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Association between neurological outcomes and prehospital time in patients with out-of-hospital cardiopulmonary arrest

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Abstract

Introduction: Out-of-hospital cardiac arrest (OHCA) remains an important health care issue. Considering the importance of such a time course after cardiac arrest, detailed evaluation of the prehospital time (i.e., time from EMS contact to a patient to hospital arrival) is essential to improve the mortality and neurologic outcome of OHCA. In this study, we aimed to evaluate the impact of prehospital time on neurological outcomes in patients with OHCA.

Methods: This retrospective observational study included adult non-traumatic OHCA patients who were transported to 2 emergency centers in Tokyo from January 2015 to December 2020. The following data were obtained retrospectively from medical records.

Results: Of the 3120 OHCA patients who were transported during the study period, 2215 patients were evaluated via the inclusion and exclusion criteria. Sixty-nine patients were alive at hospital discharge with a good neurological outcome (i.e., CPC 1 or 2). The multivariate logistic regression model showed that prehospital time (time from EMS contact to hospital arrival) was an independent predictor for hospital discharge with good neurological outcome, in addition to age, bystander CPR, initial rhythm, and cause of cardiac arrest. The GAM plot showed that the adjusted odds ratio of prehospital time for the good neurological outcome was decreased linearly according to time, and the threshold was approximately 30 min.

Conclusion: The threshold of allowable prehospital time, including field activity and transport, for OHCA patients might be 30 min at least in a Japanese urban setting.

KEYWORDS
cardiopulmonary resuscitation, emergency medical services, out-of-hospital cardiac arrest, prehospital time, transportation of patient

INTRODUCTION

Out-of-hospital cardiac arrest (OHCA) remains an important health care issue, with more than 347,000 adult OHCA cases occur each year in the United States.[1] In Tokyo, approximately 12,300 patients out of 13 million residents are transported to emergency departments annually suffering OHCA. Although one of the best medical system has been established in Tokyo, the one-month survival rate for patients with witnessed OHCA is still low at <10%.

The ultimate outcome of OHCA is neurological function. Several factors indicate a favorable neurological outcome in OHCA patients including: non-traumatic cause, presence of witnesses, presence of bystanders, shockable rhythm, high quality of cardiopulmonary resuscitation (CPR), and short time to emergency medical system (EMS) arrival.[2–8]

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Previous studies suggested a cut-off point of 20–30 min for CPR duration to achieve a good neurological function.[9–11] A recent Japanese study also concluded that the likelihood of good neurological outcome drops sharply after 20 min from the start of CPR.[12] In that study, the 90th and 99th percentiles of CPR duration in patients with good neurologic outcomes were 32.8 and 58.9 min, respectively.

Considering the importance of such a time course after cardiac arrest, a detailed evaluation of the prehospital time (i.e., time from EMS contact to a patient to hospital arrival) is essential to improve the mortality and neurologic outcome of OHCA. Japanese EMS are allowed to provide some resuscitative intervention at the scene for patients with cardiac arrest; therefore, prehospital time can partially be controlled by choosing interventions provided at the scene. However, studies on the prehospital time after an EMS contact to hospital arrival are limited. In this study, we aimed to evaluate the impact of prehospital time on neurological outcomes in patients with OHCA.

METHODS

Study design and setting

This retrospective observational study's inclusion criteria were adult non-traumatic OHCA patients who were transported to 2 emergency centers in Tokyo from January 2015 to December 2020. The emergency medical center is located in a 450-bed university hospital and handles 1800–2000 critical patient transports by ambulance and 500–550 CPA transports per year. Another emergency medical center is located in a 813-bed university hospital and handles 900–1200 critical patient transports by ambulance and 110–130 CPA transports per year.

The association between cerebral performance category (CPC) at hospital discharge and the time from EMS contact to hospital arrival was evaluated.

In Tokyo, the available EMS team, consisting of 3 ambulance crew, dispatch from the nearest fire station 24/7. According to the data of the Tokyo Fire Department in 2019, the average time required for from dispatch to arrival at the scene was approximately 6.5 min. If the ambulance crew decide that the patient is in cardiac arrest, they make a request for acceptance to the emergency medical center via the fire department by telephone. The fire department will make a sequential request for acceptance from the nearest emergency medical center, and the EMS team will transport the patient to the emergency medical center that has agreed to accept the patient. At least one of 3 ambulance crew is highly trained and allowed to insert intravenous catheterization, administer adrenaline, and use advanced airway management devices for OHCA patients, in addition to defibrillation by automated external defibrillator (AED), under the direction of an online-control physician over the phone. CPR is performed in accordance with the Japanese guidelines for cardiopulmonary resuscitation.[13] In addition, in Japan, the termination of resuscitation by the EMS team is not allowed in the prehospital setting. Therefore, almost all OHCA patients treated by EMS are transported to the hospital except in cases with systemic rigor mortis, neck and torso amputation, incineration, decomposition, etc.[13,14]

Patient selection

Consecutive non-traumatic OHCA patients who were transported to 2 emergency centers in Tokyo between January 2015 and December 2020 were included in the present study. Patients who were aged <18 years were excluded from the analysis.

Data collection

The following data were obtained retrospectively from medical records: age, sex, cause of cardiac arrest, presence or absence of bystander witness, presence or absence of bystander initiated CPR, first cardiac rhythm at EMS team contact, presence or absence of AED use, prehospital time course (EMS contact, EMS departure from the scene, EMS arrival at hospital, and total prehospital duration of resuscitation), prehospital procedures (e.g., laryngeal tube suction insertion, tracheal intubation, intravenous catheterization, epinephrine administration), cause of cardiac arrest, Return Of Spontaneous Circulation (ROSC), and cerebral performance category (CPC) at hospital discharge.

Outcomes and definition

The outcome of the study was survival at discharge with good neurological outcome defined by CPC 1 or 2.[15,16] Cause of cardiac was estimated based on clinical history, result of blood test, electrocardiogram findings after the recovery of spontaneous circulation, and computed tomography findings. We defined prehospital time as the time from the EMS team contacting the patient to the patient arriving at the hospital (Table S1).

Statistical analysis

Univariate and multivariate logistic regression models were performed to assess the association between prehospital time (i.e., time from EMS contact to a patient to hospital arrival) and the CPC at hospital discharge. Age, sex, presence or absence of witness, presence or absence of bystander CPR, location that cardiac arrest occurred (public space or facility or home), initial rhythm (shockable or not), and cause of cardiac arrest were incorporated into the multivariate logistic regression model as the explanatory variables based on subject matter knowledge. To visualize the association between prehospital time and good neurological outcome, a non-linear generalized additive model was used in which the variables used for the logistic regression analysis were adjusted (Table S2).

Data were described using median and interquartile range (IQR) for continuous variables and number and percentage (%) for categorical variables. Two-sided $p < 0.05$ was regarded to be statistically significant. All analyses were performed with R statistical software version 3.5.3 (R Foundation for Statistical Computing, Vienna, Austria).

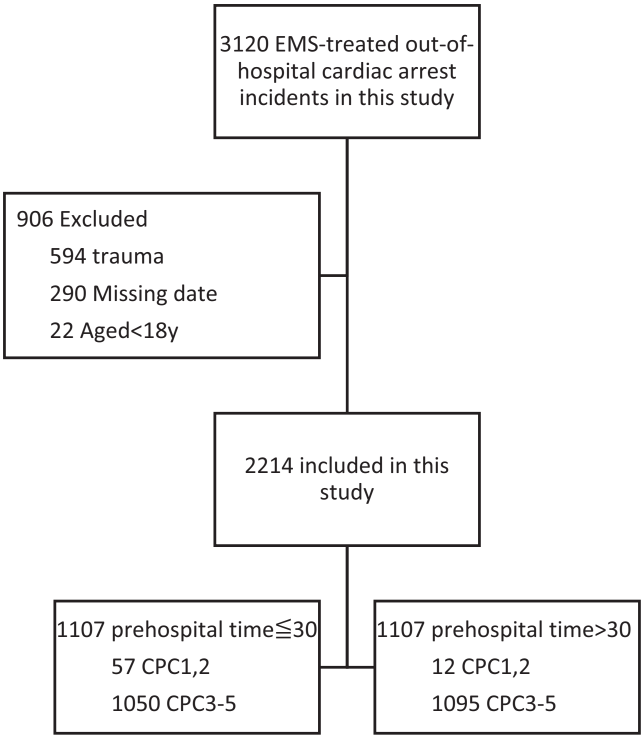

FIGURE 1 Patient flow.

RESULTS

Of the 3120 OHCA patients who were transported during the study period, 2215 patients were evaluated via the inclusion and exclusion criteria. Exclusion criteria were death by trauma, missing date, and patients under 18 years of age (Figure 1). Sixty-nine patients were alive at hospital discharge with a good neurological outcome (i.e., CPC 1 or 2). The histogram of prehospital time is shown in Figure 2.

In univariate analysis, the median time from EMS contact to EMS departure (quartiles) was 14 min (11.5–18) for the patients with CPC 1 or 2, which was significantly less than the median in the patients with CPC >2 (18 min,[15–22] $p < 0.001$). Also, the median time from EMS departure to hospital arrival was significantly shorter in patients with the CPC of 1 or 2 groups than in patients with CPC >2 (7 min (5–10.5) and 12 min,[8–17] $p < 0.001$) (Table 1).

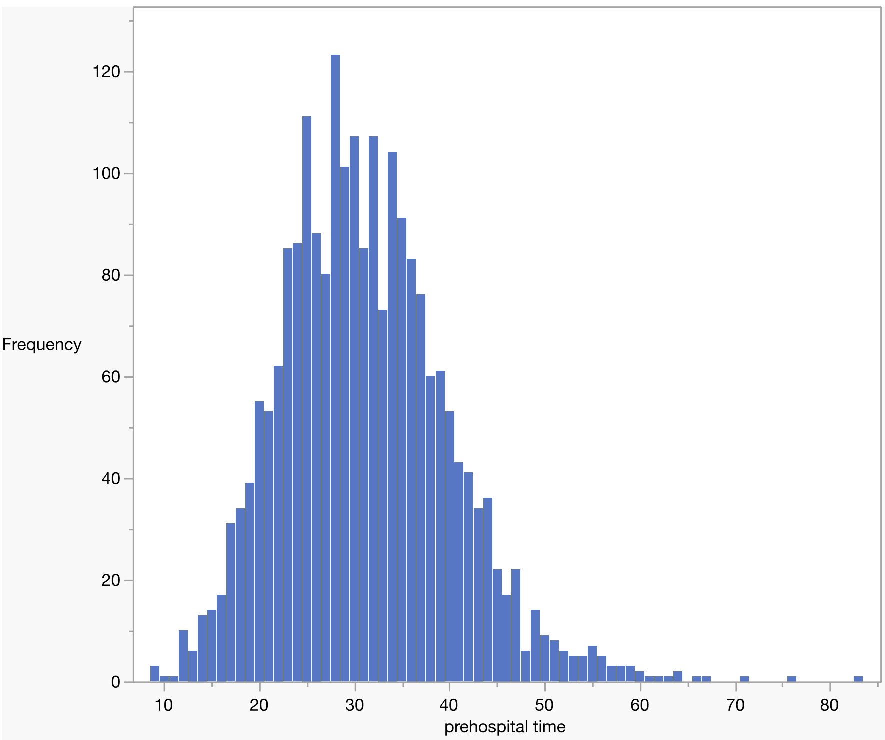

FIGURE 2 The histogram of prehospital time.

TABLE 1 Baseline characteristics of OHCA patients.

	CPC1, 2	CPC3, 4, 5	*p*-value
Age, years, median (IQR)	57 [51–69]	75 [63–83]	<0.001
Sex, *n* (%)			0.001
Male	54 (78.2)	1260 (58.7)	
Female	15 (11.8)	886 (41.3)	
Witness, *n* (%)			<0.001
Not witness	18 (26.5)	1136 (51.3)	
Bystander witness	50 (73.5)	1010 (45.6)	
Bystander CPR, *n* (%)			<0.001
No bystander CPR	20 (29.4)	1367 (63.7)	
Bystander CPR	48 (70.5)	778 (36.3)	
Location of arrest, *n* (%)			<0.001
Public space	51 (73.9)	558 (26.0)	
Home	15 (21.7)	1418 (66.1)	
Facility	3 (4.3)	170 (7.9)	
Civilian AED, *n* (%)			<0.001
Not available	42 (60.9)	2090 (97.4)	
Available	27 (39.1)	55 (2.6)	
EMS initial ECG, *n* (%)			<0.001
Asystole	3 (5.6)	1282 (60.2)	
PEA	14 (25.9)	645 (30.3)	
VF/pulseless VT	37 (68.5)	201 (9.4)	
Time from EMS contact to EMS departure, minutes, median (IQR)	14 [11.5–18]	18 [15–22]	<0.001
Time from EMS departure to hospital arrival, minutes, median (IQR)	7 [5–10.5]	12 [8–17]	<0.001
CPR duration, minutes, median (IQR)	11 [3–28]	52 [40–66]	<0.001
EMS treatment, *n* (%)			<0.001
CPR only	51 (75.0)	822 (38.4)	
CPR with airway management such as intubation and LTS	4 (5.9)	811 (37.8)	
CPR with airway management + peripheral securement	5 (7.4)	128 (6.0)	
CPR with airway management + peripheral securement + drug administration	8 (11.8)	382 (17.8)	
Causative disease, *n* (%)			<0.001
Cardiac disease (suspected)	59 (85.5)	435 (20.3)	
Cerebral nerve disease	0 (0)	121 (5.6)	
Respiratory disease	2 (2.9)	126 (5.9)	
Metabolic disease (renal disease, liver disease, diabetes, etc.)	1 (1.4)	50 (2.3)	
Gastrointestinal disease (gastrointestinal bleeding, etc.)	1 (1.4)	41 (1.9)	
Macrovascular disease	0 (0)	195 (9.1)	
Cancer	0 (0)	16 (0.7)	
Choking	2 (2.9)	160 (7.5)	
Unknown	4 (5.8)	1001 (46.6)	
ECPR, *n* (%)			0.535
Not available	61 (88.4)	1940 (90.4)	
Available	8 (11.6)	206 (9.6)	

Abbreviations: AED, Automated External Defibrillator; CPR, cardiopulmonary resuscitation; ECG, Electrocardiogram; ECPR, extracorporeal cardiopulmonary resuscitation; EMS, Emergency Medical Services; IQR, Interquartile range; VF/VT, ventricular fibrillation/tachycardia.

The multivariate logistic regression model showed that prehospital time was an independent predictors for hospital discharge with good neurological outcome, in addition to age, bystander CPR, EMS initial rhythm PEA, or VF (Table 2).

The GAM plot (Figure 3) showed that the adjusted odds ratio of prehospital time for the good neurological outcome was decreased linearly according to time, and the threshold was approximately 30 min.

DISCUSSION

In the present study, we retrospectively examined non-traumatic OHCA patients in urban settings and found that prehospital time was significantly associated with neurological outcome. The threshold of prehospital time for good neurological outcome was approximately 30 min. Previous studies have shown that a shorter EMS on-scene time is advantageous with respect to patient survival.[21] However, to our knowledge, the effect of total prehospital time, (i.e., sum of on-scene time and transport time to the hospital) on the neurological prognosis of patients has not yet been

TABLE 2 Logistic regression analysis with CPC1, 2.

	Estimate std.	Error z value	Pr (>|z|)	Adjusted odds ratio, (95%CI)	p-value
Age	−0.05	0.01 −4.10	<0.001	0.54 (0.93 to 0.96)	<0.001
Woman	0.22	0.37 0.60	0.547	1.25 (0.60 to 2.59)	0.547
Witness	−0.17	0.37 −0.45	0.652	0.85 (0.41 to 1.75)	0.652
Bystander CPR	1.02	0.36 2.82	0.005	2.77 (1.36 to 5.64)	0.005
home	−0.46	0.38 −1.23	0.2200	0.63 (0.30 to 1.32)	0.220
Facility	−1.29	1.07 −1.21	0.226	0.28 (0.03 to 2.23)	0.227
EMS initial ECG PEA	2.16	0.68 3.17	0.002	8.67 (2.28 to 32.94)	0.002
EMS initial ECG VF	3.29	0.68 4.85	<0.001	26.92 (7.11 to 101.88)	<0.001
EMS initial ECG asystol	−10.96	1.77e+04 −0.00	0.999	1.74e-05 (0.00e+00 to Inf)	0.999
Cerebralnerve disease	−17.23287	1442.36 −0.01	0.990	3.28e-08 (0.00e+00 to Inf)	0.990
Respiratory disease	−0.53	0.81 −0.66	0.512	0.59 (0.12 to 2.86)	0.512
Metabolic disease	−0.82	1.10 −0.75	0.454	0.44 (0.05 to 3.78)	0.454
Gastrointestinal disease	0.40	1.11 0.36	0.721	1.49 (0.17 to 13.07)	0.721
Disease unknown	−2.73	0.75 −3.65	<0.001	0.06 (0.01 to 0.28)	<0.001
Macrovascular disease	−17.26	1118.52 −0.02	0.988	0.06 (0.01 to 0.28)	0.988
Cancer	−15.94	4015.24 −0.00	0.997	1.19e-07 (0.00e+00 to Inf)	0.997
Choking	0.50	0.83 0.61	0.543	1.65 (0.32 to 8.44)	0.546
Prehospital time	−0.10	0.03 −3.82	<0.001	−0.91 (0.86 to 0.95)	<0.001

studied. The threshold of 30 min suggested in this study may affect the future field activity of EMS teams as the reference time.

While it is difficult to reduce the times from EMS dispatch to EMS contact and from EMS departure to hospital arrival since it was determined by the distances, it would be possible to reduce the time of field activity by the EMS team. Prior studies reported that the most important time period of CPR was the first 10–15 min in OHCA patients; the probability of good neurologic outcome decreased after 15 min.[16,17] A recent Japanese study suggested that the decision of the transport from the scene should be made 10 min after the EMS contact for patients with shockable rhythm and 8 min for patients with non-shockable rhythm.[18] Another study showed that longer transport time more than 10 min was associated with worse neurological outcome in OHCA patients with shockable rhythm.[19] According to the data of the Tokyo Fire Department in 2021, the average time required for transport was approximately 10.5 min, and the median transport time in this study was 12 min. Considering these data and the results of the present study, EMS activity at the scene over 19 min should be avoided in OHCA patients, and this target duration should be adjusted according to the region and situation.

A meta-analysis concluded that prehospital care provided by a physician was associated with better outcomes compared to that provided by paramedics due to the higher quality of procedures.[20] Paramedics should keep on training and education for quick and precise procedures, and early transport without advanced life support at the scene should be considered in case longer time is estimated for field activity. Early arrival to a hospital enables further treatment options such as resuscitation using extracorporeal membrane oxygenation or antiarrhythmic agents, although the evidence of those advanced options has been insufficient.

The present study had several limitations. First, since this study was conducted at two emergency centers in Tokyo, generalizability of the results was limited. Second limitation, this study could not evaluate the quality of CPR at prehospital setting, which may affect patient outcomes. Also, the issue of residual confounding was inevitable due to the retrospective nature of the study. Furthermore, as the number of patients who achieved CPC 1 or 2 was limited, the number of explanatory variables might be insufficient. However, the present study evaluated more than 2000 OHCA patients and proposed a time limit for prehospital care, which has significant implications for future prehospital OHCA care. Despite these limitations, our study is the first research to describe the relationship between prehospital time with neurological prognosis among OCHA patients in the large urban area in Japan. We believe that the results of this study may lead to improvements in future prehospital treatment protocols.

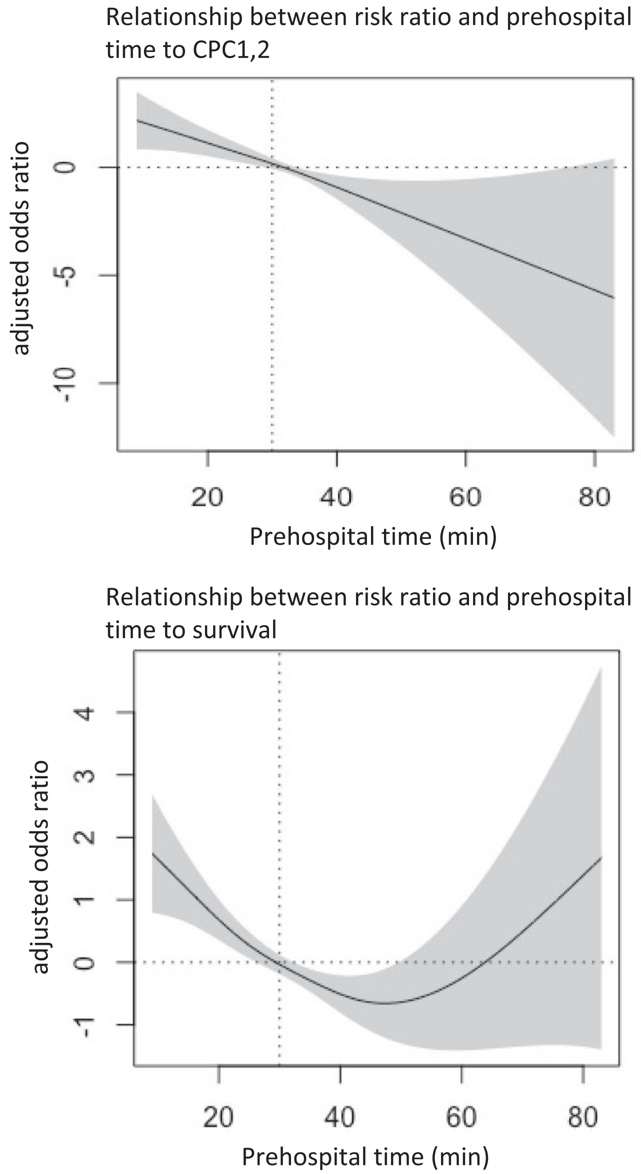

FIGURE 3 The GAM plot relationship between risk ratio and prehospital time to CPC1, 2 and relationship between risk ratio and prehospital time to survival.

CONCLUSION

The longer prehospital time from EMS contact to hospital arrival was significantly associated with worse neurological outcome of OHCA patients. The threshold of allowable prehospital time, including field activity and transport, for OHCA patients might be 30 min at least in a Japanese urban setting.

ACKNOWLEDGMENTS

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

ETHICS STATEMENT

Approval of the research protocol: This study was approved by the Institutional Review Board of Tokyo Medical and Dental University (approval number: M2023-007).
Informed consent: We applied an opt-out method on the website to obtain patient consent.
Registry and registration no. of the study/trial: N/A.
Animal studies: N/A.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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