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Clinical paper

Effect of prehospital physician presence on Out-of-Hospital cardiac arrest (OHCA) patients undergoing extracorporeal cardiopulmonary resuscitation (ECPR): A secondary analysis of the SAVE-J II study

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Abstract

Introduction: Extracorporeal cardiopulmonary resuscitation (ECPR) has been increasingly utilized for patients with out-of-hospital cardiac arrest (OHCA). However, the impact of prehospital physician presence on the outcomes of ECPR-treated OHCA patients remains uncertain. This study aimed to evaluate whether the presence of prehospital physicians improves 30-day survival and favorable neurological outcomes in this population.

Methods: This retrospective study analyzed data from the SAVE-J II study, a nationwide multicenter cohort of OHCA patients treated with ECPR in Japan. Patients were divided into two groups: prehospital physician absence and prehospital physician presence. Propensity score matching (PSM) was performed using six covariates (age, sex, witness status, presence of bystander CPR, initial heart rhythm, and location of cardiac arrest) to adjust for baseline differences. Sensitivity analyses included PSM with additional covariates (prehospital time and Low flow time), inverse probability of treatment weighting (IPTW), and varying matching ratios. Primary and secondary outcomes were 30-day survival and favorable neurological outcome (Cerebral Performance Category [CPC] 1–2), respectively.

Results: Of the 1,641 patients included, 448 were in the prehospital physician presence group and 1,193 in the prehospital physician absence group. Before PSM, 30-day survival rates were 28.2% (prehospital physician presence) vs. 25.7% (prehospital physician absence) ($p = 0.350$). After 1:1 PSM (6 covariates), the 30-day survival rate was significantly higher in the prehospital physician presence group (29.6%) compared to the prehospital physician absence group (22.7%) ($p = 0.028$), while favorable neurological outcomes showed no significant difference (prehospital physician presence: 14.5% vs. prehospital physician absence: 11.0%, $p = 0.092$). Sensitivity analyses confirmed the robustness of the findings, with 30-day survival consistently higher in the prehospital physician presence group across models, including 7-covariate PSM (31.8% vs. 23.0%, $p = 0.009$) and IPTW with 8 covariates (35.6% vs. 25.1%, $p = 0.026$). However, the 8-covariate IPTW model exhibited residual imbalance (SMD > 0.1 in four covariates). Favorable neurological outcomes did not show significant differences in any analysis.

Conclusions: Prehospital physician presence was associated with improved 30-day survival in OHCA patients undergoing ECPR. However, favorable neurological outcomes did not show significant improvement. These findings highlight the need for strategies to optimize low-flow time and explore the potential role of prehospital ECPR initiation. Further prospective studies are required to validate these findings and improve outcomes in this critical population.

Keywords: Extracorporeal cardiopulmonary resuscitation (ECPR), Out-of-hospital cardiac arrest (OHCA), Prehospital physician presence, SAVE-J II study

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Introduction

Out-of-hospital cardiac arrest (OHCA) is a life-threatening condition in which conventional cardiopulmonary resuscitation (CPR) alone may be insufficient for survival. In such cases, the introduction of extracorporeal cardiopulmonary resuscitation (ECPR) has been shown to enable the return of spontaneous circulation and, in some instances, allow for a return to normal life. Globally, the use of ECPR for OHCA patients unresponsive to standard CPR has been rapidly increasing, with evidence particularly supporting its efficacy in patients under 75 years of age with refractory ventricular fibrillation.[1] However, standardized clinical guidelines for the use of ECPR in OHCA have not yet been established, leading to significant variation in criteria and protocols across different countries and institutions.[2]

To maximize the benefits of ECPR, it is critical to minimize the time between the emergency call and the initiation of ECPR, while ensuring that high-quality CPR is consistently performed during this period. These factors significantly influence both survival rates and neurological outcomes. Emergency medical services (EMS) worldwide provide life-saving interventions for OHCA patients,[3–5] but the scope of these interventions varies by country. In Japan, EMS personnel can perform defibrillation, establish intravenous access, administer adrenaline, and perform endotracheal intubation under a physician's authorization. In contrast, in many Western countries, prehospital physicians play a vital role within EMS teams, actively intervening in severe cases, particularly cardiac arrests.[6,7] The presence of these physicians is expected to improve patient outcomes by providing advanced treatment before hospital arrival.

Some studies suggest that having prehospital physicians present during OHCA can improve both survival rates and neurological outcomes.[3,4,8–10] However, the specific benefits of having prehospital physicians present during OHCA cases where patients undergo ECPR are not yet fully understood. In some regions of Europe, efforts are underway to deploy ECPR teams and ECMO equipment directly to the prehospital scene, enabling ECPR to be initiated onsite before transporting the patient to the hospital. In Japan, although physicians are dispatched for prehospital emergencies, ECPR is rarely initiated before hospital arrival.

The potential advantages of having a physician present in the prehospital setting include administering anti-arrhythmic drugs that paramedics are not authorized to use, securing arterial and venous access necessary for ECMO initiation, and accurate endotracheal intubation. These assessments allow for early decision-making regarding the suitability of ECPR, enabling the hospital to prepare for ECMO initiation in advance, facilitating rapid deployment upon the patient's arrival.

The presence of prehospital physicians may lead to a delay in hospital arrival, potentially increasing the time before ECMO initiation and affecting patient outcomes. While some studies have shown that having prehospital physicians present is linked to better outcomes in cases of OHCA, its effectiveness in cases eligible for ECPR is still uncertain. Therefore, this study aims to evaluate the effects of prehospital physician presence on outcomes in OHCA patients who are potential candidates for ECPR Therefore, the aim of this study is to clarify the effectiveness of pre-hospital physician presence for cardiac-origin OHCA patients receiving ECPR.

Methods

Study design and data

This study is a secondary analysis of the Japanese retrospective multicenter registry "Study of Advanced Life Support for Ventricular Fibrillation by Extracorporeal Circulation II (SAVE-J II)".[11] The registry included data from 36 institutions in Japan that actively performed ECPR between 2013 and 2018. The SAVE-J II study was registered in the University Hospital Medical Information Network (UMIN) Clinical Trials Registry (registration number: UMIN000036490), and the study design and data collection methods have been previously reported.[11] This study was conducted with the approval of the Institutional Review Board (IRB) of Kagawa University (approval number: 2018-110) as well as the IRBs of all participating institutions. All institutions conducted the study in accordance with the Declaration of Helsinki (1975) and its subsequent amendments due to the retrospective nature of the study, the requirement for informed consent was waived. This secondary analysis was approved by the IRB of Toyooka Public Hospital (approval number: 222).

Study population and data collection

This study included all patients registered in the SAVE-J II registry.[11] The exclusion criteria were as follows: patients who received ECPR after admission to the intensive care unit, cases involving acute aortic syndrome/aneurysm, hypothermia, primary brain injury, infection, drug overdose, trauma, asphyxiation, drowning, or other non-cardiac causes of OHCA, patients who achieved return of spontaneous circulation (ROSC) upon hospital arrival, patients who achieved ROSC before cannulation, patients transferred from other hospitals, patients who were discharged before ECMO initiation due to ROSC after cannulation, patients with missing outcome data, and cases where the presence of a prehospital physician was unknown. To minimize the disease-selection bias, where the presence of a prehospital physician may influence the eligibility for ECPR, the above conditions were set as exclusion criteria, and the inclusion criteria for this study were restricted to cases where ECPR was performed in OHCA patients presumed to have a cardiac origin.

Collected data included patient demographics (e.g., age, sex), cardiac arrest details (e.g., location, cause, initial heart rhythm at the time of cardiac arrest), CPR-related data (e.g., presence of bystanders, use of basic life support (BLS) or external defibrillator (ED), prehospital administration of epinephrine, ROSC before hospital arrival), time to ROSC, outcome data, time intervals from emergency call to ambulance arrival and to ECMO initiation, estimated low flow time, details on the implementation of percutaneous coronary intervention (PCI) or intra-aortic balloon pumping (IABP), final OHCA diagnosis, in-hospital mortality, Cerebral Performance Category (CPC) score at discharge, and complications during ECPR.

Outcome Measures

The primary outcomes were survival rates at 30 days. The secondary outcomes were neurological outcomes at 30 days, based on the CPC. These outcomes were compared between the group of patients without a prehospital physician (prehospital physician absence group) and the group with a prehospital physician

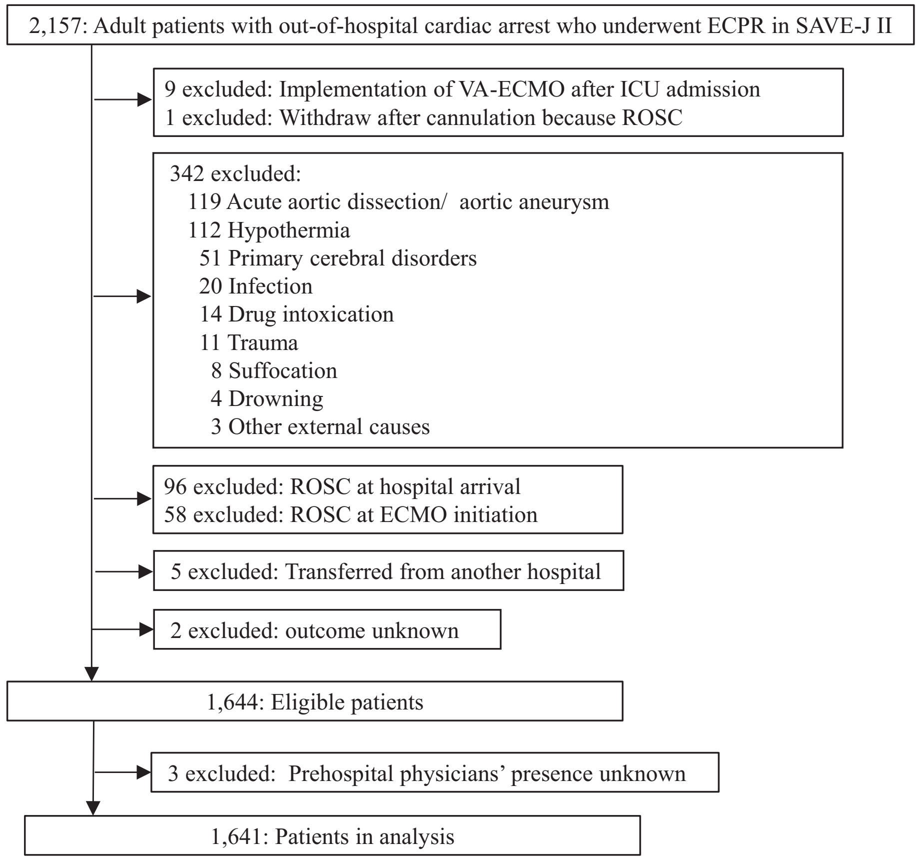

Fig. 1 – Flowchart of study enrollment. ECPR, extracorporeal cardiopulmonary resuscitation; VA-ECMO, veno-arterial extracorporeal membrane oxygenation; ICU, intensive care unit; ROSC, return of spontaneous circulation.

(prehospital physician presence group). Additionally, subgroup analyses were performed to compare the time from emergency call to hospital arrival, the time from hospital arrival to ECMO initiation, and the time from emergency call to ECMO initiation between the prehospital physician absence and prehospital physician presence groups.

Statistical analysis

The patients' characteristics and outcomes were statistically analyzed based on the presence or absence of a prehospital physician. Statistical analyses were conducted using EZR (version 1.61, Jichi Medical University, Saitama Medical Center, Japan), a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria). Continuous variables were expressed as mean ± standard deviation or median (interquartile range), and categorical variables were expressed as frequencies and percentages. Group comparisons were conducted using the *t*-test or Mann-Whitney *U* test for continuous variables, and the chi-square test or Fisher's exact test for categorical variables.

Propensity score matching (PSM) was utilized to adjust for baseline characteristics between the prehospital physician absence and prehospital physician presence groups. Propensity scores were calculated using a logistic regression model including the following six covariates: age, sex, witness status, presence of bystander CPR, initial heart rhythm, and location of cardiac arrest. 1:1 matching between the groups was performed using the nearest neighbor method without replacement, with a caliper width of 0.2 standard deviations of the logit of the propensity score. The balance of covariates before and after matching was assessed using standardized mean differences (SMD), with an SMD of less than 10% considered acceptable.

To address the potential role of additional covariates, sensitivity analyses were conducted:

PSM incorporating eight covariates, including prehospital time and Low flow time, in addition to the original six covariates.
PSM with a 1:2 matching ratio using the eight covariates.
Inverse probability of treatment weighting (IPTW) analysis using both seven covariates (excluding Low flow time) and eight covariates (including Low flow time). These sensitivity analyses were performed to ensure the robustness of the results. The SMDs were evaluated in each model to assess the balance of covariates.

To compare survival between the prehospital physician absence and prehospital physician presence groups, a log-rank test was conducted, and Kaplan-Meier survival curves were generated to illustrate differences in survival rates between the groups. In addition to the primary analysis, univariable logistic regression was performed to evaluate the association between prehospital physician presence and the primary outcome (30-day survival) in three settings: before propensity score matching (PSM), after PSM, and after inverse probability of treatment weighting (IPTW). Odds ratios (ORs)

Table 1 – Baseline characteristics of prehospital physician absence and presence groups before and after propensity score matching (PSM) (11).

	Before Propensity Score Matching				After Propensity Score Matching			
Variables	**Prehospital physician absence (n = 1193)**	**Prehospital physician presence (n = 448)**	**P values**	**SMD**	**Prehospital physician absence (n = 416)**	**Prehospital physician presence (n = 416)**	**P values**	**SMD**
Age, median [Q1-Q3] (years)	60 [49, 68]	61 [50, 69]	0.135	0.097	62 [50, 69]	61 [50, 69]	0.619	0.011
Sex Female, n (%)	176 (14.8)	78 (17.4)	0.211	0/072	67 (18.2)	61 (16.6)	0.627	0.043
Location of cardiac arrest, n (%)			0.001	0.255			0.838	0.068
Home	477 (40.1)	191 (42.7)			154 (41.8)	160 (43.5)		
Public place	225 (18.9)	67 (15.0)			55 (14.9)	56 (15.2)		
Ambulance [a]	121 (10.2)	32 (7.2)			28 (7.6)	22 (6.0)		
Others	68 (5.7)	46 (10.3)			131 (35.6)	130 (35.3)		
Initial cardiac rhythm at the scene, n (%)			0.083	0.127			0.96	0.021
Asystole	91 (7.7)	39 (8.8)			29 (7.9)	29 (7.9)		
Pulseless electrical activity	284 (24.0)	84 (18.9)			68 (18.5)	71 (19.3)		
Shockable rhythm	806 (68.2)	321 (72.3)			271 (73.6)	268 (72.8)		
Witnessed cardiac arrest, n (%)	955 (80.3)	333 (74.7)	0.015	0.136	286 (77.7)	281 (76.4)	0.726	0.032
Bystander CPR, n (%)	681 (57.7)	264 (59.9)	0.468	0.044	222 (60.3)	217 (59.0)	0.764	0.028
Prehospital intervention, n (%)								
Defibrillation	730 (61.6)	324 (73.6)	<0.001	0.26	250 (67.9)	273 (74.6)	0.056	0.147
Epinephrine administration	329 (27.9)	230 (52.3)	<0.001	0.513	129 (35.1)	185 (50.5)	<0.001	0.315
Airway management, n (%)			<0.001	0.515			<0.001	0.378
No device (bag-mask ventilation)	671 (58.9)	161 (38.9)			191 (54.1)	144 (41.1)		
Advanced airway (supraglottic airway)	392 (34.4)	163 (39.4)			133 (37.7)	135 (38.6)		
Advanced airway (endotracheal tube)	76 (6.7)	90 (21.7)			29 (8.2)	71 (20.3)		
ROSC before hospital arrival, n (%)	84 (7.1)	66 (15.1)	<0.001	0.256	22 (6.1)	47 (13.1)	0.002	0.238
Initial cardiac rhythm on hospital arrival, n (%)			0.001	0.218			0.96	0.021
Asystole	266 (22.4)	65 (14.5)			29 (7.9)	29 (7.9)		
Pulseless electrical activity	363 (30.5)	134 (30.0)			68 (18.5)	71 (19.3)		
Shockable rhythm	560 (47.1)	248 (55.5)			271 (73.6)	268 (72.8)		
Cardiac rhythm at ECMO initiation, n (%)			0.301	0.086			0.171	0.139
Asystole	190 (16.1)	64 (14.4)			67 (18.4)	54 (14.8)		
Pulseless electrical activity	386 (32.7)	134 (30.1)			109 (29.9)	98 (26.8)		
Shockable rhythm	605 (51.2)	247 (55.5)			189 (51.8)	214 (58.5)		

Variables	Before Propensity Score Matching				After Propensity Score Matching			
	Prehospital physician absence (n=1193)	Prehospital physician presence (n=448)	P values	SMD	Prehospital physician absence (n=416)	Prehospital physician presence (n=416)	P values	SMD
Time course, median [Q1-Q3] (min)								
Time from call ambulance to arrival [b]	30 [24, 36]	37 [30, 47]	<0.001	0.729	35.00 [29.00, 43.00]	35.00 [29.00, 42.00]	0.898	0.032
Time from arrival to ECMO [c]	24.5 [17.0, 35.0]	18.0 [13.0, 25.0]	<0.001	0.458	20.50 [15.00, 27.00]	18.50 [13.00, 26.00]	0.002	0.125
Time from call ambulance to ECMO [d]	56 [47, 69]	57 [48, 68]	0.183	0.037	56.00 [49.00, 68.00]	55.00 [47.00, 65.00]	0.059	0.119
Estimated low flow time [e]	54.0 [45.0, 66.0]	55.0 [46.3, 65.8]	0.188	0.044	55.00 [47.00, 64.25]	53.00 [46.00, 63.00]	0.202	0.049
ROSC after hospital arrival, n (%)			<0.001	0.268				
Before ECMO pump on	187 (20.3)	39 (10.7)			35 (12.3)	34 (11.2)	0.787	0.033
After ECMO pump on	736 (79.7)	327 (89.3)			250 (87.7)	269 (88.8)		
Emergency coronary angiography	905 (75.9)	374 (83.5)	0.001	0.189	303 (82.6)	308 (83.7)	0.755	0.03
Percutaneous coronary intervention	529 (46.4)	224 (50.1)	0.208	0.073	173 (48.5)	175 (47.7)	0.893	0.016
Intra-aortic balloon pumping	741 (62.2)	316 (70.7)	0.002	0.18	254 (69.0)	264 (71.9)	0.433	0.064
Cause of cardiac arrest, n (%)			<0.001	0.341			0.006	0.333
Acute coronary syndrome	698 (58.6)	270 (60.3)			210 (57.1)	213 (57.9)		
Arrhythmia	168 (14.1)	64 (14.3)			59 (16.0)	58 (15.8)		
Myocarditis	16 (1.3)	3 (0.7)			5 (1.4)	3 (0.8)		
Myopathy	52 (4.4)	43 (9.6)			15 (4.1)	37 (10.1)		
Other cardiac causes	72 (6.0)	31 (6.9)			26 (7.1)	24 (6.5)		
Other non-cardiac causes	36 (3.0)	11 (2.5)			11 (3.0)	9 (2.4)		
Pulmonary embolism	45 (3.8)	14 (3.1)			11 (3.0)	13 (3.5)		
Unknown	105 (8.8)	12 (2.7)			31 (8.4)	11 (3.0)		
Cause of death at hospital, n (%)			<0.001	0.267			0.228	0.184
Cardiac arrest as primary cause	767 (93.2)	283 (88.7)			245 (91.1)	223 (89.6)		
Complications	36 (4.4)	30 (9.4)			16 (5.9)	22 (8.8)		
Comorbidities	2 (0.2)	4 (1.3)			1 (0.4)	2 (0.8)		
Others	18 (2.2)	2 (0.6)			7 (2.6)	2 (0.8)		

Data are presented as medians [interquartile range: Q1-Q3] for continuous variables and as n (percentage: %) for categorical variables.

CPR, cardiopulmonary resuscitation; ECMO, extracorporeal membrane oxygenation; ROSC, return of spontaneous circulation

[a] Ambulance (Location of cardiac arrest), Patients who developed cardiac arrest after emergency medical staff (EMS) arrival with the presence of spontaneous circulation on initial EMS evaluation.

[b] Time from call ambulance to arrival (Time course), Call ambulance to arrival time is time from emergency medical services call to hospital arrival time.

[c] Time from arrival to ECMO (Time course), Arrival to ECMO time is time from hospital arrival to establishment of ECMO support.

[d] Time from call ambulance to ECMO(Time course), Call ambulance to ECMO time is time from emergency medical services call to establishment of ECMO support.

[e] Estimated low flow time (Time course), Estimated low flow time was defined as the time from cardiac arrest to the establishment of ECMO if the location of cardiac arrest was ambulance and the time from calling an ambulance to the establishment of ECMO if the location of cardiac arrest was other than ambulance.

and 95% confidence intervals (CIs) were calculated to provide a straightforward comparison of the outcomes between the prehospital physician presence and absence groups.

All statistical tests were two-sided, with a significance level set at $p < 0.05$.

Results

Of the 2,157 patients enrolled in the SAVE-J II study, 1,641 were included in the final analysis (Fig. 1). Among these, 1,193 patients were in the prehospital physician absence group, and 448 patients were in the prehospital physician presence group. The baseline characteristics of the patients in each group are presented in Table 1. The median age was 60 (49, 68) years in the prehospital physician absence group and 61 (50, 69) years in the prehospital physician presence group (p = 0.135). The proportion of females was 14.8% in the prehospital physician absence group and 17.4% in the prehospital physician presence group (p = 0.211), with no statistically significant differences observed between the groups. When comparing the overall distribution of initial rhythms (asystole, PEA, VT/VF) between the two groups, the p-value for the statistical test was 0.083, indicating no significant difference. Furthermore, when the rhythms were divided into shockable rhythms (VT/VF) and non-shockable rhythms (asystole and PEA) for individual comparison, the proportion of shockable rhythms (VT/VF) was 68.2% in the prehospital physician absence group and 72.3% in the prehospital physician presence group, with a p-value of 0.129. On the other hand, the proportion of non-shockable rhythms (asystole and PEA) was 31.8% in the prehospital physician absence group and 27.7% in the prehospital physician presence group, with no statistically significant difference (p = 0.642). The incidence of witnessed cardiac arrest (CPA) was higher in the prehospital physician absence group (80.3%) compared to the prehospital physician presence group (74.7%) (p = 0.015). The rate of bystander CPR was similar between the groups, with 57.7% in the prehospital physician absence group and 59.9% in the prehospital physician presence group (p = 0.468). Prehospital administration of epinephrine and defibrillation were significantly more frequent in the prehospital physician presence group, with rates of 52.3% and 73.6%, respectively, compared to 27.9% and 61.6% in the prehospital physician absence group (both p < 0.001). Endotracheal intubation was also performed more frequently in the prehospital physician presence group (21.7%) compared to the prehospital physician absence group (6.7%) (p < 0.001). A comparison of complications during ECPR revealed that cannula malposition and hemorrhage were significantly more frequent in the prehospital physician presence group (Table 2).

The rate of ROSC before hospital arrival was significantly higher in the prehospital physician presence group compared to the prehospital physician absence group, both before and after PSM. Before PSM, the ROSC rate was 15.1% in the prehospital physician presence group and 7.1% in the prehospital physician absence group (p < 0.001). After PSM, the prehospital physician presence group continued to show a significantly higher ROSC rate of 13.1% compared to 6.1% in the prehospital physician absence group (p = 0.002, SMD = 0.238).

Primary and secondary outcomes

The primary outcome, 30-day survival, was 28.2% in the prehospital physician presence group vs. 25.7% in the prehospital physician absence group (p = 0.350), showing no statistically significant difference. The secondary outcome, a favorable neurological outcome (CPC1-2) at 30 days, was 14.5% in the prehospital physician presence group vs. 13.4% in the prehospital physician absence group (p = 0.615), also showing no statistically significant difference (Table 3).

Propensity score matching (PSM) results

Using PSM, we adjusted for six covariates: age, sex, witness status, presence of bystander CPR, initial heart rhythm, and location of car-

Table 2 – Comparison of Complications During Extracorporeal Cardiopulmonary Resuscitation Before and After Propensity Score Matching (11).

Variables	Before Propensity Score Matching				After Propensity Score Matching			
	Prehospital physician absence (n = 1193)	Prehospital physician presence (n = 448)	P values	SMD	Prehospital physician absence (n = 416)	Prehospital physician presence (n = 416)	P values	SMD
Complications during ECPR[a], n (%)								
Cannula malposition	50 (4.2)	31 (6.9)	0.034	0.118	17 (4.0)	25 (6.0)	0.266	0.094
Unsuccessful cannulation	8 (0.7)	3 (0.7)	1	<0.001	0 (0.0)	0 (0.0)	NA	NA
Cannulation-related bleeding	175 (14.7)	58 (12.9)	0.4	0.052	52 (12.5)	50 (12.0)	0.915	0.016
Others	18 (1.5)	8 (1.8)	0.865	0.021	5 (1.2)	6 (1.4)	0.996	0.023
ECMO-related complications (including retroperitoneal hemorrhage), n (%)	15 (1.3)	6 (1.4)	1	0.015	17 (4.1)	14 (3.4)	0.696	0.043
Hemorrhage, n (%)	52 (4.5)	31 (7.0)	0.059	0.137	30 (7.2)	41 (0.9)	0.216	0.101
Ischemia, n (%)	88 (7.4)	51 (11.4)	0.013	0.107	12 (2.9)	28 (6.7)	0.017	0.192

Data are presented as n (percentage: %) for categorical variables.

ECPR, extracorporeal cardiopulmonary resuscitation; ECMO, extracorporeal membrane oxygenation

[a] Patients may have more than 1 complication

diac arrest. The 1:1 matching analysis demonstrated a significantly higher 30-day survival rate in the prehospital physician presence group compared to the prehospital physician absence group (prehospital physician presence: 29.6% vs. prehospital physician absence: 22.7%, p = 0.028). However, there was no significant difference in 30-day favorable neurological outcomes (CPC1-2) between the groups (prehospital physician presence: 14.5% vs. prehospital physician absence: 11.0%, p = 0.092). The balance of covariates was confirmed, as all standardized mean differences (SMDs) were below 0.1 (Fig. 2).

Sensitivity analyses

To assess robustness, sensitivity analyses were conducted (Table 3):

PSM using seven covariates (including prehospital time but excluding Low flow time).
PSM using eight covariates (including both prehospital time and Low flow time).
PSM using a 1:2 matching ratio.

The 30-day survival rates remained significantly higher in the prehospital physician presence group across all analyses:

•7-covariate PSM: prehospital physician presence: 31.8% vs. prehospital physician absence: 23.0% (p = 0.009).

•8-covariate PSM: prehospital physician presence: 31.6% vs. prehospital physician absence: 22.7% (p = 0.008).

•1:2 matching PSM: prehospital physician presence: 37.8% vs. prehospital physician absence: 21.8% (p < 0.001).

All covariates achieved SMDs below 0.1, indicating an adequate balance.

IPTW analyses

Inverse probability of treatment weighting (IPTW) analyses were performed with seven and eight covariates (Table 3):

•7-covariate IPTW: The 30-day survival rate was prehospital physician presence: 32.7% vs. prehospital physician absence: 24.7% (p = 0.088), with all SMDs below 0.1. Favorable neurological outcomes (CPC1-2) were prehospital physician presence: 15.8% vs. prehospital physician absence: 12.6% (p = 0.164).

•8-covariate IPTW: The 30-day survival rate was prehospital physician presence: 35.6% vs. prehospital physician absence: 25.1% (p = 0.026). However, imbalances were observed in four covariates (sex, bystander CPR, location of cardiac arrest, and Low flow time), with SMDs exceeding 0.1. Favorable neurological outcomes (CPC1-2) were prehospital physician presence: 15.0% vs. prehospital physician absence: 12.7% (p = 0.23).

Love plot results

To visually evaluate the balance of covariates, a Love Plot was generated (Fig. 2). The plot demonstrated that PSM analyses with six and seven covariates, the 1:2 matching PSM, and the 7-covariate IPTW analysis achieved SMDs below 0.1 for all covariates. In contrast, the 8-covariate IPTW analysis showed residual imbalance in four covariates, indicating potential confounding (Table 4).

Logistic regression results

Univariable logistic regression for 30-day survival consistently showed odds ratios (OR) greater than 1 across all analyses, with P-values below 0.05 (Table 5). These findings further support the

Table 3 – Outcomes Before and After PSM and IPTW: Comparison Between prehospital physician absence and prehospital physician presence groups.

Outcomes	Before PSM		PSM (6 covariates)		PSM (7 covariates)		PSM (8 covariates)		PSM (1:2 Matching)		IPTW (7 covariates)		IPTW (8 covariates)	
	Prehospital physician absence	Prehospital physician presence	Prehospital physician absence	Prehospital physician presence	Prehospital physician absence	Prehospital physician presence	Prehospital physician absence	Prehospital physician presence	Prehospital physician absence	Prehospital physician presence	Prehospital physician absence	Prehospital physician presence	Prehospital physician absence	Prehospital physician presence
30-day Survival rate (%)	25.7	28.2	22.7	29.6	23.0	31.8	22.7	31.6	21.8	37.8	24.7	32.7	25.1	35.6
P-value	0.350		0.028		0.009		0.008		<0.001		0.008		0.026	
30-day Favorable Neurological Outcome (CPC 1–2) (%)	13.4	14.5	11.0	15.2	10.8	15.8	12.3	15.5	11.3	18.4	12.6	15.8	12.7	15.0
P-value	0.615		0.092		0.061		0.246		0.005		0.164		0.375	

This table presents the outcomes of 30-day survival and 30-day favorable neurological outcome (CPC 1–2) for the prehospital physician absence and prehospital physician presence groups. Comparisons are presented for the dataset before propensity score matching (PSM), after PSM using 6 covariates (age, sex, witness status, presence of bystander CPR, initial heart rhythm, and location of cardiac arrest), PSM with 7 covariates (including prehospital time), PSM with 8 covariates (including prehospital time and Low flow time), and inverse probability of treatment weighting (IPTW) models with 7 and 8 covariates. Proportions for each outcome and their corresponding P-values are provided.

Data are presented as n (percentage: %) for outcomes.

CPC, cerebral performance category; PSM, propensity score matching; IPTW, inverse probability weighting.

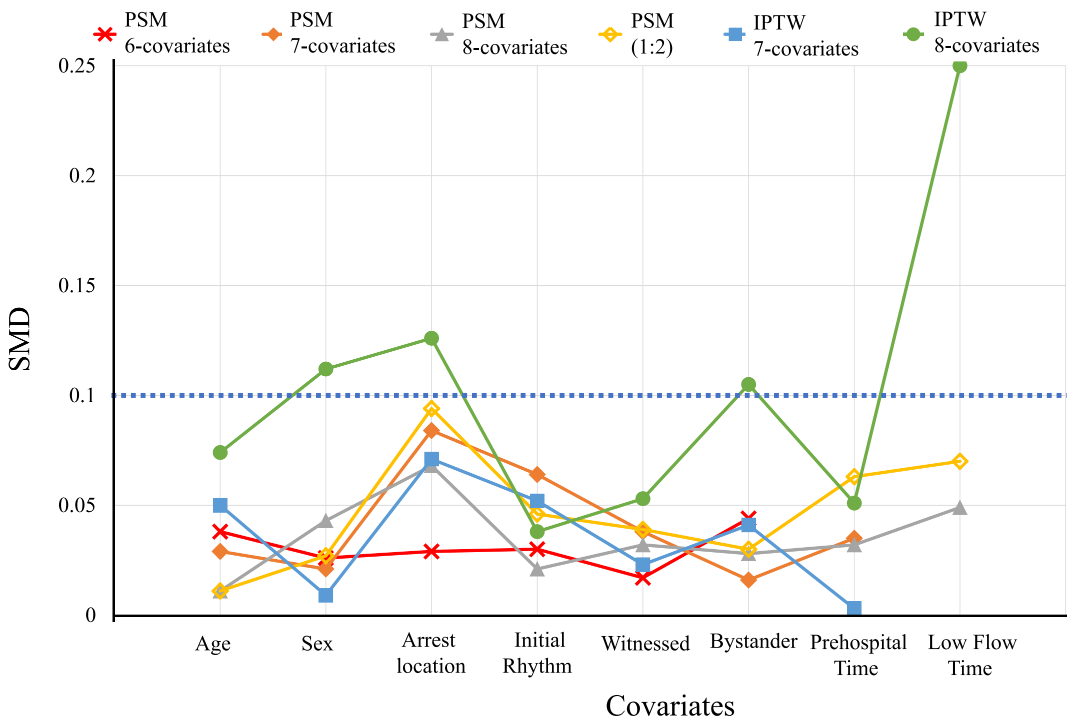

Fig. 2 – Love Plot Showing Standardized Mean Differences (SMDs) Before and After Adjustment Across PSM and IPTW Models. This Love Plot illustrates the standardized mean differences (SMDs) for the covariates before and after adjustment using propensity score matching (PSM) and inverse probability of treatment weighting (IPTW) models. Covariates include age, sex, location of cardiac arrest, initial cardiac rhythm, witnessed cardiac arrest, bystander CPR, prehospital time, and low flow time. In the PSM analyses (6-covariate, 7-covariate, and 8-covariate models) and the 7-covariate IPTW analysis, all SMDs were below the threshold of 0.1, indicating adequate balance. However, the 8-covariate IPTW analysis revealed SMDs exceeding 0.1 for four covariates (sex, bystander CPR, location of cardiac arrest, and low flow time), reflecting residual imbalance.

Table 4 – Standardized Mean Differences (SMDs) for Covariates Before and After PSM and in IPTW Analyses.

Adjusted Variables	Before PSM	PSM (6 covariates)	PSM (7 covariates)	PSM (8 covariates)	PSM (1:2 Matching)	IPTW (7 covariates)	IPTW (8 covariates)
Age	0.097	0.038	0.029	0.011	0.011	0.05	0.074
Sex	0.072	0.026	0.021	0.043	0.027	0.009	0.112
Location of cardiac arrest	0.255	0.029	0.084	0.068	0.094	0.071	0.126
Initial cardiac rhythm	0.127	0.03	0.064	0.021	0.046	0.052	0.038
Witnessed cardiac arrest	0.136	0.017	0.038	0.032	0.039	0.023	0.053
Bystander CPR	0.044	0.044	0.016	0.028	0.03	0.041	0.105
Prehospital time	0.729	N/A	0.035	0.032	0.063	0.003	0.051
Low flow time	0.044	N/A	N/A	0.049	0.07	N/A	0.25

This table presents the standardized mean differences (SMDs) for covariates across different analytical models, including the dataset before propensity score matching (PSM), after PSM using 6 covariates (age, sex, witness status, presence of bystander CPR, initial heart rhythm, and location of cardiac arrest), PSM with 7 covariates (including prehospital time), PSM with 8 covariates (including prehospital time and Low flow time), and inverse probability of treatment weighting (IPTW) analyses with 7 and 8 covariates. SMDs were calculated to assess the balance of covariates between the prehospital physician absence and prehospital physician presence groups. An SMD of less than 0.1 was considered to indicate acceptable balance. While all PSM models achieved an SMD below 0.1 for all covariates, the IPTW analysis with 8 covariates exhibited SMDs exceeding 0.1 for four covariates: sex, bystander CPR, location of cardiac arrest, and Low flow time. This indicates residual imbalance in the 8-covariate IPTW model.

PSM, propensity score matching; IPTW, inverse probability weighting.

Table 5 – Univariable Logistic Regression Results for Outcomes Before and After PSM and IPTW Across Analysis Models.

Outcomes	Before PSM	PSM (6 covariates)	PSM (7 covariates)	PSM (8 covariates)	PSM (1:2 Matching)	IPTW (7 covariates)	IPTW (8 covariates)
30-day Survival							
Odds Ratio (OR) (95% CI)	1.19 (0.93–1.53)	1.29 (1.09–1.58)	1.56 (1.13–2.17)	1.58 (1.14–2.21)	2.18 (1.61–2.96)	1.49 (1.16–1.90)	1.65 (1.30–2.09)
P-value	0.17	0.019	0.0072	0.0064	<0.001	0.0016	<0.001
30-day Favorable Neurological Outcome (CPC 1–2)							
Odds Ratio (OR) (95% CI)	1.14 (0.83–1.57)	1.21 (0.98–1.57)	1.54 (1.00–2.37)	1.25 (0.82–1.90)	1.76 (1.20–2.60)	1.30 (0.95–1.78)	1.21 (0.89–1.66)
P-value	0.41	0.069	0.048	0.30	0.0041	0.01	0.23

This table presents the univariable logistic regression results assessing the association between prehospital physician presence and outcomes, including 30-day survival and 30-day favorable neurological outcome (CPC 1–2). Analyses were conducted using the dataset before adjustment (Before PSM), after propensity score matching (PSM) with 6 covariates (age, sex, witness status, presence of bystander CPR, initial heart rhythm, and location of cardiac arrest), 7 covariates (including prehospital time), and 8 covariates (including prehospital time and Low flow time), as well as inverse probability of treatment weighting (IPTW) models with 7 and 8 covariates. For each analysis, odds ratios (ORs) with 95% confidence intervals (CIs) and P-values are shown.

CPC, cerebral performance category; PSM, propensity score matching; IPTW, inverse probability weighting.

association between prehospital physician presence and improved 30-day survival rates.

A log-rank test

A log-rank test comparing survival rates between the prehospital physician absence and prehospital physician presence groups, visualized using Kaplan-Meier survival curves, revealed a significantly higher survival rate in the prehospital physician presence group (Log-rank p = 0.02) (Fig. 3).

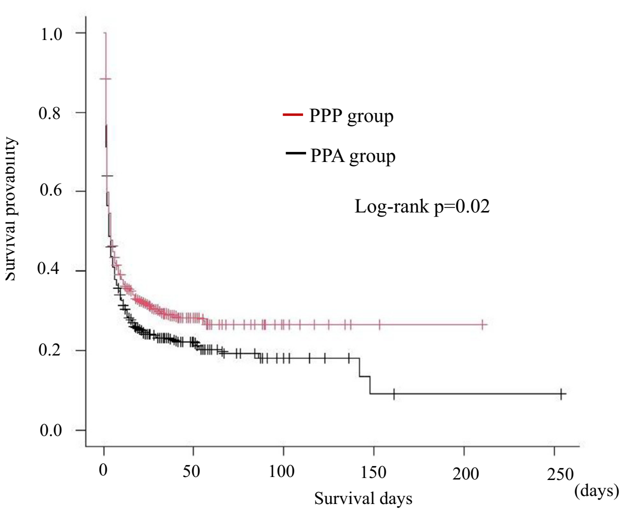

Fig. 3 – Kaplan-Meier survival curve for prehospital physician absence and prehospital physician presence groups. A log-rank test showed that the prehospital physician absence group had a significantly higher survival rate than prehospital physician presence group (p = 0.02).

The analysis of time intervals

In the analysis of time intervals (Table 1), the time from emergency call to hospital arrival was significantly longer in the prehospital physician presence group (37 [30, 47] minutes) compared to the prehospital physician absence group (30 [24, 36] minutes) (p < 0.001). Conversely, the time from hospital arrival to ECMO initiation was significantly shorter in the prehospital physician presence group (18.0 [13.0, 25.0] minutes) compared to the prehospital physician absence group (24.5 [17.0, 35.0] minutes) (p < 0.001). However, there was no significant difference in the total time from emergency call to ECMO initiation between the two groups (prehospital physician presence: 57 [48, 68] minutes; prehospital physician absence: 56 [47, 69] minutes, p = 0.183).

Discussion

Several large cohort studies have been conducted on OHCA patients who underwent ECPR in countries such as France, four other European countries, South Korea, and Japan.[12–17] The SAVE-J II study is the largest among these. Notably, it is 1.5 times the size of the previous largest study[15] and includes all types of cardiac arrest cases. This study uses continuous datasets from institutions that routinely perform ECPR, including four facilities that have conducted over 100 ECPR procedures in six years.[11] This study aimed to assess the impact of prehospital physician presence on the outcomes of ECPR in OHCA patients. To our knowledge, only two studies, including ours, have evaluated the usefulness of prehospital physician presence in ECPR-treated OHCA patients.

Another relevant study utilized data from the Japanese Association for Acute Medicine Out-of-Hospital Cardiac Arrest (JAAM-OHCA) registry, which included data from 69 tertiary emergency centers and 24 non-tertiary emergency centers across Japan. This study analyzed 1,269 ECPR-treated cases out of 57,754 OHCA patients, comparing outcomes between those with and without prehospital physician presence. It was reported that the presence of a prehospital physician did not significantly impact neurological outcomes at 30 days.[18] In contrast, our study stands out for using continuous data from institutions that frequently perform ECPR, with a high inclusion rate of approximately 76%. Additionally, we evaluated primary outcomes such as survival at 30 days and assessed time intervals from emergency call to hospital arrival, from hospital arrival to ECMO initiation, and from emergency call to ECMO initiation.

Our findings revealed that prehospital physician presence was associated with significantly higher 30-day survival rates after propensity score matching (PSM). Sensitivity analyses, including PSM with varying covariate models and inverse probability of treatment weighting (IPTW), consistently supported these results. The robustness of our findings was reinforced by additional logistic regression analyses showing that odds ratios for 30-day survival were consistently greater than 1 across all models. These results suggest that prehospital physician involvement contributes to improved survival in ECPR-treated OHCA patients.

However, no significant differences were observed in the secondary outcome of 30-day favorable neurological outcomes (CPC1-2). The lack of improvement in neurological outcomes despite higher survival rates may be due to the absence of significant differences in total low-flow time between the groups. Low-flow time, a critical determinant of neurological outcomes, remains a key target for future intervention strategies.

The prehospital physician presence was also associated with a significantly longer time from the emergency call to hospital arrival. This finding is consistent with previous studies[8,9,18] and likely reflects the additional time required for prehospital physicians to provide more advanced treatment compared to paramedics. However, unlike previous studies, the time from hospital arrival to ECMO initiation was significantly shorter in the prehospital physician presence group, resulting in no significant difference in the total time from the emergency call to ECMO initiation. This may be because prehospital physicians can issue orders for ECMO standby while en route to the hospital, enabling the ECMO team to prepare and initiate ECMO immediately upon the patient's arrival at the hospital.

These results suggest that while the presence of a prehospital physician contributes to improved survival, it does not significantly impact neurological outcomes. The lack of statistical significance in neurological outcomes may be attributed to the absence of a significant difference in the total time from the emergency call to ECMO initiation. Given that prehospital physician presence was associated with shorter times to ECMO initiation after hospital arrival, reducing the time from the emergency call to hospital arrival remains crucial, even when a prehospital physician is present.

It is crucial to minimize total prehospital time, even when there is a prehospital physician present. In some regions, a keyword-triggered dispatch system has been implemented, in this system, doctor helicopters or doctor cars are immediately dispatched when the emergency call contains specific keywords. This system saves a significant amount of time compared to the conventional approach. Additionally, efforts to minimize on-scene time and perform medical procedures during transport can further reduce time.

The significantly higher ROSC rate before hospital arrival observed in the prehospital physician presence group likely contributes to the improved survival outcomes. Prehospital physicians may facilitate advanced resuscitation efforts, such as drug administration and advanced airway management, that enhance the likelihood of achieving ROSC. However, this advantage in ROSC did not translate into significant improvements in neurological outcomes, which may be due to the absence of a significant difference in low-flow time between the groups. Low-flow time is a critical determinant of neurological outcomes, and reducing this time remains a key target for improving long-term outcomes. These findings suggest the need for further strategies to reduce low-flow time, even when prehospital physicians are present, including the potential implementation of prehospital ECPR.

Overall, the lack of difference in the total time from the emergency call to ECMO initiation may explain the absence of a significant impact on neurological outcomes. If prehospital physician presence could lead to earlier ECPR initiation, it might positively influence neurological outcomes. The potential effectiveness of prehospital ECPR initiation is suggested.[19,20] While the extent to which prehospital ECPR was performed in the SAVE-J II study is unknown, it is rarely practiced in Japan. Implementing prehospital ECPR, as done in parts of France, the Netherlands, and the UK, could further improve outcomes for patients eligible for ECPR. Bougouin et al. demonstrated that prehospital ECPR was independently associated with higher hospital discharge survival (odds ratio 2.9, 95% CI 1.5–5.9, p = 0.002) and survival with favorable neurological outcomes (odds ratio 2.9, 95% CI 1.3–6.4, p = 0.008).[12] This is likely due to the reduction in low-flow time. Petermichl et al. found that the time to ECPR was significantly shorter in patients with CPC 1,2 compared to non-survivors (40 min vs. 47 min, p = 0.010).[21]

However, establishing prehospital ECPR requires addressing several challenges, including the formation of an experienced ECPR team, procurement of equipment, transportation of staff and medical supplies, selection of a location for ECMO initiation, simulation training, criteria for prehospital ECPR indications, and the determination of appropriate transport distances.

This study has several limitations. As a retrospective study, it is inherently susceptible to selection bias and confounding factors. Additionally, variability in ECPR criteria across institutions may have introduced selection bias and heterogeneity in the data. While restricting inclusion to cardiac-origin OHCA patients minimized confounding, this approach limits the generalizability of the findings to more diverse OHCA populations. Future studies should investigate the impact of prehospital physician involvement in broader patient cohorts, including non-cardiac cases. The lack of detailed data on prehospital physician interventions – such as the timing of interventions, on-scene time, and time to hospital arrival – may affect the interpretation of our findings. Furthermore, critical information on preparations for rapid ECPR initiation, such as issuing ECMO standby orders or securing arterial and venous access, was unavailable, limiting our understanding of how prehospital physicians contribute to improved outcomes. Geographical factors, particularly the distance between the scene and the hospital, were not accounted for, despite their significant influence on outcomes. In cases with nearby hospitals, the presence of a prehospital physician might even be disadvantageous. Additionally, the dataset predominantly includes data from institutions that frequently perform ECPR, which may limit the generalizability of the findings to a broader context. While prehospital physician presence was associated with improved survival rates, it did not significantly affect neurological outcomes. This result highlights the importance of reducing Low flow time as a key target for improving neurological outcomes. However, the specific impact of Low flow time on outcomes could not be adequately assessed in this study, underscoring the need for prospective studies and causal pathway analyses. Lastly, the absence of long-term outcome data precluded an evaluation of the sustained impact of prehospital physician presence on patient prognosis. Further research is essential to address these gaps and to explore the variability in emergency medical systems across different contexts.

Conclusion

The presence of a prehospital physician significantly improved 30-day survival rates in OHCA patients undergoing ECPR, underscoring the importance of advanced prehospital interventions. However, no significant impact was observed on neurological outcomes, likely due to the lack of differences in low-flow time, a critical determinant of neurological recovery. Efforts to further optimize outcomes should focus on reducing low-flow time through strategies such as minimizing on-scene time, improving prehospital-hospital coordination, and considering the implementation of prehospital ECPR. Addressing logistical challenges and conducting prospective studies to clarify the role of Low flow time will be essential for maximizing the benefits of ECPR.

Ethics approval and consent to participate

The SAVE-J II study was approved by the institutional review board of Kagawa University (approval number: 2018-110) and of each participating institution. In all the participating institutions, the requirement for patient consent was waived due to the retrospective nature of this study. The study was conducted in accordance with the guidelines for clinical research protocols of the 1975 Declaration of Helsinki. This secondary analysis was approved by the Institutional Review Board of Toyooka Public Hospital (approval number: 222).

Availability of data and materials

Please contact the author for data requests.

Consent for publication

Not applicable.

CRediT authorship contribution statement

Futoshi Nagashima: Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Satoshi Inoue:** Writing – review & editing, Formal analysis. **Tomohiro Oda:** Formal analysis, Data curation. **Tomohiro Hamagami:** Formal analysis, Data curation. **Tomoya Matsuda:** Formal analysis, Data curation. **Makoto Kobayashi:** Formal analysis. **Akihiko Inoue:** Supervision, Project administration. **Toru Hifumi:** Supervision, Project administration. **Tetsuya Sakamoto:** Supervision, Project administration. **Yasuhiro Kuroda:** Supervision.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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REFERENCES

1. Yannopoulos D, Bartos J, Raveendran G, et al. Advanced reperfusion strategies for patients with out-of-hospital cardiac arrest and refractory ventricular fibrillation (ARREST): a phase 2, single centre, open-label, randomised controlled trial. Lancet 2020;396 (10265):1807–16.
2. Panchal AR, Bartos JA, Cabañas JG, et al. Part 3: adult basic and advanced life support: 2020 American Heart Association Guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation 2020;142(16_suppl_2):S366–468.
3. Yasunaga H, Horiguchi H, Tanabe S, et al. Collaborative effects of bystander-initiated cardiopulmonary resuscitation and prehospital advanced cardiac life support by physicians on survival of out-of-hospital cardiac arrest: a nationwide population-based observational study. Crit Care 2010;14:R199.
4. Bottiger BW, Bernhard M, Knapp J, Nagele P. Influence of EMS-physician presence on survival after out-of-hospital cardiopulmonary resuscitation: systematic review and meta-analysis. Crit Care 2016;20:4.
5. Hamilton A, Steinmetz J, Wissenberg M, et al. Association between prehospital physician involvement and survival after out-of-hospital cardiac arrest: A Danish nationwide observational study. Resuscitation 2016;108:95–101.
6. Ohbe H, Isogai S, Nakajima M, et al. Physician-manned prehospital emergency care in tertiary emergency centers in Japan. Acute Med Surg 2019;6:165–72.
7. Tanigawa K, Tanaka K. Emergency medical service systems in Japan: past, present, and future. Resuscitation 2006;69:365–70.
8. Hatakeyama T, Kiguchi T, Sera T, et al. Physician's presence in pre-hospital setting improves one-month favorable neurological survival after out-of-hospital cardiac arrest: A propensity score matching analysis of the JAAM-OHCA Registry. Resuscitation 2021;167:38–46.
9. Hagihara A, Hasegawa M, Abe T, Nagata T, Nabeshima Y. Physician presence in an ambulance car is associated with increased survival in out-of-hospital cardiac arrest: a prospective cohort analysis. PLoS One 2014;9:e84424.
10. Böttiger BW, Bernhard M, Knapp J, Nagele P. Influence of EMS-physician presence on survival after out-of-hospital cardiopulmonary resuscitation: systematic review and meta-analysis. Crit Care 2016;20:4.
11. Inoue A, Hifumi T, Sakamoto T, et al. Extracorporeal cardiopulmonary resuscitation in adult patients with out-of-hospital cardiac arrest: a retrospective large cohort multicenter study in Japan. Crit Care. 2022;26:129.
12. Bougouin W, Dumas F, Lamhaut L, et al. Extracorporeal cardiopulmonary resuscitation in out-of-hospital cardiac arrest: a registry study. Eur Heart J. 2020;41(21):1961–71.
13. Lunz D, Calabro L, Belliato M, et al. Extracorporeal membrane oxygenation for refractory cardiac arrest: a retrospective multicenter study. Intensive Care Med. 2020;46(5):973–82.
14. Choi DS, Kim T, Ro YS, et al. Extracorporeal life support and survival after out-of-hospital cardiac arrest in a nationwide registry: a propensity score-matched analysis. Resuscitation 2016;99:26–32.
15. Okada Y, Kiguchi T, Irisawa T, et al. Develop- ment and validation of a clinical score to predict neurological outcomes in patients with out-of-hospital cardiac arrest treated with extracorporeal cardiopulmonary resuscitation. JAMA Netw Open. 2020;3(11)e2022920.
16. Miyamoto Y, Matsuyama T, Goto T, et al. Association between age and neurological outcomes in out-of-hospital cardiac arrest patients resuscitated with extracorporeal cardiopulmonary resuscitation: a nationwide multicentre observational study. Eur Heart J Acute Cardiovasc Care. 2022;11(1):35–42.
17. Nakashima T, Noguchi T, Tahara Y, et al. Patients with refractory out-of-cardiac arrest and sustained ventricular fibrillation as candidates for extracorporeal cardiopulmonary resuscitation- prospective multi-center observational study. Circ J. 2019;83 (5):1011–8.
18. Nakajima S, Matsuyama T, Watanabe M, et al. Prehospital physician presence for patients with out-of-hospital cardiac arrest undergoing extracorporeal cardiopulmonary resuscitation: A multicenter, retrospective, nationwide observational study in Japan (The JAAM OHCA registry). Curr Probl Cardiol. 2023;48:101600.
19. Lamhaut L, Hutin A, Puymirat E, et al. A pre-hospital Extracorporeal Cardio Pulmonary Resuscitation (ECPR) strategy for treatment of refractory out hospital cardiac arrest: An observational study and propensity analysis. Resuscitation 2017;117:109–17.
20. Singer B, Reynolds JC, Lockey DJ, O'Brien B. Pre-hospital extra-corporeal cardio- pulmonary resuscitation. Scand J Trauma Resusc Emerg Med 2018;26:21.
21. Walter P, Alois P, Karl-Anton H, et al. Reliability of prognostic biomarkers after prehospital extracorporeal cardio- pulmonary resuscitation with target temperature management. Scand J Trauma Resusc Emerg Med. 2021;29(1):1–12.