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Clinical paper

Transient return of spontaneous circulation related to favourable outcomes in out-of-hospital cardiac arrest patients resuscitated with extracorporeal cardiopulmonary resuscitation: A secondary analysis of the SAVE-J II study

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Abbreviations: CI, confidence interval, CPA, cardiopulmonary arrest, CPC, cerebral performance category, CPR, cardiopulmonary resuscitation, ECMO, extracorporeal cardiopulmonary membrane oxygenation, EMS, emergency medical service, OHCA, out-of-hospital cardiac arrest, OR, odds ratio, ROSC, return of spontaneous circulation, ECPR, extracorporeal cardiopulmonary resuscitation

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Abstract

Aim: This study aimed to investigate the relationship between transient return of spontaneous circulation (ROSC) before extracorporeal membrane oxygenation (ECMO) initiation and outcomes in out-of-hospital cardiac arrest (OHCA) patients, who were resuscitated with extracorporeal cardiopulmonary resuscitation (ECPR).

Methods: This study was a secondary analysis of the SAVE-J II study, which was a retrospective multicentre registry study involving 36 participating institutions in Japan. We classified patients into two groups according to the presence or absence of transient ROSC before ECMO initiation. Transient ROSC was defined as any palpable pulse of ≥1 min before ECMO initiation. The primary outcome was favourable neurological outcomes (cerebral performance categories 1–2).

Results: Of 2,157 patients registered in the SAVE-J II study, 1,501 met the study inclusion criteria; 328 (22%) experienced transient ROSC before ECMO initiation. Patients with transient ROSC had better outcomes than those without ROSC (favourable neurological outcome, 26% vs 12%, $P < 0.001$; survival to hospital discharge, 46% vs 24%, respectively; $P < 0.001$). A Kaplan–Meier plot showed better survival in the transient ROSC group (log-rank test, $P < 0.001$). In multiple logistic analyses, transient ROSC was significantly associated with favourable neurological outcomes and survival (favourable neurological outcomes, adjusted odds ratio, 3.34 [95% confidence interval, 2.35–4.73]; survival, adjusted odds ratio, 3.99 [95% confidence interval, 2.95–5.40]).

Conclusions: In OHCA patients resuscitated with ECPR, transient ROSC before ECMO initiation was associated with favourable outcomes. Hence, transient ROSC is a predictor of improved outcomes after ECPR.

Keywords: Out-of-hospital cardiac arrest, Extracorporeal cardiopulmonary resuscitation, Transient return of spontaneous circulation

Introduction

Patient outcomes for those with out-of-hospital cardiac arrest (OHCA) remain poor; however, key predictors associated with favourable outcomes in OHCA patients have been reported, including younger age, shorter arrest duration, witnessed arrest, bystander cardiopulmonary resuscitation (CPR), and shockable initial cardiac rhythm.[1–6] Achieving return of spontaneous circulation (ROSC) in the field is also known to be a particularly strong predictor of favourable outcomes.[1–6] However, some OHCA patients experience refractory cardiopulmonary arrest (CPA), i.e., they do not achieve ROSC through conventional CPR. Even those who achieve transient ROSC with conventional CPR may experience re-arrest, leading to refractory CPA.[7]

It has been reported that extracorporeal cardiopulmonary membrane oxygenation (ECMO) assisted resuscitation, also known as extracorporeal resuscitation (ECPR), is potentially effective for refractory CPA.[8–22] The 2020 American Heart Association guidelines for Class IIb recommend the use of ECPR for refractory CPA with a potentially reversible aetiology.[8] While ideal candidates for ECPR initiation and its optimal timing are currently being investigated, the outcome-related factors in patients who receive ECPR are similar to those of OHCA patients who achieve ROSC with conventional CPR, such as younger age, shorter arrest duration (time from arrest to ECMO initiation), witnessed arrest, and shockable initial cardiac rhythm.[9–22] In addition, recent ECPR-related studies have reported that the experience of transient ROSC before ECMO initiation was also associated with favourable outcomes in refractory CPA; however, the numbers of included patients were relatively small. Furthermore, details concerning when transient ROSC was achieved (before or after hospital arrival) were not reported in these studies.[18–21] Therefore, the relationship between the presence or absence of transient ROSC before ECMO initiation and outcomes has not been well understood. Moreover, even if transient ROSC is achieved, it remains largely unclear what timing concerning ROSC, i.e., before or after hospital arrival, is most prognostic.

To address this knowledge gap, we used the largest ECPR registry data of OHCA in Japan to investigate the relationship between transient ROSC during resuscitation before ECMO initiation and outcomes in OHCA patients resuscitated with ECPR.[21]

Methods

Study design and setting

This study was a secondary analysis of the SAVE-J II study, which was a retrospective multicentre registry study of OHCA patients resuscitated with ECPR, involving 36 participating institutions in Japan.[22] The study design and data collection methods of the SAVE-J II study have been previously described.[22] The SAVE-J II study included consecutive OHCA patients aged ≥18 years who were resuscitated with ECPR. They were admitted to the participating institutions between 1 January 2013 and 31 December 2018. In this study, ECPR was defined as resuscitation using ECMO for patients with refractory CPA. The inclusion criterion was cardiac arrest when ECMO was initiated. The exclusion criteria were as follows: (1) patients who were transferred from another hospital; (2) patients with sustained ROSC when ECMO was initiated; and (3) aetiologies of arrest comprising non-cardiac conditions, such as acute aortic syndromes, hypothermia, primary cerebral disorders, infection, drug intoxication, trauma, suffocation, and drowning. In addition, we excluded patients with a time of >60 minutes from hospital arrival to ECMO initiation, because these patients may have achieved ROSC for a long period before ECMO initiation. We also excluded patients with missing data on transient ROSC, timing of ROSC, arrest to ECMO initiation time interval, and outcomes.

The SAVE-J II study was registered at the University Hospital Medical Information Network Clinical Trials Registry and the Japanese Clinical Trial Registry (registration number: UMIN000036490). This study was approved by the Institutional Review Board of Kagawa University (approval number: 2018-110) and each participating institution, including the Hiroshima City Hiroshima Citizens Hospital (approval number: 2019-80). This secondary analysis of de-identified data was approved by the Institutional Review Board of Hiroshima City Hiroshima Citizens Hospital (approval number: 2021-157). The need for written informed consent was waived due to the retrospective nature of this study.

The following patient data were collected from the SAVE-J II study database: age, sex, incidence of witnessed cardiac arrest and bystander-initiated CPR, initial cardiac rhythm at the scene, time interval (call or time of arrests witnessed by the emergency medical service [EMS] to hospital arrival and hospital arrival to ECMO initiation), aetiology of cardiac arrest, timing of ROSC (pre-hospital [before hospital arrival] only, in-hospital [after hospital arrival] only, or both pre- and in-hospital) in patients with transient ROSC, and outcomes. Time interval was calculated from the emergency call for those who arrested before EMS arrival, and calculated from arrest witnessed by EMS for those who arrested after EMS arrival to hospital arrival and ECMO initiation. The definition of cardiac arrest aetiology was based on a previous report.[21] Initial shockable rhythm was defined as ventricular fibrillation or pulseless ventricular tachycardia. Transient ROSC was defined as any palpable pulse or measurable blood pressure $\geq$1 min before ECMO initiation, either before and after hospital arrival.[22] The primary outcome was a favourable neurological outcome, and the secondary outcome was survival to hospital discharge. A favourable neurological outcome was defined as a cerebral performance category (CPC) of 1–2, whereas an unfavourable outcome was defined as a CPC of 3–5.

Statistical analysis

The study patients were divided into two groups according to the presence or absence of transient ROSC before ECMO initiation. We examined the relationship between transient ROSC and patient characteristics and outcomes. To investigate the association between transient ROSC and the outcomes, we performed univariate analyses. Continuous variables were presented as medians and interquartile ranges (IQR), whereas categorical variables were presented as numbers and percentages. Continuous variables were compared using a Mann–Whitney U test, and categorical variables were compared using chi-squared or Fisher's exact tests. We also depicted the association between transient ROSC and survival to hospital discharge using Kaplan–Meier survival curves, with a log-rank test to present the differences. Additionally, we performed multiple logistic analyses adjusted for patient characteristics and cardiac arrest status. Covariates were selected based on previous studies, including age, sex, bystander witness, bystander-initiated CPR, initial cardiac rhythm (shockable or not), time interval from call or EMS witnessed to ECMO initiation, and the causes of cardiac arrest (cardiac causes or not).[9–22] Data were reported as odds ratios (ORs) with 95% confidence intervals (CIs). For the subgroup analysis, we selected only patients who had transient ROSC. We stratified the patients according to timing of transient ROSC (pre-hospital only [group 1], in-hospital only [group 2], or both pre and in-hospital [group 3]), and the categories were mutually exclusive. We then compared patient characteristics and outcomes. Continuous variables were compared using a Kruskal–Wallis test, and categorical variables were compared using a chi-squared test. Furthermore, we performed multiple logistic analyses adjusted for patient characteristics and cardiac arrest status. Covariates were selected as in the primary analysis. All statistical analyses were performed using R software package version 4.0.2 (R Foundation for Statistical Computing, Vienna, Austria). Statistical significance was set at two-sided $P < 0.05$.

Results

Patient characteristics

Of 2,157 patients registered in the SAVE-J II study database, 1,501 met the inclusion criteria. Among 1,501 patients, 328 (22%) experienced transient ROSC before ECMO initiation (Fig. 1). The median age was 60 (IQR, 49–68) years, and 1,270 (85%) patients were men. A total of 1,194 (80%) arrests were witnessed by a bystander, and 868 (58%) received bystander-initiated CPR. Of all the patients, 1,043 (70%) had a shockable initial cardiac rhythm, and the median time from call or EMS witnessed to ECMO initiation was 54 min (IQR, 45–65 min). The cause of arrest in 1,289 (86%) patients was cardiac, including 885 (59%) acute coronary syndrome instances, 212 (14%) arrhythmias, 90 (6%) myopathies, and 102 (7%) other cardiac causes. In total, 221 (15%) patients had favourable neurological outcomes, and 435 (29%) survived to hospital discharge.

Comparisons between patients with and without transient ROSC before ECMO initiation

Table 1 shows a comparison between patients with and without transient ROSC before ECMO initiation. Age was higher (median, 63 years [IQR, 52–70] vs 60 [IQR, 48–68] years, $P = 0.001$), male sex was less frequent (80% vs 86%, $P = 0.01$), EMS witnessed arrests were more frequent (14% vs 10%, $P = 0.04$), initial shockable rhythm was less frequent (63% vs 72%, $P < 0.001$), and time from call or EMS witnessed to ECMO initiation was longer (median, 59 min [49–70] vs 53 min [IQR, 44–63], $P < 0.001$) in patients with transient ROSC. The time range from call or EMS witnessed to ECMO was 15–107 minutes in patients with transient ROSC, and 14–104 minutes in patients without transient ROSC. Cardiac causes of arrest were less frequent in patients with transient ROSC than in those without transient ROSC (83% vs 87%, $P < 0.001$). Further, patients with transient ROSC had significantly better outcomes than those without transient ROSC (favourable neurological outcome, 26% vs 12%, $P < 0.001$; survival to hospital discharge, 46% vs 24%, respectively; $P < 0.001$). The Kaplan–Meier plot showed significantly better survival in the transient ROSC group (log-rank test, $P < 0.001$) (Fig. 2).

Relationship between transient ROSC and outcomes

Table 2 shows the relationship between transient ROSC and outcomes using univariate and multivariate analyses. Transient ROSC was significantly associated with favourable neurological outcomes and survival (favourable neurological outcomes: adjusted OR, 3.34 [95% CI 2.35–4.73]; survival: adjusted OR, 3.99 [95% CI 2.95–5.40]). The full adjusted model is presented in Supplementary Table A1.

Comparisons among three groups divided according to timing of transient ROSC before ECMO initiation

Among 328 patients with transient ROSC, 102 (31%) achieved ROSC in the pre-hospital phase only (before hospital arrival: group 1), 159 (48%) achieved ROSC in the in-hospital phase only (after hospital arrival: group 2), and 67 (20%) achieved ROSC both pre- and in-hospital (group 3) (Table 3). Among these three groups, there

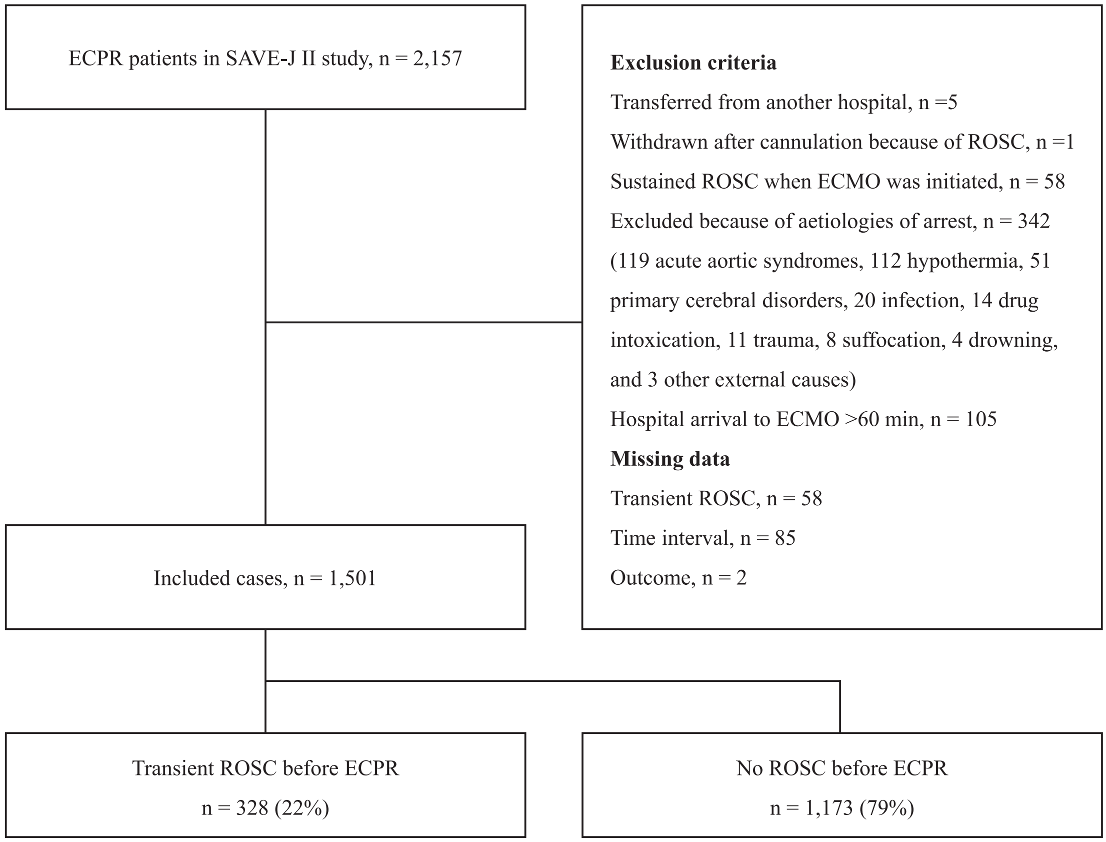

Fig. 1 – Patient selection flowchart ECMO, extracorporeal membrane oxygenation; EPCR, extracorporeal cardiopulmonary resuscitation; ROSC, return of spontaneous resuscitation.

was no difference in age, frequency of witnessed arrest, shockable initial cardiac rhythm, or aetiology of arrest. Further, bystander-initiated CPR was less frequent in group 2 than in the other groups (64%, 53%, and 72% in groups 1, 2, and 3, respectively; $P = 0.02$). Call or EMS witnessed to ECMO initiation time was the longest in group 3 (57 min [IQR 47–67], 59 min [IQR 49–70], and 63 min [IQR 53–75] in groups 1, 2, and 3, respectively; $P = 0.03$). The frequency of favourable neurological outcomes (23%, 25%, and 33% in groups 1, 2, and 3, respectively; $P = 0.30$) and survival to hospital discharge (41%, 45%, and 58% in groups 1, 2, and 3, respectively; $P = 0.07$) did not differ among the three groups. The relationship between the timing of transient ROSC and outcomes in univariate and multivariate analyses showed that group 3 had a significantly higher chance of survival to hospital discharge than group 1 (unadjusted OR, 1.99 [95% CI 1.06–3.72]; adjusted OR, 2.50 [95% CI 1.21–5.14]) (Table 4). The full adjusted model is presented in Supplementary Table A2.

Discussion

The major finding of this study was that, according to data obtained from the largest ECPR registry of OHCA in Japan, transient ROSC was independently associated with favourable outcomes in ECPR patients, regardless of the timing of transient ROSC.

ECPR has been reported as an advanced resuscitation technique for cases of refractory CPA that do not achieve ROSC with conventional CPR.[8–25] Previous studies have reported that ECPR improved neurological outcomes and survival; however, its benefit is limited and it should be considered for selected patients with reversible causes of CPA and potential for survival.[8–12] Selecting patients who are likely to benefit from ECPR is important and most ECPR studies have included younger patients with fewer comorbidities. Some studies restricted their inclusion criteria for patients with ECPR and witnessed arrest, shockable initial cardiac rhythms, shorter CPR duration, and required a certain period of conventional CPR prior to ECMO initiation;[9,10,23,24] however, the vast majority of the ECPR studies involved single centres with varying inclusion criteria and settings. Therefore, there is currently no strong evidence to define who the "selected patients" should comprise.[8] Therefore, there is a need to identify patients who are likely to benefit from ECPR.

The time from cardiac arrest to ROSC is known to be one of the key factors associated with favourable outcomes in patients who experience OHCA.[1–6] Conventional CPR is most effective within the first 20 min, at which time 90% of patients with favourable neurological outcomes have achieved ROSC.[1] Moreover, prolonged duration of CPR decreases the chances of survival. The acceptable duration (upper limit) of CPR for the achievement of favourable outcomes is approximately 40 min in patients who receive conventional CPR.[1–3] OHCA patients who have achieved transient ROSC with conventional CPR may experience re-arrest, which is known to be associated with a worse outcome;[7] whereas, OHCA patients who had experienced transient ROSC before hospital arrival and finally achieved sustained ROSC were reported to have favourable outcomes even if their CPR duration was ≥40 min.[4,11,12] Similarly, in patients with ECPR, the time from cardiac arrest to ECMO initiation

Table 1 – Comparisons between patients with and without transient ROSC prior to ECMO initiation.

	Transient ROSC *n* = 328	No ROSC *n* = 1,173	*P*-value
Age, years	63 (52–70)	60 (48–68)	0.001
Males	263 (80)	1,007 (86)	0.01
Witnessed arrest	262 (80)	932 (80)	0.93
EMS witnessed arrest	46 (14)	118 (10)	0.04
Bystander-initiated CPR	197 (61)	671 (58)	0.40
Initial cardiac rhythm			<0.001
Shockable	202 (63)	841 (72)	
Pulseless electrical activity	101 (31)	239 (21)	
Asystole	20 (6)	85 (7)	
Cardiac rhythm at ECMO initiation			<0.001
Shockable	171 (52)	635 (54)	
Pulseless electrical activity	133 (41)	340 (29)	
Asystole	24 (7)	198 (17)	
Call or EMS witnessed to hospital arrival, min	30 (23–38)	30 (24–37)	0.89
Hospital arrival to ECMO, min	27 (19–37)	21 (15–29)	<0.001
Call or EMS witnessed to ECMO, min	59 (49–70)	53 (44–63)	<0.001
Aetiology of arrest			<0.001
Cardiac causes of arrest	272 (83)	1,017 (87)	
Acute coronary syndrome	194 (59)	691 (59)	
Arrhythmia	48 (15)	164 (14)	
Myopathy	12 (4)	78 (7)	
Other cardiac causes	18 (6)	84 (7)	
Non-cardiac causes of arrest	39 (12)	65 (6)	
Pulmonary embolism	31 (10)	28 (2)	
Other non-cardiac causes	8 (2)	37 (3)	
Unknown	17 (5)	91 (8)	
Favourable neurological outcomes	85 (26)	136 (12)	<0.001
Survival to hospital discharge	152 (46)	283 (24)	<0.001

Data are presented as the number (column %) of patients or median (interquartile range).

CPR, cardiopulmonary resuscitation; EMS, emergency medical service; ECMO, extracorporeal membrane oxygenation; ROSC, return of spontaneous circulation.

The following data were missing: 2 witnessed arrest, 3 EMS witnessed arrest, 17 bystander-initiated CPR, and 13 initial cardiac rhythm.

could be an important factor related to their outcomes.[11–16,18,19,22] ECPR may enhance survival after prolonged arrest duration; however, previous studies have suggested that >60 min of CPR duration was associated with poor outcomes even with ECPR.[12,13,18,19,22,25] It is clear that prolonged cardiac arrest without ROSC precludes the possibility of ECPR; however, some reports have described patients with ECPR having had favourable outcomes even with a CPR time >60 min.[11,12,14,16,18,19,22,25] As mentioned above, re-arrest, patients who have previously achieved ROSC but who experience arrest again during resuscitation, is associated with a worse outcome;[7] however, this is only for CPA patients resuscitated with conventional CPR. Transient ROSC has been associated with favourable outcomes in patients with ECPR, with approximately 7–27% of such patients achieving transient ROSC before ECMO initiation;[18–21] however, the details of ROSC during CPR were not clearly reported and CPR duration was defined differently among these studies, with some defining it as the time from CPA to ROSC or ECMO initiation, while others defined it as the sum of times performing CPR. Patients resuscitated with ECPR who had received prolonged CPR may have experienced transient ROSC during conventional CPR, which may have led to favourable outcomes.

Our study found that patients with transient ROSC before ECMO initiation had more frequent favourable neurological outcomes and survival than those without, even though they included older patients, less frequent shockable initial cardiac rhythm, and longer call-to-

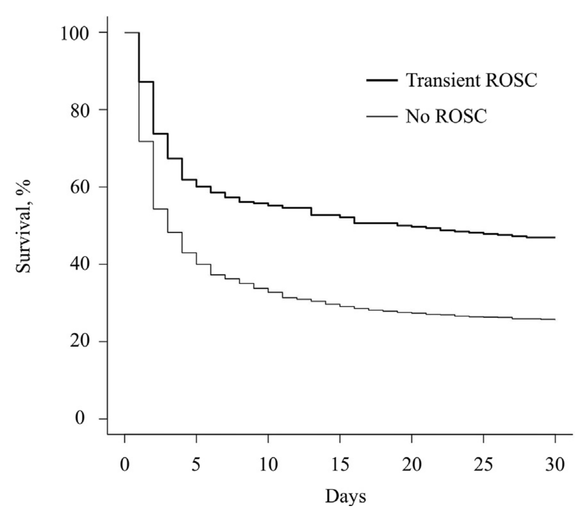

Fig. 2 – Kaplan–Meier survival curves with the log-rank test for presenting the differences between patients with and without transient ROSC The bold line indicates patients with transient ROSC and the thin line indicates patients without transient ROSC. The Kaplan–Meier plot showed significantly better survival in the transient ROSC group (log-rank test, P < 0.001). ROSC, return of spontaneous circulation.

Table 2 – Unadjusted and adjusted association between transient ROSC and clinical outcomes.

	Unadjusted odds ratios		Adjusted odds ratios*	
	Odds ratio (95% CI)	*P*-value	Odds ratio (95% CI)	*P*-value
Favourable neurological outcomes				
No ROSC	1 (Reference)		1 (Reference)	
Transient ROSC	2.67 (1.94–3.65)	<0.001	3.34 (2.35–4.73)	<0.001
Survival to hospital discharge				
No ROSC	1 (Reference)		1 (Reference)	
Transient ROSC	2.71 (2.09–3.53)	<0.001	3.99 (2.95–5.40)	<0.001

CI, confidence interval; ROSC, return of spontaneous circulation.

* Adjusted according to age, sex, bystander witness, bystander-initiated cardiopulmonary resuscitation, initial cardiac rhythm (shockable or not), time interval from call or emergency medical service witnessed to extracorporeal membrane oxygenation initiation, and the causes of cardiac arrest (cardiac causes or not).

Table 3 – Comparisons among groups divided according to timing of transient ROSC.

	Pre-hospital only (Group 1) *n* = 102	In-hospital only (Group 2) *n* = 159	Pre- and in-hospital (Group 3) *n* = 67	*P*-value
Age, years	63 (51–71)	62 (53–69)	64 (55–70)	0.62
Males	77 (76)	132 (83)	54 (81)	0.33
Witnessed arrest	79 (78)	126 (79)	57 (85)	0.46
EMS witnessed arrest	15 (15)	20 (13)	11 (16)	0.71
Bystander-initiated CPR	65 (64)	85 (53)	47 (72)	0.02
Initial cardiac rhythm				0.82
Shockable	64 (63)	100 (63)	38 (60)	
Pulseless electrical activity	32 (32)	50 (31)	19 (30)	
Asystole	5 (5)	9 (6)	6 (10)	
Call or EMS witnessed to hospital arrival, min	33 (24–44)	28 (22–35)	33 (25–40)	0.001
Hospital arrival to ECMO, min	21 (14–31)	29 (21–40)	29 (22–41)	<0.001
Call or EMS witnessed to ECMO, min	57 (47–67)	59 (49–70)	63 (53–75)	0.03
Aetiology of arrest				0.36
Cardiac causes of arrest	88 (86)	131 (82)	53 (79)	
Acute coronary syndrome	63 (62)	90 (57)	41 (61)	
Arrhythmia	14 (14)	27 (17)	7 (10)	
Myopathy	4 (4)	4 (3)	4 (6)	
Other cardiac causes	7 (7)	10 (6)	1 (2)	
Non-cardiac causes of arrest	10 (10)	17 (11)	12 (18)	
Pulmonary embolism	7 (7)	15 (9)	9 (13)	
Other non-cardiac causes	3 (3)	2 (1)	3 (5)	
Unknown	4 (4)	11 (7)	2 (3)	
Favourable neurological outcome	23 (23)	40 (25)	22 (33)	0.30
Survival to hospital discharge	42 (41)	71 (45)	39 (58)	0.07

Data are presented as the number (column %) of patients or median (interquartile range).

CPR, cardiopulmonary resuscitation; ECMO, extracorporeal membrane oxygenation; EMS, emergency medical service; ROSC, return of spontaneous circulation.

The following data were missing: 3 bystander-initiated CPR, and 5 initial cardiac rhythm.

ECMO or EMS-witnessed-to-ECMO time. In addition, transient ROSC was independently associated with favourable outcomes, regardless of the timing of the ROSC (before and/or after hospital arrival). Moreover, even if transient ROSC was achieved for the first time after hospital arrival, there was a chance of good outcomes. In the subgroup analysis with groups divided according to the timing of ROSC, patients with transient ROSC both before and after hospital arrival (group 3) were more likely to survive to hospital discharge than patients with transient ROSC before hospital arrival only (group 1). This result may reflect that a higher frequency of transient ROSC or a longer total ROSC time before ECMO initiation is associated with favourable outcomes. The results of our study using data from the largest ECPR registry in Japan support findings in previous reports.[18–21] Inclusion criteria for ECPR were not defined in the SAVE-J II study, and OHCA patients who experienced transient ROSC may have been more likely to receive ECPR; however, transient ROSC could be a predictor of favourable outcomes in patients with ECPR. Therefore, ECPR should be considered if transient ROSC was achieved at any time even when the CPR duration was prolonged.

Table 4 – Unadjusted and adjusted association between timing of transient ROSC and clinical outcomes.

	Unadjusted odds ratios		Adjusted odds ratios*	
	Odds ratio (95% CI)	*P*-value	Odds ratio (95% CI)	*P*-value
Favourable neurological outcomes				
ROSC pre-hospital only (Group 1)	1 (Reference)		1 (Reference)	
ROSC in-hospital only (Group 2)	1.15 (0.64–2.08)	0.63	1.14 (0.59–2.18)	0.70
ROSC pre- and in-hospital (Group 3)	1.68 (0.84–3.35)	0.14	1.93 (0.88–4.20)	0.09
Survival to hospital discharge				
ROSC pre-hospital only (Group 1)	1 (Reference)		1 (Reference)	
ROSC in-hospital only (Group 2)	1.15 (0.70–1.91)	0.58	1.10 (0.62–1.94)	0.74
ROSC pre- and in-hospital (Group 3)	1.99 (1.06–3.72)	0.03	2.50 (1.21–5.14)	0.01

CI, confidence interval; ROSC, return of spontaneous circulation.

* Adjusted according to age, sex, bystander witness, bystander-initiated cardiopulmonary resuscitation, initial cardiac rhythm (shockable or not), time interval from call or emergency medical service witnessed to extracorporeal membrane oxygenation initiation, and the causes of cardiac arrest (cardiac causes or not).

This study had several limitations. First, this study was based on data obtained from the largest ECPR registry in Japan; however, the decision to perform ECPR was generally made on a case-by-case basis at each institution, and the inclusion criteria for ECPR were not determined. Second, since the SAVE-J II data did not include details of ROSC (number of ROSCs and sum of total CPR times), it remains unclear whether transient ROSC itself was associated with good outcomes or whether shorter total CPR time was associated with good outcomes. This is a major limitation of this study. The shorter arrest duration is essential for favorable outcomes, and the impact of transient ROSC differs depending on the length of ROSC status and total arrest time.[11–16,18,19,22] However, it can be difficult to assess the details of ROSC and total arrest time in the resuscitation setting especially when ROSC is achieved only transiently, and most previous ECPR studies have assessed low-flow-time (time from CPR start to ECMO initiation) for the outcome related factor of whether transient ROSC was achieved or not.[11–16,18,19,22] According to our study findings, transient ROSC is independently related to favorable outcomes and this is a very simple factor that can be easily recognized during resuscitation. For these reasons, we believe that OHCA patients who experience transient ROSC should be considered for prolonged resuscitation efforts and may be candidates for ECPR, even considering this limitation. Future studies are needed to assess the relationship between transient ROSC and outcomes using the total CPR time before ECMO initiation. Third, we excluded patients who achieved sustained ROSC when ECMO was initiated, and provided cardiac rhythms when ECMO was initiated; however, we do not know how many of the patients with pulseless electrical activity had cardiac motion without a palpable pulse because the SAVE-J II data did not contain the ultrasound data during resuscitation. Fourth, approximately-one-third of the SAVE-J II study patients were not included in this analysis, mostly because of the aetiologies of arrest. Finally, because the SAVE-J II study included patients with non-witnessed OHCA, we could not assess the effect of no-flow time (the time from collapse to CPR initiation) on the outcomes.

Conclusions

In OHCA patients resuscitated with ECPR, transient ROSC before ECMO initiation was independently associated with favourable outcomes. Transient ROSC should be evaluated as a potential indication for ECPR in OHCA patients with refractory CPA.

Conflicts of interest

The authors declare that they have no conflicts of interests.

Data statement

Please contact the author for data requests.

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Appendix A. Supplementary material

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