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).

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).

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).

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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Clinical paper

Effect of time and day of admission on 1-month survival and neurologically favourable 1-month survival in out-of-hospital cardiopulmonary arrest patients☆

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ABSTRACT

Aim: We sought to examine whether the outcomes of out-of-hospital cardiopulmonary arrest (OHCA) patients differed between weekday and weekend/holiday admissions, or between daytime and nighttime admissions.

Methods: From a national registry of OHCA events in Japan between 2005 and 2008, 173,137 cases where the call-to-hospital admission interval was shorter than 120 min and collapse was witnessed by a bystander were included in this study. One-month survival rate and neurologically favourable 1-month survival rate were used as outcome measures. Logistic regression was used to adjust for potential confounding factors.

Results: No significant differences in outcome were found between weekday and holiday/weekend admissions in rates of 1-month survival or neurologically favourable 1-month survival ($p = 0.78$ and $p = 0.80$, respectively). In contrast, patients admitted in the daytime exhibited significantly better outcomes than those admitted at night, on both outcome measures ($p < 0.001$ and $p < 0.001$). After adjusting for possible confounding factors, outcomes were significantly better for daytime admissions, with odds ratios of 1.26 (95% confidence interval (CI) 1.22–1.31; $p < 0.001$) for 1-month survival, and 1.26 (95% CI 1.20–1.32; $p < 0.001$) for neurologically favourable 1-month survival. In contrast, no significant differences on either outcome measure were found between weekday and weekend/holiday cases, with odds ratios of 1.00 (95% CI 0.96–1.04; $p = 0.96$) for 1-month survival and 0.99 (95% CI 0.94–1.04; $p = 0.78$) for neurologically favourable 1-month survival.

Conclusions: Even after adjusting for confounding factors, admission day (weekday vs. weekend/holiday) had no effect on 1-month survival or neurologically favourable 1-month survival. In contrast, daytime admission was associated with significantly better outcomes than nighttime admissions.

1. Introduction

Despite recent medical advances, outcomes in cases of out-of-hospital cardiopulmonary arrest (OHCA) remain poor.[1] To address this problem, in addition to improving the treatment at medical institutions, more emphasis has been put on pre-hospital care. The "chain of survival," concept,[2] which involves improvements in immediate resuscitation techniques, including access to cardiopulmonary resuscitation (CPR), defibrillation, and advanced cardiovascular life support, has become widely accepted.[3]

To provide a desirable level of medical care, it is important to establish adequate treatment systems at night as well as during weekends and holidays. Differences in outcomes due to circadian variations and the day of occurrence have been reported. Previous studies have suggested that outcomes in cases of pulmonary embolism,[4] ischaemic cerebral infarction,[5] and ischaemic heart disease[6] are poorer at night and on weekends. There is evidence that outcomes of in-hospital cardiac arrest cases are poorer at night and on weekends, even after adjustment for patient condition and the status of the medical institutions involved.[7,8] On the other hand, some studies have reported that weekend admission is not significantly correlated with mortality, readmission rate, or admission

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period.[9,10] It was also reported that outcomes for children hospitalised in paediatric intensive care units were poorer for nighttime admissions than daytime admissions, but no difference was found between weekdays and weekends.[11] Taken together, this evidence suggests that differences in outcomes related to admission day and time depend on the specific underlying diseases and medical care systems involved. As such, further research with recent data from a large and representative sample is required.

The aim of the current study was to examine whether outcomes in cases of OHCA differed between patients admitted to hospital on weekdays and those admitted on weekends and holidays, and between those admitted in the daytime and those admitted at night time, by analysing a nationwide database of OHCA case information.

2. Methods

2.1. Setting

This study was a nationwide, observational, retrospective study of emergency transfer patients in Japan. Japan has an emergency transfer system with universal coverage. The universal emergency access number (1-1-9) is directly connected to regional fire defence headquarters. From there, the nearest available ambulance is dispatched to the incident. All expenses are covered by the local government, so there is no charge to the patient for emergency transportation.[12] The emergency transportation system operates 24 h a day, and ambulance paramedics work 24-h shifts.[13] Adrenaline (epinephrine) administration by emergency medical technicians was allowed in April 2008, if conducted under instruction from physicians. A 'Doctor-Heli' programme has been implemented, but its coverage is still limited. The first Doctor-Heli operation started in 2001, and as of the 2008 fiscal year, 18 Doctor-Heli programmes were operational. These programmes have been used 5625 times, treating 5182 patients.[14] Although tertiary emergency facilities operate 7 days a week, 365 days a year, many secondary emergency facilities do not operate every day of the week. Among designated emergency hospitals, 3717 operate an emergency department of internal medicine, 71.9% of which operate 7 days a week. 33.3% of multiple trauma departments operate 7 days a week.[15] The data used in the present study were from a national registry of OHCA patient data, recorded according to a modified Utstein-style format.[16] Items included in this database were patients' sex, age, estimated time of collapse (where the sudden loss of consciousness was either seen or heard by a witness), time of the emergency call, the first documented cardiac rhythm (ventricular fibrillation (VF), pulseless ventricular tachycardia (pulseless VT), pulseless electrical activity (PEA), asystole and others), aetiology (presumed cardiac origin or non-cardiac origin), CPR time, first defibrillation time, time of return of spontaneous circulation (ROSC), time of hospital admission, 1-month survival rate, 1-month cerebral performance category (CPC), and others. These data were transferred from the regional fire defence headquarters to the Fire and Disaster Management Agency.

2.2. Participants

From the national OHCA patient database recorded over a 4-year period between January 1, 2005 and December 31, 2008 (total n = 431,968), all cases where the call-to-hospital admission interval was within 120 min and the collapse was witnessed by bystanders were included in the present study (n = 173,137).

Measures of time and date were based on the day/time that a patient was admitted to hospital. Days between Monday and Friday, except national holidays (68 days in the 4-year observation period), were categorised as 'weekdays', while Saturday, Sunday, and national holidays were categorised as 'weekends and holidays'. Admissions between 9:00 and 16:59 were categorised as 'daytime', and admissions between 17:00 and 8:59 on the next day were categorised as 'nighttime'.

Although estimated collapse times were recorded in this database, because this time was based on bystander interviews we used call-to-hospital admission interval as a measurement of time, which is recorded by emergency medical services (EMS) system. To eliminate the effects of outliers, we analysed data from patients transported within 120 min from the time of emergency call. According to a previous report, 99.7% of all emergency cases in Japan (not limited to cardiopulmonary arrest) are transported within this time period.[17]

EMS recorded the presumed causes of cardiopulmonary arrest, 1-month survival, and 1-month CPC in cooperation with attending physicians at medical institutions. Data were recorded in the registry at local fire stations. Anonymised data were then transferred to the national registry system on the Fire and Disaster Management Agency database server. No data were obtained for 1-month survival in three patients (0.002%) or for neurologically favourable 1-month survival in 360 patients (0.21%). These patients were also excluded from the analysis.

We obtained permission to analyse the data for this study from the Fire and Disaster Management Agency of Japan, and the Agency provided the anonymised dataset. In accord with the Ministry of Education, Culture, Sports, Science and Technology and the Ministry of Health Labour and Welfare's "a guideline for epidemiology studies", studies are exempt from the requirement to obtain individual informed consent from each patient if they are an analysis of secondary data from a pre-existing dataset. As such, we did not obtain individual consent from the study participants. This study was approved by the Institutional Review Board of Nara Medical University.

2.3. Measurements

One-month survival rate, and neurologically favourable (CPC1; good cerebral performance [conscious, alert, able to work and lead a normal life], or 2; moderate cerebral disability [conscious, with sufficient cerebral function for part-time work in sheltered environment or independent activities of daily life])[18,19] 1-month survival rate were used as outcome measures.

2.4. Analysis

Patient characteristics, including sex distribution, average age, proportion of cardiac origin, first recorded rhythm, bystander CPR, adrenaline (epinephrine) administration, and average call-to-hospital admission interval were calculated and divided by weekday vs. weekend/holiday and daytime vs. nighttime admissions.

Subsequently, 1-month survival rate and neurologically favourable 1-month survival rate by day (Monday to Friday, except national holidays, and Saturday, Sunday, and national holidays), and 1-month survival rate and neurologically favourable 1-month survival rate by time (calculated in 1-h intervals; daytime vs. nighttime) were calculated. We analysed differences in outcome measurement between weekday and weekend/holiday admissions, and between daytime and nighttime admissions.

We used a logistic regression model to examine the association between admission day (weekday vs. weekend/holiday) and time (daytime vs. nighttime) and outcomes, adjusting for possible confounders such as gender, age, bystander CPR, public AED use, initial recorded rhythm (VF/pulseless VT vs. other rhythm), adrenaline, and call-to-hospital admission interval. In this model, age and call-to-hospital admission interval were used as continuous variables,

Table 1
Patient characteristics.

	Total $n=173,137$	Day of the week of admission			Time of admission		
		Weekday $n=114,300$	Weekend or holiday $n=58,837$	*p*-Value	9:00–16:59 $n=69,061$	17:00–8:59 $n=104,076$	*p*-Value
Male (%)	106,577 (61.6%)	70,091 (61.3%)	36,486 (62.0%)	0.005	42,546 (61.6%)	64,031 (61.5%)	0.73
Average age (SD)	71.6 (17.8)	71.6 (17.7)	71.6 (18.0)	0.58	72.2 (17.6)	71.2 (18.0)	<0.001
Cardiac origin (%)	95,192 (55.0%)	62,982 (55.1%)	32,210 (54.7%)	0.16	37,328 (54.1%)	57,864 (55.6%)	<0.001
First recorded rhythm							
Ventricular fibrillation (%)	21,764 (12.5%)	14,345 (12.5%)	7419 (12.6%)	0.75	9580 (13.8%)	12,184 (11.7%)	<0.001
Pulseless ventricular tachycardia (%)	818 (0.5%)	550 (0.5%)	268 (0.5%)	0.46	319 (0.5%)	499 (0.5%)	0.61
Pulseless electrical activity (%)	57,520 (33.1%)	38,401 (33.5%)	19,119 (32.4%)	<0.001	23,588 (34.1%)	33,932 (32.5%)	<0.001
Asystole (%)	76,763 (44.2%)	50,128 (43.7%)	26,635 (45.1%)	<0.001	28,846 (41.7%)	47,917 (45.9%)	<0.001
Other (%)	16,738 (9.6%)	11,166 (9.7%)	5572 (9.4%)	0.04	6889 (10.0%)	9849 (9.4%)	<0.001
Layperson CPR (%)	60,174 (34.8%)	39,427 (34.5%)	20,747 (35.3%)	0.001	25,277 (36.6%)	34,897 (33.5%)	<0.001
Adrenaline (%)	8965 (5.3%)	5983 (5.3%)	2982 (5.2%)	0.14	3608 (5.3%)	5357 (5.2%)	0.49
Collapse-to-call interval, min (SD)	5.6 (9.4)	5.6 (9.3)	5.7 (9.5)	0.16	5.3 (9.1)	5.8 (9.6)	<0.001
Call-to-arrival interval, min (SD)	7.3 (4.2)	7.2 (4.1)	7.3 (4.4)	0.01	7.2 (4.4)	7.3 (4.0)	<0.001
Call-to-CPR interval, min (SD)	11.4 (8.2)	11.2 (8.1)	11.2 (8.2)	0.11	10.9 (8.1)	11.4 (8.2)	<0.001
Call-to-hospital interval, min (SD)	32.3 (12.9)	32.2 (12.7)	32.5 (13.1)	<0.001	31.3 (12.8)	32.9 (12.9)	<0.001

whereas the others were binominal parameters. Chi-square tests and t-tests were used to test for differences between two groups as appropriate. A value of $p<0.05$ was considered as significant. SPSS 16.0J (SPSS Japan Inc., Tokyo, Japan) was used for statistical analyses.

3. Results

Patient characteristics, divided by admission day (weekday vs. weekend/holiday) and time (daytime vs. nighttime) are shown in Table 1. Age by admission time revealed that patients admitted in the daytime were significantly older (72.2 years old) than those admitted at night time (71.2 years old; $p<0.001$). The rate of bystander CPR administration was significantly higher for cases admitted in the daytime (36.6%) compared with those admitted at night time (33.5%; $p<0.001$).

Average 1-month survival rates by admission day (weekday vs. weekend/holiday) are shown in Fig. 1a. Neurologically favourable 1-month survival rates divided by admission day are shown in Fig. 1b. Average 1-month survival rates were 8.8% in total, 8.8% on weekdays, and 8.8% on weekend and holidays. Average neurologically favourable 1-month survival rates were 4.5% in total, 4.5% on weekdays, and 4.6% on holidays. No significant effect of admission day was noted on either 1-month survival rate or neurologically favourable 1-month survival rate ($p=0.78$ and $p=0.80$, respectively).

Average 1-month survival rates and neurologically favourable 1-month survival rates divided by admission time are shown in Fig. 2a and b, respectively. Average 1-month survival rates were 8.8% in total, 10.2% for daytime admissions and 7.9% for nighttime admissions. Average neurologically favourable 1-month 1-month survival rates were 4.5% in total, 5.3% for daytime admissions, and 4.0% for nighttime admissions. Thus, outcomes were significantly more favourable for cases admitted in the daytime in terms of both 1-month survival rates ($p<0.001$) and neurologically favourable 1-month survival rates ($p<0.001$).

After adjusting for potential cofounders, outcomes were still significantly higher when admission was during the daytime, with odds ratios of 1.26 (95% confidence interval (CI) 1.22–1.31; $p<0.001$) for 1-month survival and 1.26 (95% CI 1.20–1.32; $p<0.001$) for neurologically favourable 1-month survival. On the other hand, we found no significant effect of admission day (i.e. weekday compared with weekend and holiday) after adjustment, with odds ratios of 1.00 (95% CI 0.96–1.04; $p=0.96$) for 1-month survival and 0.99 (95% CI 0.94–1.04; $p=0.78$) for neurologically favourable 1-month survival (Table 2).

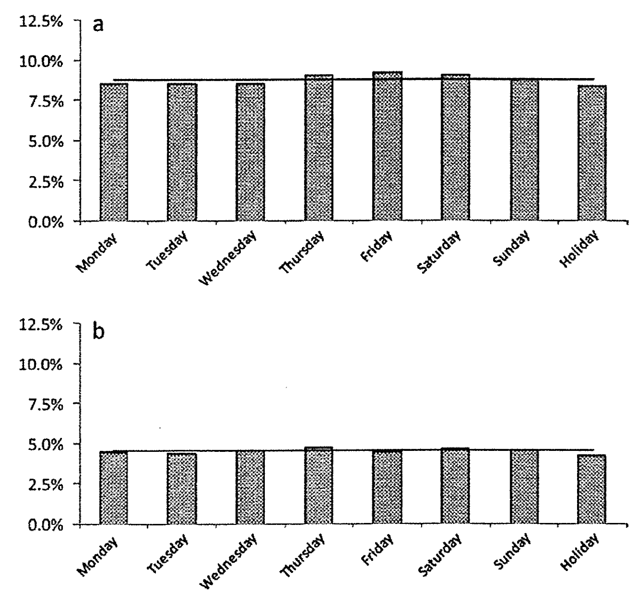

Fig. 1. (a) One-month survival rate by admission day. One-month survival was 8.81% in total (solid line), 8.80% for weekday admissions (bold dashed line), and 8.84% for weekend/holiday admissions (thin dashed line). The difference was not significant ($p=0.78$). (b) Neurologically favourable 1-month survival rate by admission day. Neurologically favourable 1-month survival rate was 4.55% in total (solid line), 4.54% for weekday admissions (bold dashed line), 4.57% for weekend/holiday admissions (thin dashed line). The difference was not significant ($p=0.80$).

4. Discussion

In the present study, the average 1-month survival rate was 8.8% and the rate of neurologically favourable 1-month survival was 4.5%. In previous studies, the reported outcome of OHCA varied both in terms of measurement methodology and results. Sasson et al.[20] conducted a systematic review and meta-analysis, and reported survival-to-hospital discharge rates of between 0.3% and 20.4% (median 6.4%), and an aggregated survival rate of 7.6%. Another study in Sweden reported overall 1-month survival rates of OHCA with CPR of 8.1% in 1992, and 14.0% in 2005.[21] In Japan, a 1-month survival rate of 23.8% and a rate of survival with minimal neurological impairment of 14.4% was reported for bystander witnessed Vf patients.[22]

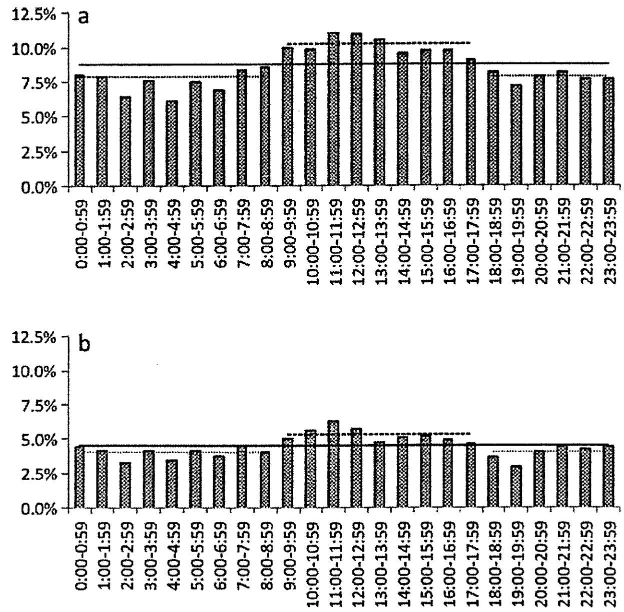

Fig. 2. (a) One-month survival rate by the admission time. One-month survival rate was 8.81% in total (solid line), 10.23% for daytime admissions (bold dashed line), and 7.87% for nighttime admissions (thin dashed line). The difference was significant ($p < 0.001$). (b) Neurologically favourable 1-month survival rate by admission time. Neurologically favourable 1-month survival rate was 4.55% in total (solid line), 5.35% for daytime admissions (bold dashed line), and 4.02% for nighttime admissions (thin dashed line). The difference was significant ($p < 0.001$).

4.1. Hospital admission day and outcome of OHCA patients

In the present study, we examined the effects of day and time of admission on outcome in cases of OHCA in Japan. Even after adjusting for potential confounding factors such as gender, age, bystander CPR, public AED, initial recorded rhythm, adrenaline, call-to-hospital admission interval and time of admission (daytime/nighttime), we found that the day of admission (weekday vs. weekend/holiday) had no significant effect on rates of 1-month survival or neurologically favourable 1-month survival.

In a previous study conducted in Japan, the 28-day fatality rate in cases of acute subarachnoid haemorrhage was found to be higher when patients were transported to hospital on weekdays compared with holidays.[23] One study of acute myocardial infarction (AMI) found no significant difference in the incidence, admission, and case-fatality of AMI between weekdays and weekends.[24] Another study of AMI found no significant difference in 30-day and 1-year survival rates between weekend and weekday admissions.[25] In a study of stroke outcomes, reduced access to computed tomography (CT) tests at weekends because of longer admission times at a stroke unit was found to have a negative effect on stroke outcome in England, Wales, and Northern Ireland.[26]

Although aetiologies might differ depending on the day and time of admission in some contexts, the characteristics of the healthcare system in Japan may have reduced the effect of admission day on outcomes in the present study.

4.2. Hospital admission time and outcome of OHCA patients

We found that cases in which patients were admitted in the daytime were associated with significantly better outcomes in terms of both 1-month survival and neurologically favourable 1-month survival, compared with cases admitted at night. The rate of 1-month survival and neurologically favourable 1-month survival rates increased as the morning progressed, peaked around noon, then declined into the afternoon.

This pattern is consistent with that reported in previous studies. Several studies in the United States reported that circadian rhythm was associated with out-of-hospital sudden deaths, such that rates of cardiac arrest increased rapidly between 06:00 and noon.[27,28] In addition, with the exception of ventricular fibrillation, the circadian variation in arrest rhythm was reported to be identical between cardiac and non-cardiac patients.[29] The causes of this type of circadian variation have also been examined in animal models. It was reported that global cerebral ischaemia during the light phase impaired survival in mice, because of increasing microglia activation and proinflammatory cytokine production, suggesting a biological response.[30]

Table 2
Logistic regression analysis.

	1-month survival		Neurologically favourable 1-month survival	
	OR (95% CI)	*p*-Value	OR (95% CI)	*p*-Value
Sex				
Male	Reference		Reference	
Female	1.05 (1.01–1.09)	0.01	0.94 (0.89–0.99)	0.03
Age	0.99 (0.99–0.99)	<0.001	0.98 (0.98–0.98)	<0.001
Layperson				
No CPR	Reference		Reference	
With CPR	1.09 (1.05–1.13)	<0.001	1.18 (1.12–1.24)	<0.001
Public AED				
Without AED	Reference		Reference	
With AED	4.22 (3.68–4.83)	<0.001	6.42 (5.54–7.43)	<0.001
Initial recorded rhythm				
Other than VF/pulselessVT	Reference		Reference	
VF/pulseless VT	4.22 (4.06–4.39)	<0.001	5.63(5.35–5.91)	<0.001
EMT intervention				
No adrenaline	Reference		Reference	
Adrenaline	0.76 (0.70–0.83)	<0.001	0.35 (0.30–0.41)	<0.001
Call-admission interval	0.99 (0.99–0.99)	<0.001	1.00 (0.99–1.00)	<0.001
Day of the week				
Weekday	Reference		Reference	
Weekend or holiday	1.00 (0.96–1.04)	0.96	0.99 (0.94–1.04)	0.78
Time of admission				
Nighttime	Reference		Reference	
Daytime	1.26 (1.22–1.31)	<0.001	1.26 (1.20–1.32)	<0.001

OR; odds ratio, CI; confidence interval.

In Japan, the emergency transport systems function 24-h a day on every day of the year. Senior physicians are typically on call at weekends, and CT tests are conducted in emergency medical institutions.[25] In addition, ambulances are available free of charge. Highly invasive surgeries, such as stent implantation for AMI, are widely performed because of universal coverage by the public healthcare system.[31] One of the possible reasons for worse outcomes in nighttime admissions is a shortage of staff. Moreover, less comprehensive nighttime facilities are likely to provide less exhaustive treatment, potentially affecting patients' outcomes.

4.3. Limitations

This study involved several limitations. First, details regarding the specific underlying diseases, courses, and complications were not recorded and so these may have acted as confounding factors. Second, we did not have access to individual information about the medical institutions involved. Thus, the distribution of the quality of treatment or characteristics of hospitals may have differed between cases. Potentially useful additional information for future studies includes details of the therapeutic care available at each facility, whether ambulances could be accepted only in the daytime or also at night time, and details of the treatment and techniques available at each institution. A third limitation is that the quality of medical care systems and available resources and the effect of day and time may differ between countries. Thus, it is unclear whether our results can be generalised to other countries with different medical systems, although our findings are relevant to other countries with similar medical systems to Japan. Fourth, since we did not obtain information regarding the location of collapse or how many bystanders were present, the quality of CPR arrests might have been affected. For example, nighttime might be associated with the presence of fewer bystanders, but systematic data are not available. Fifth, our study participants were limited to witnessed cases and more than half of reported OHCA cases are non-witnessed. As might be expected, more OHCA events are non-witnessed during the nighttime (data not shown), which could affect the interpretation of the OHCA data as a whole.

Despite these limitations, the findings of the current study are particularly important because the populations of many countries (especially developed countries including Japan) are rapidly aging.

5. Conclusions

Overall, we found that after adjusting for confounding factors, the day of admission (weekday vs. weekend/holiday) had no significant effect on rates of 1-month survival or neurologically favourable 1-month survival in cases of OHCA in Japan between 2005 and 2008. However, daytime admission was associated with significantly better outcomes compared with admission at night time. This finding indicates that nighttime medical care systems in Japan should be improved. We propose that the operation of emergency transport and medical care systems on both weekdays and holidays in Japan may ameliorate the effect of admission day on OHCA outcomes compared with other countries.

Conflicts of interest statement

The authors declare that they have no conflicts of interest to disclose.

Acknowledgements

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CRITICAL CARE

RESEARCH Open Access

Collapse-to-emergency medical service cardiopulmonary resuscitation interval and outcomes of out-of-hospital cardiopulmonary arrest: a nationwide observational study

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Abstract

Introduction: The relationship between collapse to emergency medical service (EMS) cardiopulmonary resuscitation (CPR) interval and outcome has been well documented. However, most studies have only analyzed cases of cardiac origin and Vf (ventricular fibrillation)/pulseless VT (ventricular tachycardia). We sought to examine all causes of cardiac arrest and analyze the relationship between collapse-to-EMS CPR interval and outcome in a nationwide sample using an out-of-hospital cardiac arrest (OHCA) registry.

Methods: This was a retrospective observational study based on a nationwide OHCA patient registry in Japan between 2005 and 2008 (n = 431,968). We included cases where collapse was witnessed by a bystander and where collapse and intervention time were recorded (n = 109,350). Data were collected based on the Utstein template. One-month survival and neurologically favorable one-month survival were used as outcome measures. Logarithmic regression and logistic regression were used to examine the relation between outcomes and collapse-to-EMS CPR interval.

Results: Among collapse-to-EMS CPR intervals between 3 and 30 minutes, the logarithmic regression equation for the relationship with one-month survival was $y = -0.059 \ln(x) + 0.21$, while that for the relationship with neurologically favorable one-month survival was $y = -0.041 \ln(x) + 0.13$. After adjusting for potential confounders in the logistic regression analysis for all intervals, longer collapse-to-EMS CPR intervals were associated with lower rates of one-month survival (odds ratio (OR) 0.93, 95% confidence interval (CI): 0.93 to 0.93) and neurologically favorable one-month survival (OR 0.89, 95% CI 0.89 to 0.90).

Conclusions: Improving the emergency medical system and CPR in cases of OHCA is important for improving the outcomes of OHCA.

Introduction

The recovery rate in patients suffering cardiopulmonary arrest is generally very low for out-of-hospital cases [1]. In spite of a substantial effort, studies have found that the overall survival in out of hospital cardiac arrest (OHCA) has been stable for almost 30 years [2], or has shown little improvement [3]. As such, establishing an effective emergency medical system (EMS) as well as improving the quality of basic life support (BLS) and advanced cardiac life support (ACLS) are important health policy issues. A number of previous studies have reported that starting cardiopulmonary resuscitation (CPR) earlier results in better outcomes, applying regression models [4], logistic regression models [5,6], and reciprocal models [7] to describe the relationship between collapse-to-EMS CPR interval and outcome.

This study examined the relationship between collapse-to-EMS CPR interval and outcomes based on a

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nationwide OHCA registry. As such, this study is one of the largest studies conducted, in terms of its study population and coverage. There is currently limited documentation on the effects of collapse-to-CPR interval on this scale. Most previous studies have analyzed cardiac origin only, especially initial rhythms of ventricular fibrillation (Vf) or pulseless ventricular tachycardia (VT), A nationwide analysis of all causes of OHCA could provide useful information for establishing more effective EMS systems and the most appropriate allocation of resources.

The aim of this study was to analyze the relationship between the collapse-to-EMS CPR interval, one-month survival, and neurologically favorable outcome using a nationwide OHCA registry between 1 January 2005 and 31 December 2008. This study sought used curve-fitting analysis and potential confounder adjusted odds ratios of the collapse-to-EMS CPR interval. In addition, we sought to discuss the implications of our results for improving EMS systems and the survival of OHCA patients.

Materials and methods

Study design

This study was an observational, retrospective study based on an analysis of a nationwide OHCA registry in Japan from January 2005 to December 2008.

Setting

Japan is a country with a population of 126 million and universal health insurance coverage. The universal emergency access number enables direct connection to a dispatch center located in the regional fire defense headquarters. Upon receiving a call, the nearest available ambulance is sent to the incident. All expenses for transport are covered by the local government and there is no charge to the patient [7]. The emergency network covers the whole country and almost all OHCA patients undergo emergency transfer to a hospital. Treatment fees for medical services at a hospital are also covered by health insurance. The data used in this study were recorded based on the Utstein template [8]. Items included in the database were the patient's name, sex, age, time of collapse (the time at which sudden falling into unconsciousness was either seen or heard by a witness), the first documented cardiac rhythm, etiology, the CPR or first defibrillation time, the time to return of spontaneous circulation (ROSC), the one-month survival rate, and the one-month CPC (cerebral performance category; as a measure of neurologically favorable survival) [9,10]. Location of arrest, survival at discharge, neurological outcome at discharge were not stored in the database. Cardiac etiology was composed of confirmed and presumed cardiac etiology. Although we could not confirm that all times in the database were recorded with standardized timing methods, the proportion of EMS teams practicing daily clock synchronization increased from 39% in December 2005 to 43% in July 2007 [11]. These data were transferred from regional fire defense headquarters to the Fire and Disaster Management Agency. Time data were recorded in the system in the unit of minutes.

Selection of participants

Among the 431,968 OHCA emergency-transferred patients between January 2005 and December 2008, our analysis included cases where collapse was witnessed (that is, collapse was heard or seen by a bystander) but not witnessed by paramedics, the onset time was recorded, and intervention time was less than 120 minutes. A total of 109,350 cases were included in the analysis (Figure 1).

One-month survival was not recorded in 2,131 patients (1.9%) and neurologically favorable survival of 2,356 patients (2.2%) was not recorded in the data registry. These cases were excluded from the logistic regression analysis for outcome.

We obtained permission to analyze the data from the Fire and Disaster Management Agency of Japan, and the Agency provided an anonymized dataset. This study was approved by the Institutional Review Board of the Nara Medical University.

Methods of measurement

Our primary outcome measurement was one-month survival. Neurologically favorable (CPC 1 (Good Cerebral Performance) or 2 (Moderate Cerebral Disability) was used as secondary outcome measurement. Etiology, one-month survival, and neurologically favorable one-month survival were recorded by EMS personnel in cooperation with attending physicians at medical institutions [12].

Primary data analysis

After obtaining the patient characteristics and stratified outcome data, the relationship between collapse to EMS CPR interval and outcomes, logarithmic regression analyses were conducted for cases where collapse-to-EMS CPR time was between 3 and 30 minutes.

Logistic regression analyses where the dependent variable was one-month survival or neurologically favorable one-month survival and the independent variables were potential confounders including study year (2005 to 2006/2007 to 2008), sex (male/female), age (seven categories), etiology (cardiac origin/non-cardiac origin), bystander CPR (0/1), public Automated External Defibrillator (AED) (0/1) and collapse-to-EMS CPR interval (minutes) were then performed. In these logistic regression models, collapse-to-EMS CPR interval was treated

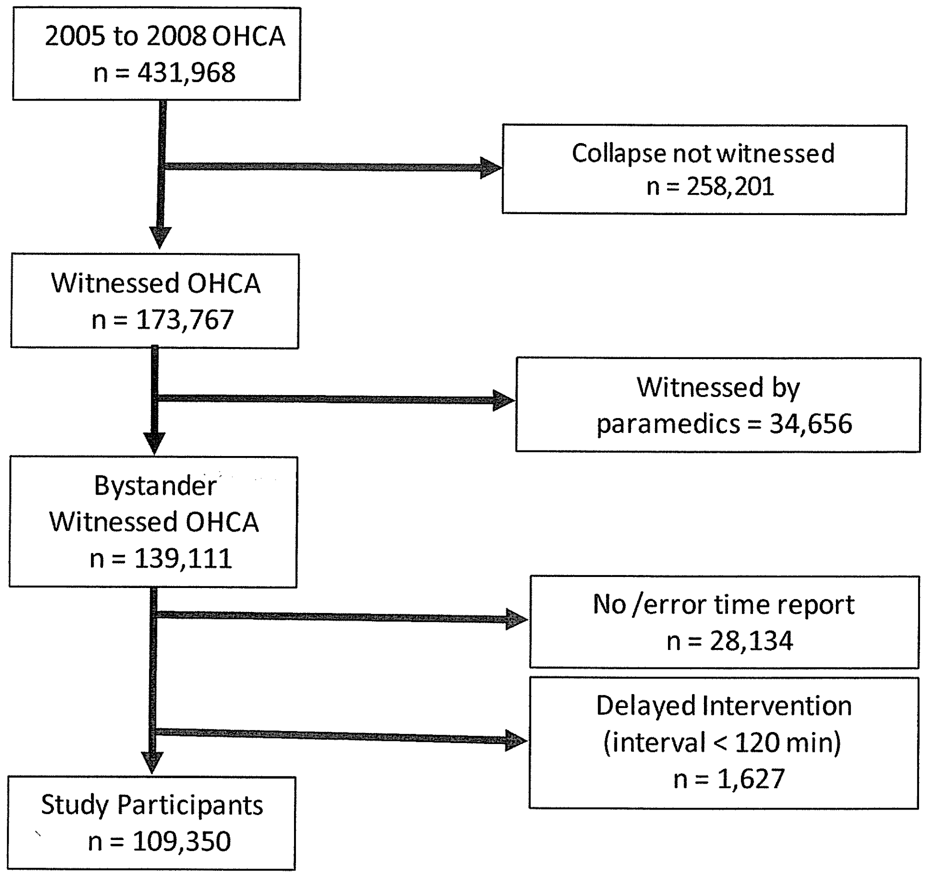

Figure 1 Selection of study participants.

as a continuous variable and included in the model as an independent variable. SPSS 16.0J (SPSS Japan Inc, Tokyo, Japan) was used for statistical analysis.

Results

Characteristics of study subjects

The characteristics of study participants are presented in Table 1. Among 109,350 study participants, 67,583 (61.8%) were male with mean age ± standard deviation (SD) of 72.9 ± 18.2 years old. The presumed etiology in 59,693 (54.6%) cases was cardiac origin, and non-cardiac origin in 49,657 (45.4%) cases. Bystander CPR was given in 49,122 (44.9%) cases, and 914 (0.8%) were treated by public AED. The mean collapse-to-EMS CPR interval (± SD) was 14.5 (± 9.3) minutes. The mean collapse-to-EMS CPR interval exhibited a positively skewed distribution (Figure 2). The other outcomes stratified by intervention or participant characteristics are presented in Table 2.

Main results

Among cases where collapse-to-EMS CPR intervals (x) were between 3 and 30 minutes, the logarithmic regression equation for the relationship to one-month survival (y) was $y = -0.059 \ln(x) + 0.21$ ($R^2 = 0.98$), and that with neurologically favorable one-month survival (y) was $y = -0.041 \ln(x) + 0.13$ ($R^2 = 0.95$; Figure 3).

The results of the logistic regression analyses for one-month survival and neurologically favorable one-month survival revealed that the 2007 to 2008 period, male, cardiac origin, younger age, bystander CPR, public AED usage were all associated with higher rates of one-month survival and neurologically favorable one-month survival. After adjusting for the potential confounders presented above, the collapse-to-EMS CPR interval (minutes) was associated with lower survival (odds ratio (OR); 0.93, 95% CI (confidence interval); 0.93 to 0.93 (0.925 to 0.933)) and neurologically favorable one-month survival (OR; 0.89, 95% CI; 0.89 to 0.90; Table 3).

Discussion

The present study was an analysis of data from 109,350 patients whose cardiac arrest onset was witnessed. Among cases where the collapse-to-EMS CPR interval was between 3 and 30 minutes, the duration of the

Table 1 Characteristics of study participants

Variable	No.(%) of patients	
Survey year		
2005	24,955	(22.8)
2006	26,861	(24.6)
2007	28,126	(25.7)
2008	29,408	(26.9)
Male sex	67,583	(61.8)
Age, mean (SD), year	72.9	(18.2)
Etiology		
Presumed cardiac	59,693	(54.6)
Non-cardiac	49,657	(45.4)
cerebrovascular disease	*5,331*	*(10.7)*
respiratory diseases	*7,041*	*(14.2)*
cancer	*3,982*	*(8.0)*
exogenous causes	*20,320*	*(40.9)*
other non-cardiac origin	*12,983*	*(26.1)*
non-cardiac origin, subtotal	*49,657*	*(100.0)*
Bystander CPR	49,122	(44.9)
family	*27,997*	*(57.0)*
friend	*2,202*	*(4.5)*
colleague	*1,610*	*(3.3)*
passerby	*1,767*	*(3.6)*
others	*15,546*	*(31.6)*
type of bystander subtotal	*49,122*	*(100.0)*
Public AED	914	(0.8)
Intubation	52,123	(47.7)
Drug	6,410	(5.9)
Interval, mean (SD), minutes		
collapse-to-call interval	5.4	(8.1)
collapse-to-arrival	12.8	(9.0)
collapse-to-EMS contact	14.0	(9.2)
collapse-to-EMS CPR	14.5	(9.3)
collapse-to-EMS defibrillation	16.7	(10.1)
collapse-to-hospital transfer	36.7	(14.5)

collapse-to-EMS CPR interval was fitted to a logarithmic regression equation to examine its relationship with one-month survival and neurologically favorable one-month survival. After adjusting for potential confounders in a logistic regression analysis, we found that longer collapse-to-EMS CPR intervals were associated with lower one-month survival and neurologically favorable one-month survival.

Consistent with previous studies, the rate of one-month survival decreased sharply and gradually leveled off with increasing collapse-to-EMS CPR intervals. The nature of the relationship was the same after adjusting potential confounders including survey year, sex, age, etiology, bystander CPR and public AED. However, in previous studies, 20% to 34.1% [13-15] of cases were of non-cardiac origin, whereas the proportion of non-cardiac origin cases in the present study was 45.4%. This difference in etiological proportion should be considered when interpreting the results. The rate of survival following out-of-hospital cardiac arrest of non-cardiac origin has been previously reported to be lower than the survival rate in cases of cardiac arrest of cardiac origin [16]. Most previous studies limited the sample to cardiac origin only, De Mario *et al.* [17] analyzed all cardiac cases of arrest meeting the Utstein Criteria (9,273 patients) between 1991 and 1997, and confirmed that survival exhibited an exponential relationship with time. As our study has a much larger sample, our results provide additional evidence confirming the shape of the survival curve.

The shape of this survival curve suggests two ways to improve the survival of OHCA patients; shortening the collapse-to-CPR interval, or, alternatively, shifting the curve upward by improving the quality of resuscitation attempt.

To quicken response times, potential bystanders could be better educated to activate EMS as soon as possible. In addition, the ambulance system response could be streamlined, strengthening the "chain of survival" [18] concept and reinforcing the importance of an appropriate sequence of pre-hospital care. In Japan, the Fire and Disaster Management Agency reported that the mean response time (call-to-arrival interval) was 7.0 minutes in 2007, increasing from 6.1 minutes in 1997 [19]. In the same period, the number of traffic accidents and accompanying emergency transfers decreased. However, there has been a steady increase in the number of requests for ambulance services. The number of ambulance requests in Japan reached almost 5.3 million per year (almost a 50% increase in 10 years), but not all calls were genuine emergency cases. It was found that 51.7% of cases eventually did not require hospitalization. For fully utilizing limited resources in the most appropriate manner, the public should be better educated to call ambulance service only in case of an emergency. In addition, assessment and triage systems should be established at emergency control centers. These changes should be accompanied by improved transportation systems, including methods for determining the hospital to which the transfer should be made as rapidly as possible.

Starting CPR as early as possible would shift the survival curve left. In addition, the survival curve could be shifted upward by improving the quality of resuscitation

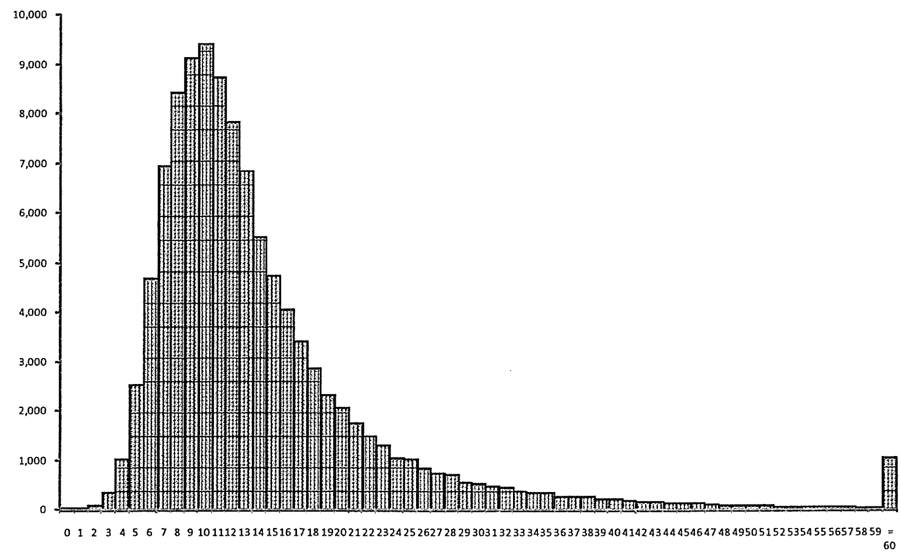

Figure 2 Distribution of collapse-to-EMS CPR intervals (minutes). The distribution of patients by collapse-to-EMS CPR interval (minutes) was presented for 109,350 cases. Cases where the interval was equal or longer than 60 minutes were categorized into one group.

Table 2 One-month survival and neurologically favorable one-month survival

	One-month survival No. (%) of patients		Neurologically favorable one-month survival No. (%) of patients	
Survey Year				
2005 to 2006	3,758	(7.3)	1,545	(3.0)
2007 to 2008	5,269	(9.2)	2,803	(4.9)
Sex				
Male	6,087	(9.0)	3,134	(4.6)
Female	2,940	(7.0)	1,214	(2.9)
Age (year)				
<40	940	(13.3)	593	(8.4)
40 to 49	569	(12.1)	388	(8.3)
50 to 59	1,304	(12.7)	779	(7.6)
60 to 69	1,846	(11.1)	966	(5.8)
70 to 79	2,116	(7.6)	866	(3.1)
80 to 89	1,760	(5.9)	606	(2.0)
≥90	492	(3.8)	150	(1.2)
Etiology				
Non-cardiac	3,557	(7.2)	1,212	(2.4)
Presumed cardiac	5,470	(9.2)	3,136	(5.3)
Bystander CPR				
no bystander CPR	3,974	(6.6)	1,496	(2.5)
bystander CPR	5,053	(10.3)	2,852	(5.8)
Public defibrillation				
no public AED	8,414	(8.0)	3,927	(3.7)
public AED	343	(37.5)	296	(32.4)
Total	9,027	(8.3)	4,348	(4.0)

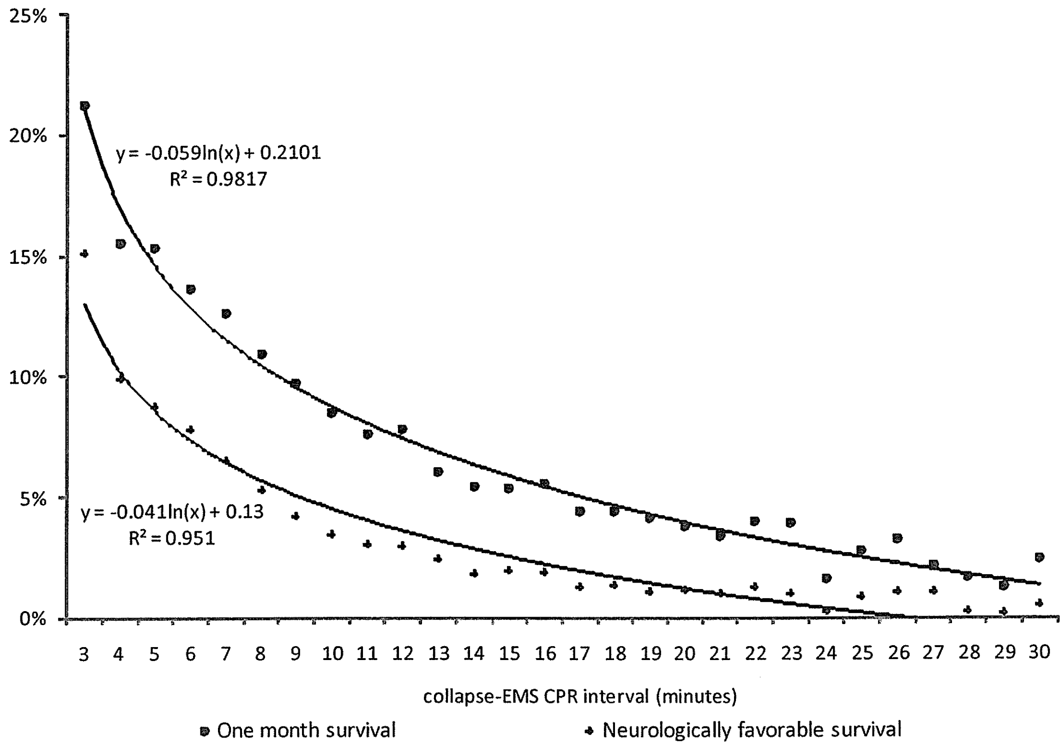

Figure 3 Collapse-EMS CPR interval and outcomes. The relationship between collapse-to-EMS CPR interval and one-month survival (dots) and neurologically favorable one-month survival (crosses) are presented for all cases where collapse-to-EMS CPR interval was between 3 to 30 minutes. Logarithmic regression equations for outcome (y) by collapse-to-EMS CPR interval (x) with R^2 were calculated and plotted in the graph.

attempts. High-quality CPR is a cornerstone of a system of care that can optimize outcomes [20]. It has been found that improved CPR quality administered by bystanders [21] and ACLS [22] are correlated with survival rates [23]. Various educational courses including mass CPR training and targeted CPR training for family members of patients suffering from cardiovascular diseases are currently available in Japan. Since 1995, new driver's license applicants have been required to take three hours of basic life support (BLS) training at driving schools [24], an attempt to expand BLS knowledge to the general public. Since 2003, Emergency Medical Technicians, (the highest level of ambulance personnel), have been authorized to use AED without online medical control. In the same year, orotracheal intubation was included as a sanctioned method of clearing airways by Emergency Life-Saving Technicians (ELSTs) with 262 hours of additional national standard training. Adrenaline administration by ELSTs with 220 hours of training became legal in 2006 [25]. These combined efforts to improve all four chains of survival could shift the survival curve upward, substantially improving the rate of survival in cases of OHCA.

Several limitations of this study should be considered. First, the time of collapse was based on interviews with laypersons. The witnesses might have been unable to accurately report the time of collapse. Unless there is an exceptional situation (for example, an OHCA event that is videotaped in a casino [26]), obtaining accurate collapse time is problematic, especially based on interviews with laypeople in emergency situations. Isaacs and colleagues [27] reported that layperson estimation of the time and actual measured intervals in cardiac arrest situations were not strongly correlated. As such, the quality of the time interval data represents a serious limitation of the current study. However, this limitation was minimized in the current analysis by excluding values that appeared to be due to error. In addition, the duration of the collapse-to-EMS CPR interval exhibited a positively skewed distribution, suggesting that the remaining potential errors in a set of 109,350 cases did not substantially affect the overall conclusions of this study.

A second limitation is that our data were obtained in Japan only. As such, the emergency system and demography might affect the results as unpredicted confounding factors. In our study, more than half of the study

Table 3 Results of regression analysis

	One-month survival OR (95%)	Neurologically favorable one-month survival OR (95%)
Survey year		
2005 to 2006	Reference	Reference
2007 to 2008	1.16 (1.11 to 1.22)	1.41 (1.31 to 1.51)
Sex		
Male	Reference	Reference
Female	0.91 (0.87 to 0.96)	0.83 (0.77 to 0.90)
Age (year)		
<40	Reference	Reference
40 to 49	0.89 (0.79 to 1.01)	0.91 (0.78 to 1.07)
50 to 59	0.95 (0.86 to 1.05)	0.82 (0.72 to 0.94)
60 to 69	0.83 (0.75 to 0.92)	0.63 (0.56 to 0.72)
70 to 79	0.56 (0.52 to 0.62)	0.34 (0.30 to 0.39)
80 to 89	0.41 (0.37 to 0.45)	0.18 (0.15 to 0.20)
≥90	0.24 (0.21 to 0.27)	0.09 (0.07 to 0.11)
Etiology		
Non-cardiac origin	Reference	Reference
Cardiac origin	1.29 (1.23 to 1.35)	2.61 (2.41 to 2.84)
Bystander CPR		
No bystander CPR	Reference	Reference
Bystander CPR	1.49 (1.40 to 1.54)	1.95 (1.81 to 2.09)
Public defibrillation		
No public AED	Reference	Reference
Public AED	2.91 (2.44 to 3.47)	3.52 (2.88 to 4.31)
Collapse-EMS CPR interval (minutes)	0.93 (0.93 to 0.93)	0.89 (0.89 to 0.90)

CI, confidence interval; OR, odds ratio.

participants were 70 years old or older. It is known that the survival rate following CPR in elderly patients is lower than for younger people [28,29]. Although age factors were adjusted for in our logistic regression model, the results of this study may be problematic when applied to other countries with younger population compositions. However, our results will be useful for informing health policy makers in many developed countries with similar emergency systems and demographic profiles.

Third, we did not have data on the hospitals to which patients were transferred, meaning that the data did not reflect the quality of the hospital at which treatment was received. A recent study revealed that treatment at critical care medical centers was associated with better outcomes in cardio pulmonary arrest patients [30]. This may have also acted as a potential confounder.

Despite these limitations, our data provide a valuable investigation of almost all cases of OHCA subjects in Japan over a four-year period, constituting the largest-scale study of this issue to date.

Conclusions

Our analysis of one of the largest samples of OHCA patients, including cases of cardiac and non-cardiac origin, revealed that shorter collapse-to-EMS CPR intervals were associated with better outcomes. Both one-month survival and neurologically favorable one-month survival curves against collapse-to-EMS CPR interval indicated that improving OHCA outcomes requires interventions to move the curve leftward (by shortening the response time) and upward (by improving the quality of CPR). Improving the emergency medical system, and the speed and quality of CPR in cases of OHCA are the key methods for improving the outcomes of OHCA.

Key messages

- A nationwide HCA patient registry in Japan confirmed that shorter collapse-to-EMS CPR intervals were associated with better outcomes
- The logarithmic regression equation for the relationship with one-month survival was $y = -0.059 \ln(x) +$

0.21, and that for the relationship with neurologically favorable one-month survival was y = -0.041 ln(x) + 0.13

- The logistic regression analysis after adjusting for potential confounders showed that longer collapse-to-EMS CPR intervals were associated with lower rates of one-month survival (OR 0.93, 95% CI: 0.93 to 0.93) and neurologically favorable one-month survival (OR 0.89, 95% CI 0.89 to 0.90)
- Improving the emergency medical system, and the speed and quality of CPR in cases of OHCA are key measures for improving the outcomes of OHCA

Abbreviations

ACLS: advanced cardiac life support; AED: automated external defibrillator; BLS: basic life support; CI: confidence interval; CPC: cerebral performance category; CPR: cardiopulmonary resuscitation; ELSTs: emergency life-saving technicians; EMS: emergency medical service; OHCA: out-of-hospital cardiac arrest; ROSC: return of spontaneous circulation; SD: standard deviation; Vf: ventricular fibrillation; VT: entricular tachycardia.

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Authors' contributions

SK and TI jointly conceived and designed this study. TO conducted data cleaning. SK, TO, ST, MA, HY, HH, SM and TI jointly analyzed and interpreted the data. SK drafted the manuscript. All of the authors jointly reviewed and discussed the manuscript and revised it critically for important intellectual content and approved the draft for submission.

Competing interests

The authors declare that they have no competing interests.

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CLINICAL RESEARCH STUDY

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The Effects of Sex on Out-of-Hospital Cardiac Arrest Outcomes

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ABSTRACT

OBJECTIVE: We examined the effects of sex on out-of-hospital cardiac arrest outcomes. There is evidence that women are more likely to survive cardiac arrest than men. However, few large studies have examined these sex differences in detail. It is unknown whether the female survival advantage is age-specific or whether sex affects neurologic outcomes after cardiac arrest events.

METHODS: Data were analyzed from a nationwide population-based out-of-hospital cardiac arrest database (between January 2005 and December 2007) involving 318,123 patients (male: 188,357, female: 129,766) to assess the effects of sex on out-of-hospital cardiac arrest outcomes in Japan. We selected 276,590 patients aged 20 to 89 years with out-of-hospital cardiac arrest and compared the frequencies of initial cardiac rhythms, 1-month survival rates, and favorable neurologic outcome rates between sexes.

RESULTS: The incidence of out-of-hospital cardiac arrest was higher in men than in women (men: 0.12%; women: 0.07%). Men were witnessed more often while out-of-hospital cardiac arrest was occurring (men: 42.1% and women: 36.9%), typically presented with initial ventricular fibrillation/ventricular tachycardia rhythms, and had a higher 1-month survival rate overall after out-of-hospital cardiac arrest events (men: 5.2% and women: 4.3%). However, the rate of survival with a favorable neurologic outcome for women aged 30 to 49 years was significantly higher than that for men within the same age range. Among patients initially presenting with ventricular fibrillation/ventricular tachycardia, the rate of survival with favorable neurologic outcome was higher for women than men in the group aged 40 to 59 years.

CONCLUSION: Our results suggest that men have a higher 1-month survival rate after out-of-hospital cardiac arrest because of a higher frequency of ventricular fibrillation/ventricular tachycardia presentation compared with women. Although patients of both sexes with out-of-hospital cardiac arrest initially presenting with ventricular fibrillation/ventricular tachycardia exhibited similar overall survival rates, the rate of survival with favorable neurologic outcome was significantly higher for women than men in the group aged 40 to 59 years.
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KEYWORDS: Cardiopulmonary resuscitation; Out-of-hospital cardiac arrest; Sex; Survival rate; Ventricular fibrillation

Cardiopulmonary arrest is associated with a high mortality rate, even when patients receive appropriate treatment in accord with the "chain of survival" concept, consisting of rapid access to the emergency medical service, cardiopulmonary resuscitation, and defibrillation.[1-5] A meta-analysis reported a 6.7% overall survival rate to hospital discharge for patients with out-of-hospital cardiac arrest.[6] The out-

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