RESUSCITATION 136 (2019) 85–92

Available online at www.sciencedirect.com

Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation

Clinical paper

Hospitals' extracorporeal cardiopulmonary resuscitation capabilities and outcomes in out-of-hospital cardiac arrest: A population-based study

Yoshinori Matsuoka[a,b], *Tatsuyoshi Ikenoue*[c], *Natsumi Hata*[b], *Masataka Taguri*[d], *Takahiro Itaya*[a], *Koichi Ariyoshi*[b], *Shunichi Fukuhara*[a,e], *Yosuke Yamamoto*[a,*]

[a] *Department of Healthcare Epidemiology, Graduate School of Medicine and Public Health, Kyoto University, Yoshidakonoe-cho, Sakyo-ku, Kyoto-city, Kyoto, 606-8501, Japan*

[b] *Department of Emergency Medicine, Kobe City Medical Center General Hospital, 2-1-1 Minatojima-Minamimachi, Chuo-ku, Kobe-city, Hyogo, 650-0047, Japan*

[c] *Department of Human Health Science, Graduate School of Medicine, Kyoto University, 53 Kawahara-cho, Shogoin, Sakyo-ku, Kyoto-city, Kyoto, 606-8507, Japan*

[d] *Department of Data Science, School of Data Science, Yokohama City University, 22-2 Seto, Kanazawa-ku, Yokohama-city, Kanagawa, 236-0027, Japan*

[e] *Center for Innovative Research for Communities and Clinical Excellence (CIRC2LE), Fukushima Medical University, 1 Hikarigaoka, Fukushima-city, Fukushima, 960-1295, Japan*

Abstract

Aim: Extracorporeal cardiopulmonary resuscitation (ECPR) is the emerging resuscitative strategy to save refractory ventricular fibrillation (VF) or pulseless ventricular tachycardia (VT) patients. We investigated whether the receiving hospitals' ECPR capabilities are associated with outcomes in out-of-hospital cardiac arrest (OHCA) patients who have refractory VF or pulseless VT.

Methods: In a population-based cohort study performed in Kobe City, Japan, between 2010 and 2017, we identified all OHCA patients who had refractory VF or pulseless VT. Based on their ECPR capabilities, hospitals were categorised into ECPR facilities and conventional cardiopulmonary resuscitation (CCPR) facilities. We compared patient survivals between ECPR facilities and CCPR facilities by applying inverse probability weighting using a propensity score.

Results: Of all 10,971 OHCA patients, 518 had refractory VF or pulseless VT. The proportion of favourable neurologic outcomes was 43/188 (22.9%) in ECPR facilities and 28/330 (8.5%) in CCPR facilities. In the propensity analysis, hospitals' ECPR capabilities were associated with favourable neurologic outcomes (adjusted risk difference [ARD], 9.7% [95% confidence interval [CI], 3.7%–15.7%]; adjusted risk ratio [ARR], 2.01 [95% CI, 1.31–3.09]), and overall survival (87/188 [46.3%] vs. 67/330 [20.3%]; ARD, 19.0% [95% CI, 11.1%–26.9%]; ARR, 1.88 [95% CI, 1.45–2.44]).

Conclusions: Hospitals' ECPR capabilities were associated with favourable neurologic outcomes in OHCA patients who had refractory VF or pulseless VT. We should take each hospital's ECPR capability into consideration when developing a regional system of care for OHCA.

Keywords: Extracorporeal cardiopulmonary resuscitation, Out-of-hospital cardiac arrest, Emergency medical services, Hospital characteristics

* Corresponding author.
E-mail address: yamamoto.yosuke.5n@kyoto-u.ac.jp (Y. Yamamoto).

https://doi.org/10.1016/j.resuscitation.2019.01.013

Received 24 October 2018; Received in revised form 4 January 2019; Accepted 8 January 2019

Introduction

Sudden cardiac death is a major public health problem in industrialised countries. The outcome is dismal among those who had refractory ventricular fibrillation (VF) or pulseless ventricular tachycardia (VT). Despite advances in the chain of survival, patient survival at one month has continued to remain at 20.4%, and only 5.6% of patients experienced favourable neurologic outcomes at one month after VF or pulseless VT without return of spontaneous circulation (ROSC).[1] Several advanced medical procedures, such as therapeutic hypothermia and percutaneous coronary intervention (PCI), have been introduced to treat patients with out-of-hospital cardiac arrest (OHCA).[2–4] In addition, the concept of extracorporeal cardiopulmonary resuscitation (ECPR) is a promising resuscitative approach to saving patients with refractory VF or pulseless VT.[5–7] According to the American Heart Association (AHA) guidelines and the European Resuscitation Council, ECPR may be considered for select patients in settings where it can be rapidly implemented.[8,9] However, the number of facilities that can afford to implement ECPR is limited, as ECPR requires specially-trained medical professionals and significant resources. Therefore, we need to develop emergency medical service (EMS) protocols and systems, to transport possible ECPR candidates directly to regional centres with ECPR capabilities.

Given such limited medical resources, EMS should transport OHCA patients to appropriate facilities where advanced medical practice, including ECPR, can be provided. This idea is consistent with the AHA recommendation that OHCA patients should be treated under an established regional system of care.[10,11] There has been growing evidence of the relationship between hospitals' capabilities for medical practice, such as PCI capability and the level of intensive care, and survival.[12–20] Although some studies have demonstrated that the receiving hospital's characteristics were associated with better outcomes for OHCA patients,[12–17] others failed to show such a relationship between the hospital's capacity and outcomes.[13–20] The discrepancy still remains unresolved. However, this could be explained partially by differences in target populations, as well as the statistical methods used to address confounding factors. Furthermore, the receiving hospital's ECPR capability would be a more important factor than PCI capabilities and level of intensive care for refractory VF or pulseless VT patients. However, to the best of our knowledge, it is still unclear whether transporting OHCA patients with VF or pulseless VT without ROSC to ECPR-capable facilities is associated with better patient outcomes.

The purpose of the present study was to evaluate the longitudinal relationship between hospitals' ECPR capabilities and outcomes in OHCA patients with refractory VF or pulseless VT.

Methods

Study design and setting

This was a population-based cohort study conducted in Kobe City, Japan from January 2010 to December 2017. Data from all OHCA patients who were treated in the city by EMS personnel and transported to hospitals were collected prospectively from the OHCA registry using the Utstein style.[21] Cardiac arrest was defined as the cessation of mechanical activity, determined by the absence of signs of circulation.[21] The ethics committee of Kobe City Medical Center General Hospital approved the study's protocols (zn180621). The requirement of informed consent was waived, as all the information that could identify patients in the present study was removed from the database.

Kobe City has a population of 1.5 million residents in an area of approximately 557 km^2 including both its urban and rural communities. As of 2017, the municipal government provided EMS at 10 fire and ambulance stations with 29 emergency dispatch centres. EMS personnel perform cardiopulmonary resuscitation (CPR) according to Japanese CPR guidelines, which are based on the AHA and the International Liaison Committee on Resuscitation guidelines.[22] Almost all OHCA patients were transported to the nearest appropriate hospital, as EMS personnel in Japan are not allowed to terminate resuscitation out of hospital. The exceptions are as follows: decapitation, incineration, decomposition, rigor mortis, and dependent cyanosis.

Selection of participants

From all the OHCA patients in the registry, we enrolled adult patients aged 18 years and older with refractory VF or pulseless VT, defined as cardiac arrest without ROSC after receiving conventional resuscitation by EMS in the field. We excluded patients with an aetiology of cardiac arrest from trauma, other external causes, known pregnancy, or known terminal-stage malignancies.

Data collection

EMS personnel in charge of the patients completed the run-sheets, followed up on all the survivors for up to one month, and obtained details of the patients' outcomes from the hospitals.

From the OHCA registry, we extracted data including age, sex, witness status, bystander CPR, bystander use of public-access automated external defibrillators (AEDs), defibrillation by EMS, adrenaline (epinephrine) administration, insertion of intravenous lines, prehospital intubation, time from EMS arrival on the scene to the departure, time from the call to the hospital arrival, survival at 1 month, and neurologic status 1 month after cardiac arrest.

Information on hospitals' ECPR and PCI capabilities was obtained from Kobe City Fire Bureau and Kobe City municipal office. Information regarding certified levels of intensive care was obtained from the Japanese Ministry of Health, Labour and Welfare's website.[14,15,23]

Hospitals' ECPR capabilities and other hospital characteristics

Hospitals were categorised into two groups according to their ECPR capabilities: ECPR facilities (four hospitals) and CCPR facilities (38 hospitals). ECPR-capable facilities were defined as hospitals where they could perform ECPR at any time (24 h/day, 365 days/year) and establish ECPR within 15 min of the patients' arrival, along with simultaneous catheterisation laboratory activation. With regard to CCPR facilities, we defined two types: conditionally ECPR-capable facilities (seven hospitals) and ECPR-incapable facilities (31 hospitals). Conditionally ECPR-capable facilities had limited ECPR capabilities, and offered ECPR during restrictive hours. ECPR-incapable facilities could not perform ECPR at all.

With regard to other hospital characteristics, we identified five 24/7 PCI-capable facilities and two critical care centres in the city. We defined the certified level of intensive care as that provided by a critical care medical centre.

Outcome measures

The primary outcome measure was survival with a favourable neurologic outcome at one month after cardiac arrest. We defined a favourable neurologic outcome as a Cerebral Performance Category score of 1 (good performance) or 2 (moderate disability).[21] The secondary outcome measure was overall survival at one month.

Statistical analysis

We presented the data as medians with interquartile ranges (IQRs) for continuous variables and as counts and proportions for categorical variables.

In the primary analysis, we compared outcomes between two groups: patients who were transported to ECPR facilities and those transported to CCPR facilities. We analysed the adjusted risk differences and risk ratios by applying inverse probability weighting using a propensity score. The propensity score was the estimated probability that OHCA patients were transported to either ECPR or CCPR facilities, calculated by a logistic regression model using the following variables: age (in 10-year increments), sex, witness status, bystander CPR, bystander use of a public-access AED, adrenaline administration, and time from call to hospital arrival (categorised into quartiles). We selected the variables for propensity score based on biological plausibility and preexisting knowledge. To assess whether other hospital characteristics (24/7 PCI capability and certified intensive care level) are associated with patient outcomes, we additionally performed the same propensity score analyses as above.

In the secondary analyses, we compared outcomes between three groups: patients transported to ECPR-capable facilities, conditionally ECPR-capable facilities, and ECPR-incapable facilities. We analysed adjusted risk differences by applying inverse probability weighting using a propensity score. The propensity score was calculated as the estimated probabilities that patients were transported to either ECPR, conditionally ECPR-capable, or ECPR-incapable facilities using a multinomial regression model and the same variables as in the primary analysis.

Standardised differences were calculated as the difference in means or proportions divided by the pooled standard deviation in both propensity score analyses, and we defined an absolute standardised difference of less than 0.1 as negligible.[24]

In the subgroup analysis, we evaluated the association between favourable neurologic outcomes and transport of patients to ECPR-capable facilities and CCPR facilities, dividing patients into predefined groups by age (≥65, 55–65, <55 years), time from call to hospital arrival (≥30, 20–30, ≤20 min), witness (yes or no), and bystander CPR (yes or no), using the same analysis method as the primary analysis.

All statistical analyses were conducted using STATA version 15.1 (StataCorp, College Station, TX). All hypothesis tests were 2-tailed with a significance level of $P < 0.05$.

Results

Study population

From a total of 10,971 patients with OHCA, 578 patients were confirmed with refractory VF or pulseless VT. After excluding patients with cardiac arrest due to trauma and other external causes (28), known terminal stages of malignancies (10), and missing data (22), we included 518 patients for our analyses (Fig. 1).

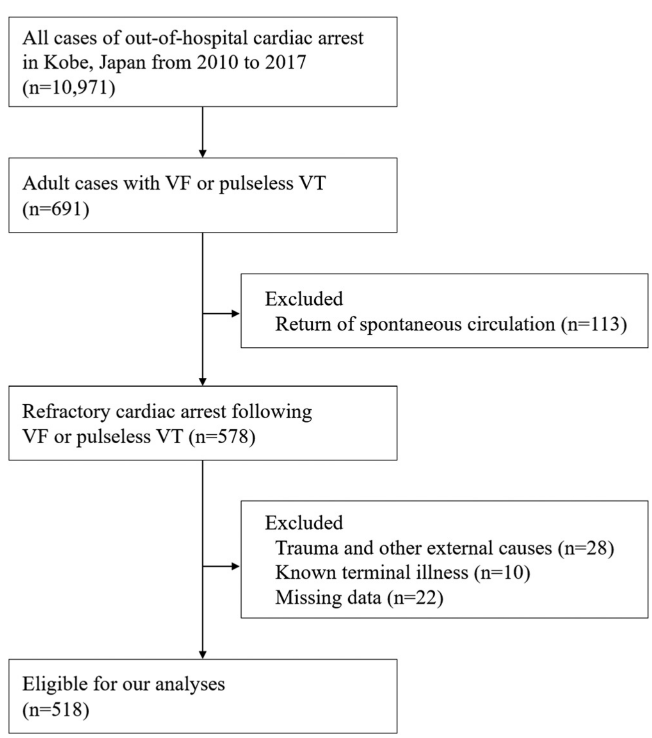

Fig. 1 – Flowchart of the study.

Table 1 – Characteristics of out-of-hospital cardiac arrest patients with refractory ventricular fibrillation or pulseless ventricular tachycardia.

Characteristics	Total (n = 518)	ECPR facility (n = 188)	CCPR facility (n = 330)
Year of cardiac arrest, n (%)			
2010	66 (13)	14 (7.4)	52 (16)
2011–2015	342 (66)	120 (64)	222 (67)
2016–2017	110 (21)	54 (29)	56 (17)
Timing of cardiac arrest			
Daytime[a], n (%)	240 (46)	73 (39)	167 (51)
Weekday[b], n (%)	376 (73)	138 (73)	238 (72)
Age, median (IQR)	68 (58–77)	66 (57–75)	69 (59–78)
Male, n (%)	408 (79)	147 (78)	261 (79)
Witnessed, n (%)	395 (76)	144 (77)	251 (76)
Bystander CPR, n (%)	238 (46)	91 (48)	147 (45)
Bystander use of public-access AED, n (%)	21 (4.1)	10 (5.3)	11 (3.3)
Defibrillation by EMS, n (%)	503 (97)	185 (98)	318 (96)
Adrenaline administration, n (%)	145 (28)	39 (21)	106 (32)
Insertion of intravenous line, n (%)	257 (50)	85 (45)	172 (52)
Time from EMS scene arrival to departure, median (IQR), min	14 (11–18)	12 (10–16)	15 (12–19)
Time from call to hospital arrival, median (IQR), min	31 (24–37)	28 (23–34)	32 (25–39)

ECPR, extracorporeal cardiopulmonary resuscitation; CCPR, conventional cardiopulmonary resuscitation; IQR, interquartile range; CPR, cardiopulmonary resuscitation; AED, automated external defibrillator; EMS, emergency medical service.
[a] Daytime indicates time between 9:00 AM–17:00 PM.
[b] Weekday indicates Monday–Friday.

Patient characteristics

Table 1 shows the baseline characteristics of OHCA patients with refractory VF or pulseless VT by ECPR capabilities of hospitals to which they were transported. The median age for all patients was 68 (IQR, 58–77) years and 79% of patients were male. Patients were more likely to receive public-access AED from a bystander, but less adrenaline administration and insertion of intravenous lines when transported to ECPR facilities than to CCPR facilities. Both the time from EMS arrival on the scene to departure, and from call to hospital arrival were shorter in patients who were transported to ECPR facilities.

Outcomes

ECPR vs. CCPR facilities

Table 2shows the primary and secondary outcomes in patients with refractory VF or pulseless VT, who were transported to ECPR and CCPR facilities. In the primary analysis, the proportion of favourable neurologic outcomes was significantly higher in the patients transported to ECPR facilities than in those transported to CCPR facilities (43/188 (22.9%) vs. 28/330 (8.5%); adjusted risk difference [ARD], 9.7% [95% confidence interval [CI], 3.7%–15.7%]; adjusted risk ratio [ARR], 2.01 [95% CI, 1.31–3.09]). Survival at one month after cardiac arrest was significantly higher in the patients who were transported to ECPR facilities than in those who were transported to CCPR facilities (87/188 (46.3%) vs. 67/330 (20.3%); ARD, 19.0% [95% CI, 11.1%–26.9%]; ARR, 1.88 [95% CI, 1.45–2.44]). All covariates between the groups were well balanced after applying the inverse probability weighting (all standardised differences were <0.1). A summary of the balance before and after applying inverse probability weighting is shown in Supplemental Tables 1 and 2.

Other hospital characteristics: PCI capability and certified intensive care level

Neither of these two hospital characteristics were associated with favourable neurologic outcomes, but they were associated with

Table 2 – ECPR capabilities and outcomes in out-of-hospital cardiac arrest patients with refractory ventricular fibrillation or pulseless ventricular tachycardia.

Outcome	Number of patients with outcome/total patients (%)		Unadjusted analysis (ECPR vs. CCPR)		Adjusted analysis (ECPR vs. CCPR)	
	ECPR facilities	CCPR facilities	Risk difference (95% CI), %	Risk ratio (95% CI)	Risk difference (95% CI), %	Risk ratio (95% CI)
Favourable neurologic outcome[a]	43/188 (22.9)	28/330 (8.5)	14.4 (7.7–21.1)	2.70 (1.73–4.19)	9.7 (3.7–15.7)	2.01 (1.31–3.09)
Survival at one month	87/188 (46.3)	67/330 (20.3)	26.0 (17.6–34.3)	2.28 (1.75–2.97)	19.0 (11.1–26.9)	1.88 (1.45–2.44)

ECPR, extracorporeal cardiopulmonary resuscitation; CCPR, conventional cardiopulmonary resuscitation; CI, confidence interval. These risk differences and risk ratios were adjusted by applying inverse probability weighting using a propensity score. The propensity score was calculated by a logistic regression model using the following variables: age, sex, bystander witness status, bystander cardiopulmonary resuscitation, bystander use of a public access automated external defibrillator, adrenaline administration, and time from call to hospital arrival.
[a] Favourable neurologic outcome was defined as cerebral performance category of 1 or 2 at one month.

Table 3 – Hospital characteristics and outcomes in out-of-hospital cardiac arrest patients with refractory ventricular fibrillation or pulseless ventricular tachycardia.

1. PCI capabilities (24/7)[a]

Outcome	Number of patients with outcome/Total patients (%)		Unadjusted analysis (PCI vs. non-PCI)		Adjusted analysis (PCI vs. non-PCI)	
	PCI-capable (24/7)	non-PCI-capable	Risk difference (95% CI), %	Risk ratio (95% CI)	Risk difference (95% CI), %	Risk ratio (95% CI)
Favourable neurologic outcome[a]	43/259 (16.6%)	28/259 (10.8%)	5.8 (−0.1 to 11.7)	1.54 (0.99–2.39)	3.7 (−2.0 to 9.4)	1.32 (0.86–2.03)
Survival at one month	94/259 (36.3%)	60/259 (23.2%)	13.1 (5.3–20.9)	1.57 (1.19–2.06)	12.0 (4.4–19.5)	1.51 (1.15–1.98)

2. Certified intensive care level[a]

Outcome	Number of patients with outcome/Total patients (%)		Unadjusted analysis (Critical care medical centre vs. non-critical care medical centre)		Adjusted analysis (Critical care medical centre vs. non-critical care medical centre)	
	Critical care medical centre	Non-critical care medical centre	Risk difference (95% CI), %	Risk ratio (95% CI)	Risk difference (95% CI), %	Risk ratio (95% CI)
Favourable neurologic outcome[b]	39/229 (17.0%)	32/289 (11.1%)	6.0 (−0.1 to 12.0)	1.54 (1.00–2.37)	3.3 (−2.3 to 9.0)	1.28 (0.84–1.95)
Survival at one month	85/229 (37.1%)	69/289 (23.9%)	13.2 (5.3–21.2)	1.55 (1.19–2.03)	11.1 (3.6–18.7)	1.46 (1.13–1.90)

PCI, percutaneous coronary intervention; CI, confidence interval. These risk differences and risk ratios were adjusted by applying inverse probability weighting using a propensity score. The propensity score was calculated by a logistic regression model using the following variables: age, sex, bystander witness status, bystander cardiopulmonary resuscitation, bystander use of a public access automated external defibrillator, adrenaline administration, and time from call to hospital arrival.

[a]We defined PCI capability as 24/7 PCI availability, and the certified level of intensive care as that provided by a critical care medical centre.

[b]Favourable neurologic outcome was defined as cerebral performance category of 1 or 2 at one month.

survival at one month after cardiac arrest (Table 3). All covariates between the groups were well balanced after applying the inverse probability weighting (all the standardised differences were <0.1).

ECPR vs. conditionally ECPR-capable vs. ECPR-incapable facilities

Table 4 shows the primary and secondary outcomes in refractory VF or pulseless VT patients transported to ECPR, conditionally ECPR-capable, or ECPR-incapable facilities. The proportion of survival with a favourable neurologic outcome and overall survival at one month was significantly higher in the patients transported to ECPR facilities than in those transported to ECPR-incapable facilities, but was similar between the patients transported to conditionally ECPR-capable facilities and those transported to ECPR-incapable facilities. All covariates between the three groups were well balanced with inverse probability weighting (Supplemental Table 2).

Table 4 – Association between hospitals' ECPR capabilities and outcomes in out-of-hospital cardiac arrest patients with refractory ventricular fibrillation or pulseless ventricular tachycardia.

Outcome	Number of patients with outcome/Total patients (%)			Adjusted Risk Difference (95% CI), %	
	ECPR facilities[a]	Conditionally ECPR-capable facilities[a]	ECPR-incapable facilities[a]	ECPR facilities vs. ECPR-incapable facilities	Conditionally ECPR-capable facilities vs. ECPR-incapable facilities
Favourable neurologic outcome[b]	43/188 (22.9)	18/229 (7.9)	10/101 (9.9)	9.4 (1.8–17.1)	−0.4 (−7.5 to 6.7)
Survival at one month	87/188 (46.3)	46/229 (20.1)	21/101 (20.8)	18.8 (8.5–29.1)	−0.4 (−10.1 to 9.4)

ECPR, extracorporeal cardiopulmonary resuscitation; CI, confidence interval. These risk differences were adjusted by applying inverse probability weighting using a propensity score. The propensity score was calculated by a multinomial regression model using the following variables: age, sex, bystander witness status, bystander CPR, bystander use of a public access automated external defibrillator (AED), adrenaline administration, and time from call to hospital arrival.

[a] ECPR facilities could perform ECPR all the time with rapid implementation. Conditionally ECPR-capable facilities had limited ECPR capabilities, and offered ECPR during restrictive hours. ECPR-incapable facilities could not perform ECPR at all.

[b] Favourable neurologic outcome was defined as cerebral performance category of 1 or 2 at one month.

Table 5 – Subgroup analyses of associations with hospitals' ECPR capabilities and favourable neurologic outcomes after refractory ventricular fibrillation or pulseless ventricular tachycardia.

Subgroup	Number of patients with outcome/total patients (%)		Adjusted risk difference (95% CI), %
	ECPR facilities	CCPR facilities	
Age			
≥ 65	16/106 (15.1)	10/204 (4.9)	7.4 (0.6–14.2)
55–65	12/43 (27.9)	10/72 (13.9)	6.3 (−7.1 to 19.8)
<55	15/39 (38.5)	8/54 (14.8)	17.8 (0.7–34.8)
Time from call to hospital arrival, min			
≥30min	12/76 (15.8)	10/191 (5.2)	6.8 (−0.5 to 14.1)
20–30 min	24/88 (27.3)	16/108 (14.8)	11.4 (0.1–22.8)
≤20 min	7/24 (29.2)	2/31 (6.5)	22.2 (3.5–40.8)
Witness			
Yes	37/144 (25.7)	24/251 (9.6)	11.1 (3.9–18.2)
No	6/44 (13.6)	4/79 (5.1)	4.2 (−6.2 to 14.6)
Bystander CPR			
Yes	18/91 (19.8)	15/147 (10.2)	2.9 (−5.2 to 11.0)
No	25/97 (25.8)	13/183 (7.1)	14.8 (6.2–23.3)

ECPR, extracorporeal cardiopulmonary resuscitation; CCPR, conventional cardiopulmonary resuscitation; CI, confidence interval; CPR, cardiopulmonary resuscitation.

These risk differences were adjusted by applying inverse probability weighting using apropensity score. The propensity score was calculated by a logistic regression model using the following variables: age, sex, bystander witness status, bystander CPR, bystander use of a public access automated external defibrillation (AED), adrenaline administration, and time from call to hospital arrival. Favourable neurologic outcome was defined as cerebral performance category of 1 or 2 at one month.

Subgroup analysis

The results of the subgroup analyses are shown in Table 5. There were differences in ARD between the subgroups according to age, time from call to hospital arrival, witness status, and bystander CPR. Younger age, shorter time from call to hospital arrival, and witnessed cardiac arrest were associated with higher favourable neurologic outcomes, whereas bystander CPR was associated with a lower likelihood of favourable neurologic outcomes.

Discussion

In our analyses of data from a population-based registry in Japan, OHCA patients with refractory VF or pulseless VT were likely to experience better neurologic outcomes in ECPR facilities than in CCPR facilities. Patient outcomes were similar between CCPR facilities that were categorised into conditionally ECPR facilities and ECPR-incapable facilities.

The present study suggests that the receiving hospitals' ECPR capabilities should be considered when developing EMS systems and protocols for transporting patients with refractory VF or pulseless VT. The results of this study may be reasonably explained by previous observational studies and a systematic review, which demonstrated that ECPR improves the survival of patients with refractory VF or pulseless VT compared with CCPR.[5,6,25] However, we should consider the overlap between ECPR capabilities and other hospital characteristics, such as PCI capability and level of intensive care.[17,20] Therefore, we conducted additional analyses in order to evaluate whether other hospital characteristics (24/7 PCI capabilities and certified level of intensive care) were associated with patient outcomes. Inconsistent with previous observational studies, no significant association was evident between these hospital characteristics and favourable neurologic outcomes.[12–15] Our results suggest that, regardless of 24/7 PCI capability and certified intensive care level, patient outcomes may not be improved without a system designed for rapid implementation of ECPR. Considering these results, hospitals' ECPR capabilities might be the single independent identifier for the selection of hospitals for refractory VF or pulseless VT patients.

In the secondary analysis, results showed that the outcomes of OHCA patients with refractory VF or pulseless VT were similar between conditionally ECPR-capable and ECPR-incapable facilities. Because a 24/7 ECPR program requires specially-trained medical professionals and significant resources, the Canadian ECPR Research Working Group discussed the feasibility of offering ECPR during more restrictive hours (e.g. business hours).[26] The results suggest that 24/7 ECPR programs may be better than more restrictive programs. There are multifactorial reasons to explain the results. First, in a setting requiring time-sensitive and complicated interventions, we need enough experience to maintain sufficient provider skill levels. A similar situation was discussed in other emergency settings, such as trauma, ST-elevation myocardial infarction, and stroke.[10,27–29] Furthermore, a recent systematic review speculated that the outcome variation in the previous studies might be affected by the structure and experience of the team performing ECPR.[30] Second, ECPR in conditional settings may cause delays in implementation secondary to determination of inclusion.[31] The delay to implement ECPR has been reported as an important prognostic factor in several studies.[32–34] Finally, it is possible that ECPR was undertaken in conditionally ECPR-capable hospitals, though there has been a consensus that OHCA patients with presumed cardiac origin, such as refractory VF or pulseless VT, should receive ECPR.[6,35,36] Conditional centres may not be fully vested in their ECPR programs.

In the subgroup analyses, we found that younger age, shorter time to transport, and witnessed cardiac arrest were all positively associated with patient outcomes at a population level based on the results of risk differences. While our sample size was too small to make a strong inference from subgroup analyses, previous studies also revealed similar associations.[32–34,36,37] Considering these results, the benefit of treating OHCA patients with ECPR appears to be maximised in the patients described above. We cannot explain why the effect of ECPR was attenuated in those who received bystander CPR, though this might be explained partially by the fact that without appropriate bystander CPR, patients with refractory VF or pulseless VT might not benefit from highly advanced interventions.[7]

The strength of the present study is that we used a population-based registry in a relatively large city, where all data of transported OHCA patients were collected using a uniform method of data collection and consistent definitions. Such a registry is suitable for assessing the association between patient outcomes and regional hospitals' characteristics to minimise potential sources of selection bias. Further, we estimated the adjusted risk difference by inverse probability weighting using a propensity score to deal with potential confounding factors.

This observational study has several limitations. First, in-hospital treatment information was not available. Although our main purpose was to evaluate whether the receiving hospitals' ECPR capabilities are associated with patient outcomes, there is a need for further study to evaluate which in-hospital factors are associated with patient outcomes. Second, it may be difficult to generalise our results to other communities due to differences in EMS systems and the geospatial locations of the regional hospitals. These differences must be considered, when our results are implemented in different communities. For example, a "scoop and run" strategy is generally accepted in Japanese EMS protocols, while the "stay and treat" approach is more common in several countries. Third, we did not assess the risk caused by bypassing the nearest hospitals. To establish regional systems of care, we need further studies to compare the two strategies, namely, transporting the patient to the nearest hospital, or bypassing the hospital and transporting the patient to an ECPR facility. Finally, our findings might be confounded by unmeasured factors. We dealt with potential confounders using a propensity score and confirmed that the covariate balance was well controlled between patients transported to ECPR facilities and those who were transported to CCPR facilities. However, we could not ascertain whether unmeasured confounding factors were balanced between the groups.

Conclusions

In conclusion, this population-based cohort study demonstrated that patients transported to ECPR-capable facilities had better outcomes than those transported to CCPR facilities. When transported to conditionally ECPR-capable facilities and ECPR-incapable facilities, patient outcomes were poorer than when they were transported to ECPR capable facilities. We should therefore take ECPR capabilities into consideration in order to develop regional systems of care for OHCA patients who have refractory VF or pulseless VT.

Conflicts of interest

None.

Sources of funding

None.

Acknowledgements

We thank all EMS personnel and related health-care providers involved in this study. We are especially indebted to the staff of Kobe City Fire Department for their support, and to Mr. Geoff Rupp for his assistance in English editing.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.resuscitation.2019.01.013.

REFERENCES

1. Sakai T, Iwami T, Tasaki O, et al. Incidence and outcomes of out-of-hospital cardiac arrest with shock-resistant ventricular fibrillation: data from a large population-based cohort. Resuscitation 2010;81:956–61.
2. Bernard SA, Gray TW, Buist MD, et al. Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia. N Engl J Med 2002;346:557–63.
3. Hypothermia after Cardiac Arrest Study Group. Mild therapeutic hypothermia to improve the neurologic outcome after cardiac arrest. N Engl J Med 2002;346:549–56.
4. Callaway CW, Donnino MW, Fink EL, et al. Part 8: Post-cardiac arrest care: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation 2015;132:S465–82.
5. Siao FY, Chiu CC, Chiu CW, et al. Managing cardiac arrest with refractory ventricular fibrillation in the emergency department: conventional cardiopulmonary resuscitation versus extracorporeal cardiopulmonary resuscitation. Resuscitation 2015;92:70–6.
6. Sakamoto T, Morimura N, Nagao K, et al. Extracorporeal cardiopulmonary resuscitation versus conventional cardiopulmonary resuscitation in adults with out-of-hospital cardiac arrest: a prospective observational study. Resuscitation 2014;85:762–8.
7. Hutin A, Abu-Habsa M, Burns B, et al. Early ECPR for out-of-hospital cardiac arrest: best practice in 2018. Resuscitation 2018;130:44–8.
8. Link MS, Berkow LC, Kudenchuk PJ, et al. Part 7: Adult advanced cardiovascular life support: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation 2015;132:S444–64.
9. Soar J, Nolan JP, Bottiger BW, et al. European Resuscitation Council guidelines for resuscitation 2015: section 3. Adult advanced life support. Resuscitation 2015;95:100–47.
10. Nichol G, Aufderheide TP, Eigel B, et al. Regional systems of care for out-of-hospital cardiac arrest: a policy statement from the American Heart Association. Circulation 2010;121:709–29.
11. Kronick SL, Kurz MC, Lin S, et al. Part 4: Systems of care and continuous quality improvement: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation 2015;132:S397–413.
12. Wnent J, Seewald S, Heringlake M, et al. Choice of hospital after out-of-hospital cardiac arrest—a decision with far-reaching consequences: a study in a large German city. Crit Care 2012;16:R164.
13. Mumma BE, Diercks DB, Wilson MD, Holmes JF. Association between treatment at an ST-segment elevation myocardial infarction center and neurologic recovery after out-of-hospital cardiac arrest. Am Heart J 2015;170:516–23.
14. Matsuyama T, Kiyohara K, Kitamura T, et al. Hospital characteristics and favourable neurological outcome among patients with out-of-hospital cardiac arrest in Osaka, Japan. Resuscitation 2017;110:146–53.

15. Kajino K, Iwami T, Daya M, et al. Impact of transport to critical care medical centers on outcomes after out-of-hospital cardiac arrest. Resuscitation 2010;81:549–54.
16. Stub D, Smith K, Bray JE, Bernard S, Duffy SJ, Kaye DM. Hospital characteristics are associated with patient outcomes following out-of-hospital cardiac arrest. Heart 2011;97:1489–94.
17. Cournoyer A, Notebaert E, de Montigny L, et al. Impact of the direct transfer to percutaneous coronary intervention-capable hospitals on survival to hospital discharge for patients with out-of-hospital cardiac arrest. Resuscitation 2018;125:28–33.
18. Chocron R, Bougouin W, Beganton F, et al. Are characteristics of hospitals associated with outcome after cardiac arrest? Insights from the Great Paris registry. Resuscitation 2017;118:63–9.
19. Callaway CW, Schmicker R, Kampmeyer M, et al. Receiving hospital characteristics associated with survival after out-of-hospital cardiac arrest. Resuscitation 2010;81:524–9.
20. Hunter BR, O'Donnell DP, Kline JA. Receiving hospital characteristics associated with survival in patients transported by emergency medical services after out-of-hospital cardiac arrest. Acad Emerg Med 2016;23:905–9.
21. Jacobs I, Nadkarni V, Bahr J, et al. Cardiac arrest and cardiopulmonary resuscitation outcome reports: update and simplification of the Utstein templates for resuscitation registries. A statement for healthcare professionals from a task force of the international liaison committee on resuscitation (American Heart Association, European Resuscitation Council, Australian Resuscitation Council, New Zealand Resuscitation Council, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation, Resuscitation Council of Southern Africa). Resuscitation 2004;63:233–49.
22. Japanese Resuscitation Council. 2015 Japanese guidelines for emergency care and cardiopulmonary resuscitation. Tokyo: Igaku-Shoin; 2016.
23. Ministry of Health, Labour and Welfare. Evaluation of the quality of Critical Care Medical Center (in Japanese). (Accessed 24 October 2018, at https://www.mhlw.go.jp/stf/seisakunitsuite/bunya/0000063335.html).
24. Cohen J. Statistical power analysis for the behavioral sciences. Hillsdale, New Jersey: Lawrence Erlbaum Associates; 1988.
25. Kim SJ, Kim HJ, Lee HY, Ahn HS, Lee SW. Comparing extracorporeal cardiopulmonary resuscitation with conventional cardiopulmonary resuscitation: a meta-analysis. Resuscitation 2016;103:106–16.
26. Brooks SC, Shemie SD, Torrance S, et al. Barriers and opportunities related to extracorporeal cardiopulmonary resuscitation for out-of-hospital cardiac arrest in Canada: a report from the first meeting of the Canadian ECPR Research Working Group. CJEM 2018;1–11.
27. Sewalt CA, Wiegers EJA, Venema E, et al. The volume-outcome relationship in severely injured patients: a systematic review and meta-analysis. J Trauma Acute Care Surg 2018;85:810–9, doi:http://dx.doi.org/10.1097/TA.0000000000002043.
28. Canto JG, Every NR, Magid DJ, et al. The volume of primary angioplasty procedures and survival after acute myocardial infarction. National Registry of Myocardial Infarction 2 Investigators. N Engl J Med 2000;342:1573–80.
29. Saposnik G, Baibergenova A, O'Donnell M, Hill MD, Kapral MK, Hachinski V. Hospital volume and stroke outcome: does it matter? Neurology 2007;69:1142–51.
30. Beyea MM, Tillmann BW, Iansavichene AE, Randhawa VK, Van Aarsen K, Nagpal AD. Neurologic outcomes after extracorporeal membrane oxygenation assisted CPR for resuscitation of out-of-hospital cardiac arrest patients: a systematic review. Resuscitation 2018;130:146–58.
31. Choi DH, Kim YJ, Ryoo SM, et al. Extracorporeal cardiopulmonary resuscitation among patients with out-of-hospital cardiac arrest. Clin Exp Emerg Med 2016;3:132–8.
32. Kim SJ, Jung JS, Park JH, Park JS, Hong YS, Lee SW. An optimal transition time to extracorporeal cardiopulmonary resuscitation for predicting good neurological outcome in patients with out-of-hospital cardiac arrest: a propensity-matched study. Crit Care 2014;18:535.
33. Haneya A, Philipp A, Diez C, et al. A 5-year experience with cardiopulmonary resuscitation using extracorporeal life support in non-postcardiotomy patients with cardiac arrest. Resuscitation 2012;83:1331–7.
34. Kagawa E, Inoue I, Kawagoe T, et al. Assessment of outcomes and differences between in- and out-of-hospital cardiac arrest patients treated with cardiopulmonary resuscitation using extracorporeal life support. Resuscitation 2010;81:968–73.
35. Brooks SC, Anderson ML, Bruder E, et al. Part 6: Alternative techniques and ancillary devices for cardiopulmonary resuscitation: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation 2015;132:S436–43.
36. Debaty G, Babaz V, Durand M, et al. Prognostic factors for extracorporeal cardiopulmonary resuscitation recipients following out-of-hospital refractory cardiac arrest. A systematic review and meta-analysis. Resuscitation 2017;112:1–10.
37. Goto T, Morita S, Kitamura T, et al. Impact of extracorporeal cardiopulmonary resuscitation on outcomes of elderly patients who had out-of-hospital cardiac arrests: a single-centre retrospective analysis. BMJ Open 2018;8:e019811.