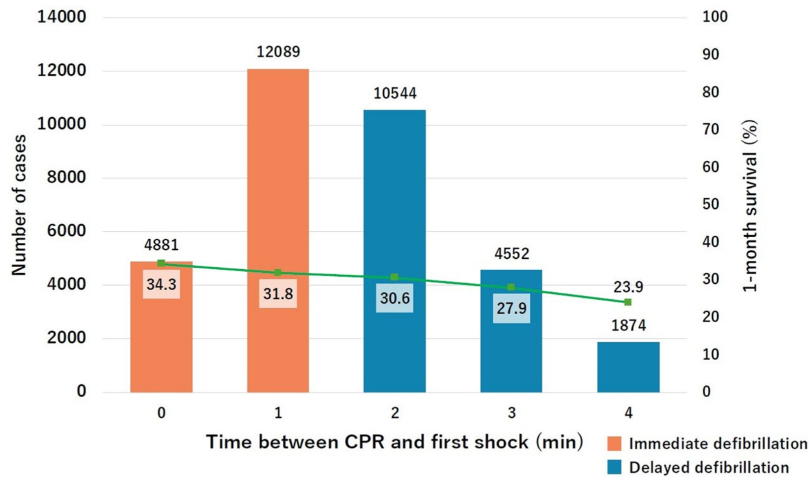

Figure 2. 1-month survival by time between CPR and first shock.
CPR = cardiopulmonary resuscitation; immediate defibrillation = 0 min ≤ CPR–defibrillation ≤ 1 min; delayed defibrillation = 2 min ≤ CPR–defibrillation ≤ 4 min

Table 2. Association between immediate defibrillation and outcomes after out-of-hospital cardiac arrest.

	Patients with outcome, No/total No (%)					
Outcome	Immediate defibrillation		Delayed defibrillation		A[a]OR	(95%CI)
Primary analysis						
1-month survival	5519/16970	(32.5)	4946/16970	(29.1)	1.18	(1.12, 1.24)
ROSC	5767/16970	(34.0)	5060/16970	(29.8)	1.21	(1.16, 1.27)
CPC1-2	3829/16970	(22.6)	3204/16970	(18.9)	1.27	(1.20, 1.34)

Immediate defibrillation = 0 min ≤ CPR–defibrillation ≤ 1 min; delayed defibrillation = 2 min ≤ CPR–defibrillation ≤ 4 min; AOR = adjusted odds ratio; CI = confidence interval; ROSC = return of spontaneous circulation; CPC = cerebral performance category; a = The explanatory variables were propensity score (increments of 0.2); advanced airway management (yes/no); timing of defibrillation (immediate defibrillation; delayed defibrillation); adrenaline (yes/no); time from initial defibrillation by EMS to hospital arrival (min/continuous variable); and number of defibrillations (≤3, >3).

of cases, which effectively addressed previous concerns regarding low statistical power (6,11–16).

Immediate defibrillation is positively associated with patient prognosis. This may be because defibrillation was performed while myocardial adenosine triphosphate (ATP), which represents a physiological state, was still present (25–27). An increase in myocardial blood flow caused by CPR generates ATP in the myocardium, restores ion pump function, and stabilizes the electrical potential of myocardial cell membranes, which is thought to increase the likelihood of ROSC via defibrillation (28). However, myocardial ATP is consumed over time during CPR, decreasing the likelihood of successful defibrillation (29). Therefore, it is considered that in the immediate defibrillation group, defibrillation was performed at a time when success was more likely, before myocardial ATP was depleted, resulting in early ROSC and a good long-term prognosis. Consequently, defibrillation strategies for OHCA should conform to the CoSTR 2020 consensus, which states that high-quality CPR should be performed until defibrillation is available and that defibrillation should be performed expeditiously if the presenting rhythm is shockable.

Although the association between immediate defibrillation and 1-month survival was not statistically significant in the <5 min response time group, immediate defibrillation consistently showed a trend toward better outcomes in both the <5 min and ≥5 min groups. According to the 3-phase model of cardiac arrest, patients with short EMS response times are more likely to be in the electrical phase or early circulatory phase, during which myocardial ATP levels are relatively high, and the myocardium is well-preserved, resulting in a high probability of successful defibrillation regardless of the duration of preceding CPR. This may explain the relatively favorable outcomes even in the delayed defibrillation group, narrowing the between-group difference and likely preventing detection of any association with 1-month survival. In contrast, when the response time is prolonged, patients are more likely to have entered the metabolic phase, in which myocardial ATP depletion has progressed. In this phase, the ongoing depletion of myocardial ATP makes every passing second more critical for defibrillation success; the sooner the defibrillation, the higher the likelihood of success. From the aforementioned, these findings suggested that immediate defibrillation was more important for achieving favorable outcomes in this subgroup (25–27).

The consistent directionality of the effect across both subgroups suggests a potentially beneficial effect of immediate defibrillation even in shorter response time scenarios. As the response time increases, the duration of VF is expected to increase, leading to significant ATP depletion in the myocardium and instability in the myocardial cell membranes. Consequently, for patients with a response time of 5 min or longer, a strategy has been proposed to perform 180 s of CPR before defibrillation, aiming to regenerate ATP in the depleted myocardium and enhance the chances of successful defibrillation (5). The physiological differences in patients with OHCA due to varying response times suggest that different defibrillation strategies may be appropriate, highlighting the difficulties in universally recommending immediate defibrillation, as per the CoSTR 2020 guidelines (4). However, this study supports the CoSTR 2020 recommendations, as the optimal defibrillation strategy was consistent regardless of response time. These results may serve as evidence for future guidelines that recommend immediate defibrillation. Furthermore, a subgroup analysis stratified by time period

(2010–2014 and 2015–2019) showed that the significant association between immediate defibrillation and patient outcomes remained consistent across both periods. This finding suggests that the effectiveness of immediate defibrillation was not significantly influenced by changes in JRC resuscitation guideline or EMS practices over the past decade in Japan, further supporting the robustness of this strategy.

A systematic review concluded that 1) further studies using sufficiently large sample sizes and 2) further country-specific studies are needed to clarify the optimal timing for defibrillation (6). In a previous observational study, the sample size was 11,941 (immediate defibrillation: $n=267$; delayed defibrillation: $n=6{,}407$; others: $n=5{,}267$) and the number of events was 3,125 (immediate defibrillation: $n=66$; delayed defibrillation: $n=1{,}780$; others: $n=1{,}279$) (10). In addition, the subgroup analysis of response time had a small sample size, which was insufficient for the analysis. In this study, a sufficient sample size was used, which increased the statistical power. Furthermore, because EMS systems vary by country and region, an analysis on an EMS basis is necessary. Japan has a single-tiered response system that includes 3 EMTs (16,29). However, some countries have adopted a 2-tiered response system (30,31). Additionally, while the average response time in Japan is approximately 10 min (1), there are some areas in the United States and Taiwan where the response time is approximately 6 min (32,33). As such, there are large regional differences depending on the EMS system; therefore, analysis on an EMS basis is extremely important. We believe that this study has supplemented the findings of previous studies and has highlighted the importance of immediate defibrillation.

Limitations

This study has several limitations. First, as this was an observational, retrospective study, causation cannot be definitively established. Additionally, unmeasured or uncontrolled confounder—such as variations in CPR quality, EMS personnel skills, bystander CPR quality, underlying comorbidities, the total amount of adrenaline administered, or real-time EMS decision-making constraints—may have influenced the results. Furthermore, long-term trends in EMS practices, such as the increased use of dispatch-assisted CPR in Japan, may also have acted as confounding factors. Second, the Utstein data did not include hospital information, which may be an unmeasured confounder. In particular, patients with refractory VF/pVT may have been indicates for extracorporeal CPR, which has been shown to improve outcomes at discharge (34). Therefore, hospital information may have influenced the results. Third, it remains unclear whether delayed defibrillation in this study was the result of an intentional decision by EMS or due to situational factors that made timely defibrillation infeasible. Fourth, this study used data exclusively from Japan, and therefore, the transportability of the findings to other countries or EMS systems may be limited.

Conclusions

In patients with OHCA and an initial shockable rhythm, defibrillation within 2 min of CPR initiation by EMS was associated with improved outcomes. These findings support the CoSTR 2020 recommendations, which emphasize the importance of early initiation of high-quality CPR, timely rhythm assessment, and prompt defibrillation when a shockable rhythm is present. A longer interval between CPR initiation and defibrillation may reduce the likelihood of favorable outcomes.

Authorship Statement

R. Kimura was responsible for conceptualization, data curation formal analysis, investigation, methodology, project administration, visualization, writing of the original draft, and writing review and editing. K. Nakagawa was responsible for conceptualization, investigation, methodology, project administration, supervision, visualization, writing of the original draft, and writing review and editing. T. Kinoshi was responsible for supervision and writing review and editing. H. Tanaka was responsible for supervision and writing review and editing.

Disclosure Statement

The authors report there are no competing interests to declare.

Declaration of Generative AI in Scientific Writing

The authors did not use a generative artificial intelligence (AI) tool or service to assist with preparation or editing of this work. The authors take full responsibility for the content of this publication.

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