Available online at ScienceDirect

Resuscitation

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

Clinical paper

Clinical outcomes among out-of-hospital cardiac arrest patients treated by extracorporeal cardiopulmonary resuscitation: The CRITICAL study in Osaka

Yohei Okada[a,b], Taro Irisawa[c], Tomoki Yamada[d], Kazuhisa Yoshiya[e], Changhwi Park[f], Tetsuro Nishimura[g], Takuya Ishibe[h], Hitoshi Kobata[i], Takeyuki Kiguchi[j], Masafumi Kishimoto[k], Sung-Ho Kim[l], Yusuke Ito[m], Taku Sogabe[n], Takaya Morooka[o], Haruko Sakamoto[p], Keitaro Suzuki[q], Atsunori Onoe[r], Tasuku Matsuyama[s], Daisuke Kobayashi[a], Norihiro Nishioka[a], Satoshi Matsui[t], Satoshi Yoshimura[a], Shunsuke Kimata[a], Shunsuke Kawai[a], Yuto Makino[a], Kosuke Kiyohara[u], Ling Zha[t], Tetsuhisa Kitamura[t], Taku Iwami[a,]*

Abstract

Aim: Extracorporeal cardiopulmonary resuscitation (ECPR) is performed in refractory out-of-hospital cardiac arrest (OHCA) patients, and the eligibility has been conventionally determined based on three criteria (initial cardiac rhythm, time to hospital arrival within 45 minutes, and age <75 years) in Japan. Owing to limited information, this study descriptively determined neurological outcomes after applying the three criteria among OHCA patients who underwent ECPR.

Methods: This study conducted a post-hoc analysis of data from the Comprehensive Registry of Intensive Care for OHCA Survival (CRITICAL) study. This was a multi-institutional prospective observational study of OHCA patients in Osaka Prefecture, Japan. All adult (aged ≥18 years) OHCA patients with internal medical causes treated with ECPR between 1 July 2012 and 31 December 2019 were evaluated. We described one-month neurological favourable outcomes based on the three criteria (initial shockable, time to hospital arrival within 45 minutes, and age <75 years), and we compared them using the chi-square test.

Results: Among 18,379 patients screened from the CRITICAL study database, we included 517 OHCA patients treated by ECPR; 311 (60.2%) patients met all three criteria. Favourable neurological outcomes were as follows: patients meeting no or one criterion: 2.3% (1/43), those meeting two criteria: 8% (13/163), and those meeting all criteria: 16.1% (50/311) (P-value = 0.004).

Conclusions: In this study, approximately 60% of patients treated by ECPR met the three criteria (initial shockable, time to hospital arrival within 45 minutes, and age <75 years), and the greater the number of criteria met, the better were the neurological outcomes achieved.

Keywords: Ventricular fibrillation, ECPR, SAVE-J study, Out-of-hospital cardiac arrest

* Corresponding author at: Department of Preventive Services, School of Public Health, Kyoto University, Postal code: 606-8501, Yoshida-Konoe-Cho, Sakyo, Kyoto, Japan. Fax: +81 75 753 2424.

E-mail address: iwami.taku.8w@kyoto-u.ac.jp (T. Iwami).

https://doi.org/10.1016/j.resuscitation.2022.06.007

Received 12 April 2022; Received in Revised form 25 May 2022; Accepted 9 June 2022

Available online xxxx

Introduction

Extracorporeal cardiopulmonary resuscitation (ECPR) is one of the advanced procedures expected to improve the clinical outcomes of patients with refractory out-of-hospital cardiac arrest (OHCA).[1,2] However, ECPR is an invasive and expensive technique and requires abundant medical resources.[3,4] Therefore, there is a need for valid criteria for selecting appropriate candidates. Currently, clinical practice guidelines indicate the target population of ECPR vaguely, including 'selected patients experiencing cardiac arrest when conventional advanced life support measures fail'.[5,6] Furthermore, a previous systematic review reported several patterns of an ECPR protocol. In those patterns, there are no widely accepted criteria for deciding patient eligibility for ECPR.

In Japan, the first large prospective observational study (SAVE-J study) indicated the potentially favourable effect of ECPR by assessing 46 institutions from 2008 to 2011.[2,7] Since then, such a landmark study or clear guidelines have not yet been published to date in Japan. Thus, eligibility information reported in the SAVE-J study has been conventionally considered one of the important references in Japan.[2,7] Regarding the eligibility, the following three criteria have been particularly considered as being clinically important: (i) the initial cardiac rhythm is ventricular fibrillation (VF) or pulseless ventricular tachycardia (pVT), (ii) time duration from emergency call initiation to hospital arrival is within 45 minutes, and (iii) patient age younger than 75 years. However, little is known about clinically relevant outcomes when applying these three criteria. We believe that descriptive data of clinical outcomes based on these criteria will be valuable for considering the indications for ECPR. To address this knowledge gap, this study aimed to descriptively determine neurological outcomes in patients meeting those criteria and those not meeting the criteria, and the patient population included OHCA patients treated by ECPR.

Methods

The Ethics Committee of Kyoto University and each participating institution approved this study protocol (R1045), and the need for written informed consent was waived.

Study design and setting

This study was a post-hoc analysis of data extracted from the database of the Comprehensive Registry of Intensive Care for OHCA Survival (CRITICAL) study. This was a multi-institutional prospective observational study of OHCA patients in Osaka Prefecture, Japan. Pre-hospitalisation data were obtained from the All-Japan Utstein Registry of the Fire and Disaster Management Agency (FDMA).[8–11] In-hospital data were obtained from 15 tertiary critical care medical centres (CCMCs) and one non-CCMC community hospital with an emergency department, all located in Osaka Prefecture in Japan. Osaka Prefecture is an urban region with an area of 1,905 km^2, and it has a residential population of approximately 8.8 million in 2015.[12] In Osaka Prefecture, 7,500 OHCA cases occur every year,[13] and approximately one in four OHCA patients (approximately 2,000 cases or more) have been registered every year from 2012 to 2019. This registry is ongoing, with an undefined study period. In-hospital data were recorded by the physicians in charge of the patients and registered by the physicians or medical administrators using a predefined online form. Finally, the working group checked and confirmed the quality of the data. If the data were incomplete, then they were returned to each institution, and the data were then completed.[11] A detailed description of the All-Japan Utstein Registry of FDMA and the CRITICAL study has been previously published.[11]

Study participants

From the CRITICAL study database, we included all adult (aged ≥18 years) OHCA patients with internal medical causes who were treated with ECPR between 1 July 2012 and 31 December 2019. We defined ECPR as the initiation of cardiopulmonary bypass using veno-arterial extracorporeal membrane oxygenation through emergency cannulation of a large vein and artery for OHCA patients at hospital arrival during resuscitation before the return of spontaneous circulation (ROSC).[14] We excluded patients who met the following criteria: those who did not receive any resuscitation or treatment in the hospital, those with an unavailable or incomplete pre-hospital record, those aged ≤17 years or with unknown information on age, or those who collapsed due to cardiac arrest involving external causes such as trauma, drowning, or hanging, and those who did not undergo ECPR. The implementation of ECPR was decided by the physicians in charge of the patients or by each institution's protocol.

Outcomes

The primary outcome in this study was one-month survival with favourable neurological outcome, defined as Cerebral Performance Category 1 or 2.[10] The secondary outcome was one-month survival.

Measurements

From the CRITICAL study database, information on the following clinical variables was obtained: sex, age, cause of cardiac arrest (cardiogenic including presumed cardiogenic), witnessed by a bystander, CPR performed by a bystander, initial cardiac rhythm during contact with paramedics, a cardiac rhythm at hospital arrival, resuscitation time course, and outcomes. Resuscitation time courses were defined as the time from emergency call initiation for an ambulance to hospital arrival and to start ECPR in the hospital. Regarding the initial cardiac rhythm at contact with paramedics, if the data were missing because the patients had collapsed to cardiac arrest after contact with paramedics and during transport, we defined the case as 'Other'. Furthermore, the three criteria about patient age, initial cardiac rhythm, and time to hospital arrival used in the SAVE-J study were as follows: (i) age <75 years, (ii) initial cardiac rhythm: VF or pVT, and (iii) time from emergency call initiation to hospital arrival of <45 min.

Sample size and missing information

We did not estimate the sample size because our analysis was a secondary analysis of already available data.[15] For missing values, we did not perform the imputation method and described it as 'unknown' because this is a descriptive study.

Statistical analysis

Data of patients' characteristics are shown as medians and interquartile ranges (IQRs) for continuous variables and as numbers and percentages for categorical variables. First, we described the primary and secondary outcomes for each criterion. Second, we indicated the outcomes regarding the number of criteria met by the patient. Third, we determined the outcomes among patients who

Please cite this article as: Y. Okada, T. Irisawa, T. Yamada et al., Clinical outcomes among out-of-hospital cardiac arrest patients treated by extracorporeal cardiopulmonary resuscitation: The CRITICAL study in Osaka, Resuscitation, https://doi.org/10.1016/j.resuscitation.2022.06.007

met two of the three criteria to investigate the specific lacking criterion that had led to the worse outcome. For data analyses, we used Pearson's chi-square test or Kruskal–Wallis rank-sum test if appropriate. Statistical analyses were performed using R software (version 4.0.3). All statistical results were considered significant at a two-sided P value of <0.05.

Results

Patient characteristics

Among 18,379 patients identified from the CRITICAL study database, we included and analysed 517 OHCA patients treated by ECPR before ROSC. A flowchart of the study patient selection process is shown in Fig. 1. The Median (IQR) patient age was 60 [47–68] years, and men accounted for 438 (84.7%) patients among the total. Other patient characteristics are described in Table 1. One-month survival with a favourable neurological outcome and one-month survival were noted in 64 (12.4%) and 115 (22.2%) patients, respectively. Moreover, 311 (60.2%) patients met all the three criteria. The other details of patient characteristics are described in the Supplementary file (S-Table 1, 2, 3, and 4).

Table 1 – Characteristics of the study patients.

Characteristic	Overall, n = 517
Age	60.0 (47.0, 68.0)
Sex (men)	438 (85%)
Cardiac aetiology	463 (90%)
Witness	416 (80%)
Bystander CPR	220 (43%)
Initial cardiac rhythm	
VF/pVT	376 (73%)
PEA	83 (16%)
Asystole	38 (7.4%)
Other/Unknown	20 (3.9%)
Time from call initiation to hospital arrival	30 (25, 37)
Cardiac rhythm on hospital arrival	
VF/pVT	280 (54%)
PEA	136 (26%)
Asystole	101 (20%)
Time from call initiation to ECPR	53 (45, 64)

Continuous variables are summarised as median and interquartile range (IQR), whereas categorical variables are summarised as frequencies and percentages (%).

CPR: cardiopulmonary resuscitation, VF: ventricular fibrillation, pVT: pulseless ventricular tachycardia, PEA: pulseless electrical activity, ROSC: return of spontaneous circulation, ECPR: extracorporeal cardiopulmonary resuscitation.

Outcomes in terms of each criterion

One-month survival with a favourable neurological outcome in terms of age was as follows: age <75 years, 13.3% (62/466) patients, and ≥75 years, 3.9% (2/51) patients (P-value: 0.088). For time from emergency call to hospital arrival, the outcomes were <45 minutes, 13.1% (60/459) patients and ≥45 minutes, 6.9% (4/58) patients (P-value: 0.257). For initial cardiac rhythm, the outcomes were VF/pVT, 14.6% (55/376) patients and PEA/Asys/Others, 6.4% (9/141) patients (P-value: 0.017) (Fig. 2). Furthermore, one-month survival in terms of age was as follows: Age <75 years, 23.6% (110/466)

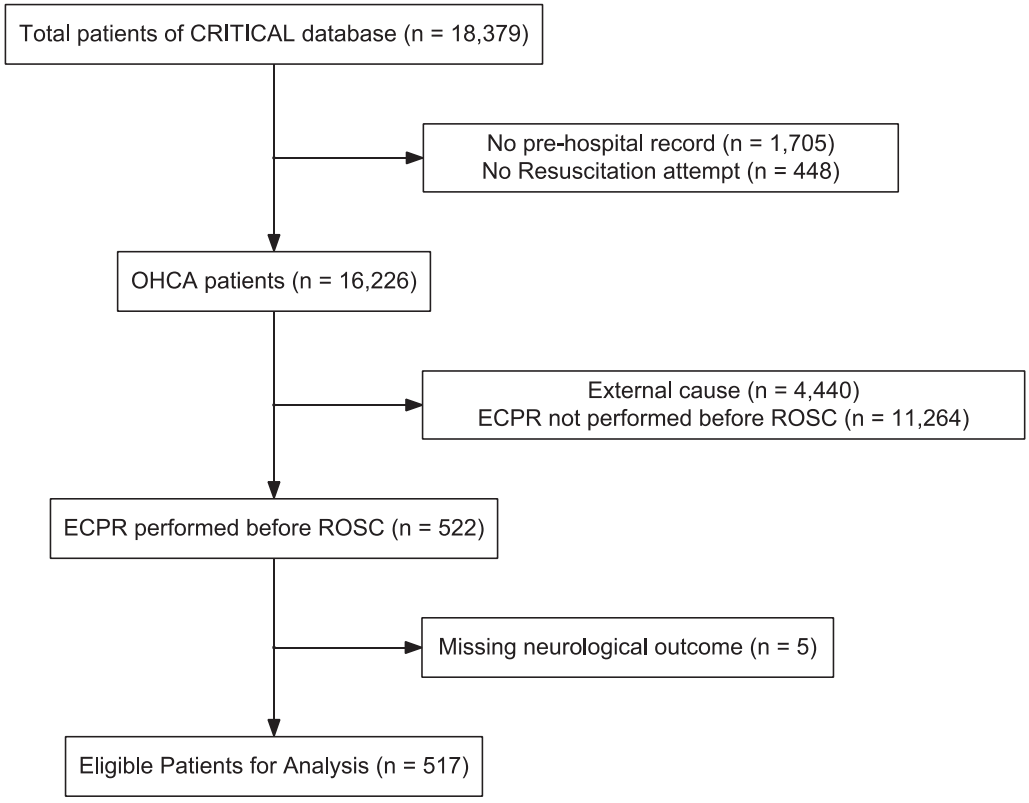

Fig. 1 – Flowchart of the study patient selection process. OHCA: out-of-hospital cardiac arrest, ECPR: extracorporeal cardiopulmonary resuscitation, ROSC: return of spontaneous circulation.

patients and ≥75 years, 9.8% (5/51) patients (P-value: 0.038). For time from emergency call to hospital arrival, the outcomes were <45 minutes, 23.3% (107/459) patients, and ≥45 minutes, 13.8% (8/58) patients (P-value: 0.140). For initial cardiac rhythm, the outcomes were VF/pVT, 26.6% (100/376) patients, and PEA/Asystole/Others, 10.6% (15/141) patients (P-value: <0.001) (Fig. 2).

Outcomes by number of meeting criteria

Patients were divided into three groups based on the number of criteria met (0–1, 2, and 3), and one-month survival with favourable neurological outcome based on this group was as follows: 0–1 criterion: 2.3% (1/43) patients, 2 criteria: 8% (13/163) patients, and 3 criteria: 16.1% (50/311) (P-value: 0.004) (Fig. 3). Furthermore, one-month survival based on this group was as follows: 0–1 criterion: 7% (3/43) patients, 2 criteria: 13.5% (22/163) patients, and 3 criteria: 28.9% (90/311) patients (P-value <0.001) (Fig. 3).

Outcomes in patients with two of the three criteria

Among the group that met two of the three criteria, one-month survival with favourable neurological outcomes was as follows: patients who did not meet the criterion of age <75 years, 3.6% (1/28); those who did not meet the criterion of time from emergency call initiation to hospital arrival of <45 minutes, 9.1% (3/33), and those who did not meet the criterion of initial VF/pVT, 8.8% (9/102). Furthermore, one-month survival outcomes were as follows: patients who did not meet the criterion of age <75 years, 10.7% (3/28), those not meeting the criterion of time from emergency call initiation to hospital arrival of <45 minutes, 15.2% (5/33), and those not meeting the criterion of initial VF/pVT, 13.7% (14/102).

Discussion

Key observation

This study descriptively indicated that approximately 60% of OHCA patients who were treated by ECPR and who met all the three criteria (initial shockable rhythm, time from emergency call initiation to hospital arrival being less than 45 minutes, and patient age younger than 75 years) and those meeting all the three criteria achieved better neurological outcomes than those not meeting the criteria. Our

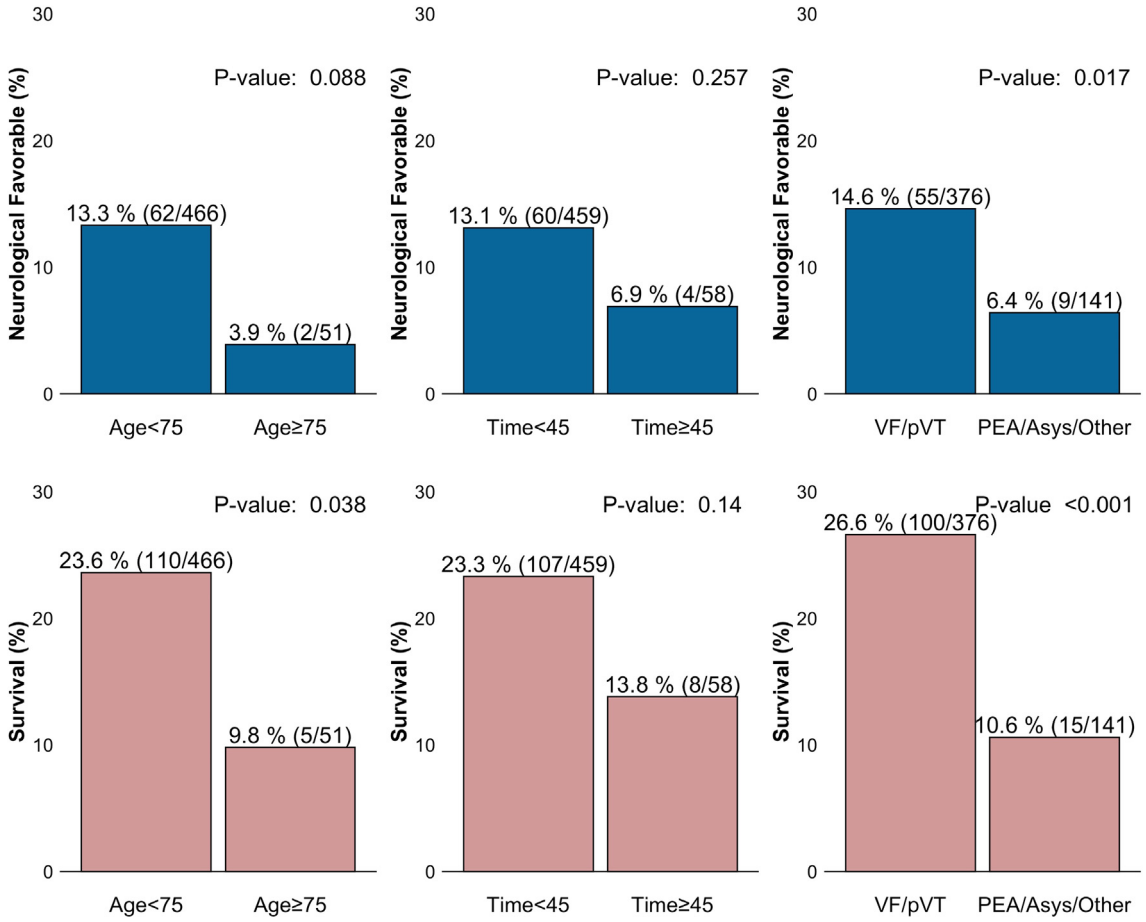

Fig. 2 – Outcomes in terms of each criterion. Upper: One-month favourable neurological outcome, Lower: One-month survival. The criterion is age, time from emergency call initiation to hospital arrival, and initial cardiac rhythm during contact with paramedics. Time duration of <45 minutes is defined as the time from emergency call initiation to hospital arrival within 45 minutes. Time duration of ≥45 minutes is defined as the time from emergency call initiation to hospital arrival beyond 45 minutes. VF/pVT is ventricular fibrillation (VF) or pulseless ventricular tachycardia (pVT). PEA/Asys/Other refers to pulseless electrical activity (PEA), asystole, or other. Other refers to no record about cardiac rhythm during contact with paramedics and almost all patients had cardiac arrest after paramedic contact. P-value: Pearson's chi-square test.

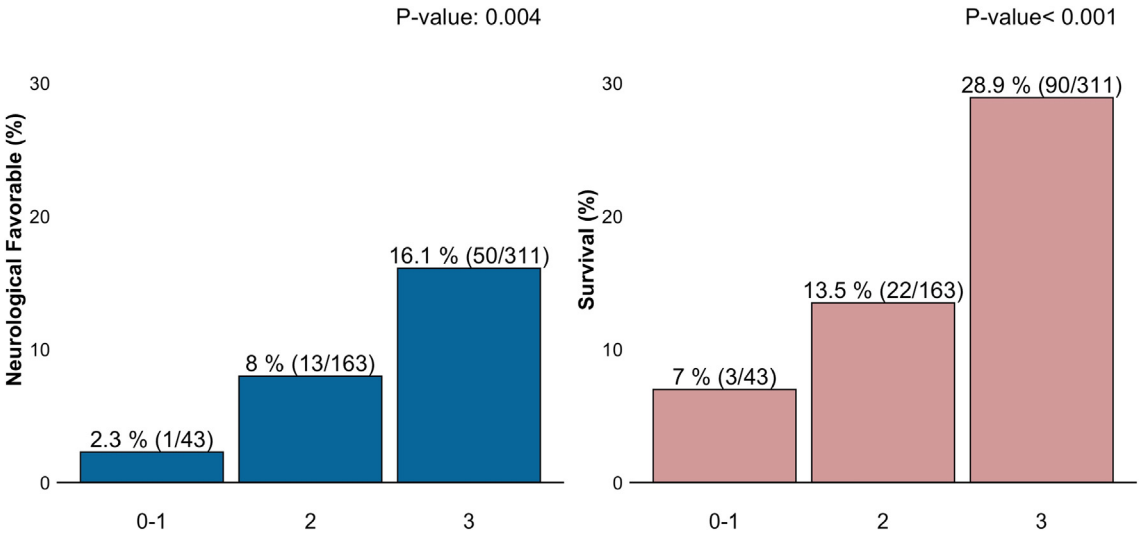

Fig. 3 – One-month outcomes by number of patients who met the criteria. X-axis: Number of patients who met the criteria. Y-axis: Left: One-month favourable neurological outcome, right: One-month survival. Three criteria for age, initial cardiac rhythm, and time to hospital arrival: 1) age <75 years, 2) initial cardiac rhythm: ventricular fibrillation (VF) or pulseless ventricular tachycardia (pVT), and 3) time from emergency call initiation to hospital arrival that is lesser than 45 minutes. When all three criteria were met, then the number of patients who met the criteria was 3; contrarily, when no criterion was met, then the number of patients was 0. P-value: Pearson's chi-square test.

results suggest that the application of the criteria may aid in selecting the appropriate candidates for ECPR.

Strengths and clinical implications

This study has the following strengths and clinical implications. First, this is the first study to indicate the clinical outcomes based on three criteria and its combination met among OHCA patients undergoing ECPR. We believe that this information would help select appropriate candidates for ECPR. Generally, ECPR is an invasive and expensive procedure that requires sufficient resources.[3,4] Thus, it cannot be practically performed for all patients with cardiac arrest, and clinicians should consider selecting only those patients who are expected to have a higher probability of favourable outcomes than the threshold to be acceptable. For example, we consider that it may be reasonable to implement the ECPR if OHCA patients fully meet the criteria because 28.9% (90 of 311) of the patients who met all three criteria in this study achieved survival, and this probability of survival may be acceptable for performing ECPR for most clinicians or the patients' family. On the contrary, patients who met all three criteria accounted for only 60% of all included patients; thus, we should also discuss the indications for ECPR for patients not meeting all the criteria. If the patients met only one or no criterion, then we suggest that the indication for ECPR should be carefully considered because the probability of favourable outcomes was extremely low among them, and it might be lower than the threshold to accept the invasion or expense in some cases. If the patients met two criteria, then it may generate controversy. However, if the patients met the criteria of time and initial rhythm but were aged above 75 years, then survival with favourable neurological outcomes was very limited (3.6%, 1/28 patients, Fig. 4); thus, ECPR should be carefully performed in those cases.

Second, the criteria were expected to be more suitable for considering eligibility for ECPR than single factors previously reported to be associated with outcomes such as age, time to ECPR, pH value of arterial blood gas assessment at hospital arrival [16–20] because applying these single factors for decision-making means ignoring other important factors, and this situation may lead to misses in identifying patients who would achieve a favourable outcome. For example, in this study, the proportion of a favourable neurological outcome in patients with initial VF or pVT was higher than that with PEA, asystole, or other (Fig. 2). However, some patients with PEA, asystole, or others, achieved favourable neurological outcomes (6.4%, 9/141); thus, if a candidate for ECPR is considered only by the initial rhythm, they may lose the opportunity for ECPR. On the contrary, the criteria including several factors potentially can minimise the harm of false-negative results. Previously, we reported the usefulness of a simple predicting model 'Tips65 score' to predict a neurological outcome among OHCA patients treated by ECPR [21]; however, this 'Tips65 score' requires the results of blood gas assessment, and it is expected to be used in in-hospital settings and just before implementation of ECPR. Contrarily, the three criteria in this study may be applicable just after hospital arrival or even in the pre-hospital situation if the time to the hospital can be predicted. Thus, it may have a different role from that of the Tips65 score, and it is easier to be applied than the score in some clinical settings. Furthermore, a combination of the three criteria and the Tips65 score might be more helpful for selecting a suitable candidate for ECPR.

Interpretation

There are some points to discuss regarding the interpretation of the results in this study. Regarding age, a previous study published by Haas et al. indicated no apparent difference in outcomes by age groups in ECPR cases, which was inconsistent with our results.[22] However, in that study, the study participants were relatively young (median age: 52 years, IQR [45–62]), and the number of patients who were 70 years or older was limited (18 of 217 patients were ≥70 years).[22] On the contrary, several studies conducted in Japan

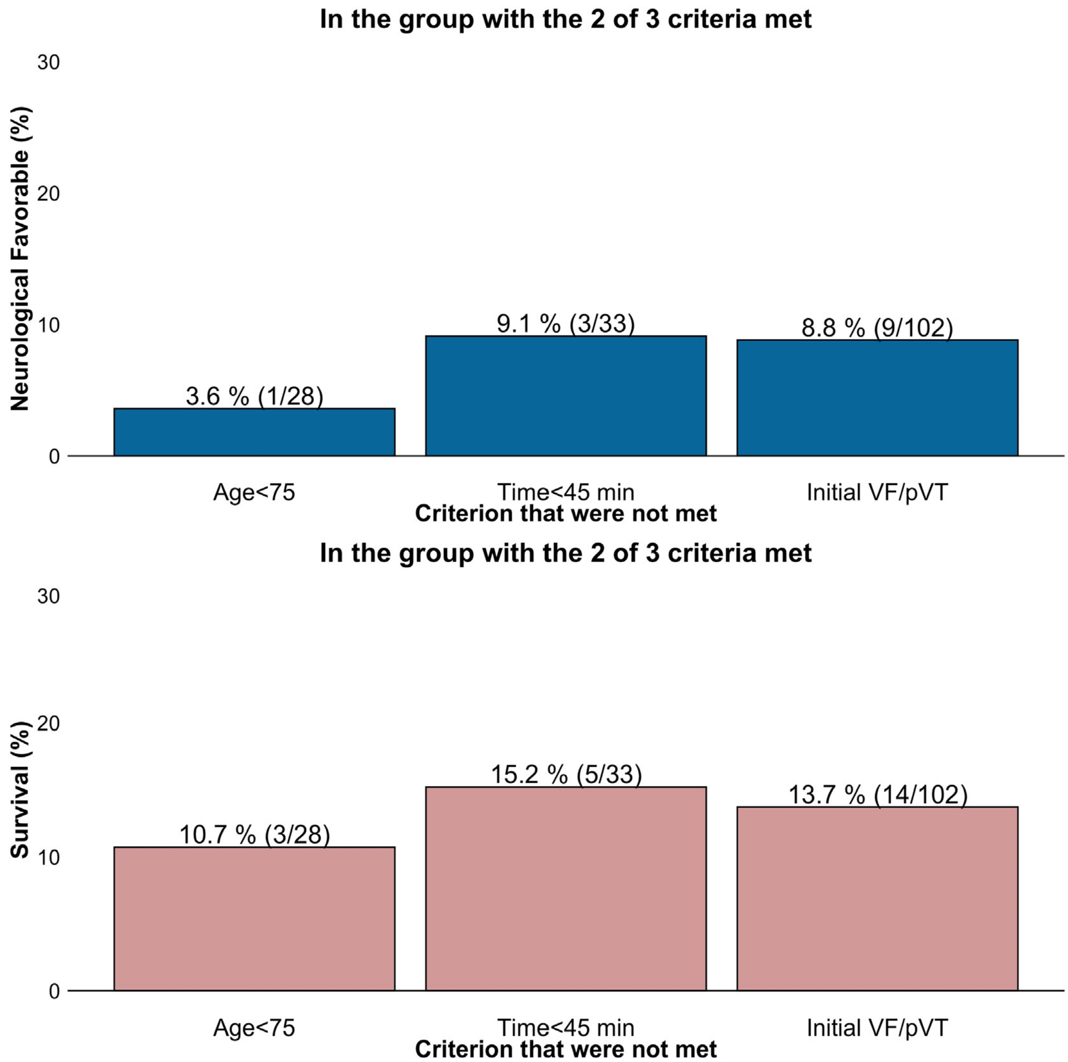

Fig. 4 – One-month outcomes among patients whose condition met two of the three criteria. Upper: One-month favourable neurological outcome, Lower: One-month survival. Ventricular fibrillation (VF) or pulseless ventricular tachycardia (pVT): Initial rhythm ventricular fibrillation or pulseless electrical activity, Time duration of <45 minutes: Time from emergency call initiation to hospital arrival that is lesser than 45 minutes. The chi-square test is not performed owing to limited number of outcomes. The figures indicate the outcomes of patients with out-of-hospital cardiac arrest treated by extracorporeal resuscitation and whose condition met two of the three SAVE-J criteria. Favourable outcome in patients whose condition did not meet the criterion of age <75 years is limited among patients whose condition met two of the three criteria.

indicated that favourable outcomes in patients aged 75 years or older treated by ECPR were rare.[19,20,23] This finding was in line with that reported in our study (3.9%, 2 of 51 patients). When compared with the study published by Haas et al., these studies and our study included a greater number of patients aged $\geq$75 years; thus, it may be reasonable that the outcomes in patients aged $\geq$75 years treated by ECPR have not shown promising results.

Regarding time, we agree that there is a criticism that one of the criteria used in this study, namely, time to hospital arrival being less than 45 minutes, is an arbitrary number, or it is unclear why this duration is used in this study. We consider that there is a dose-response relationship between time to hospital arrival or low-flow time and outcomes in OHCA patients treated by ECPR, and this finding was suggested in some studies.[18,24] We also consider that it is difficult to determine the 'golden period to start ECPR' because it may depend on the threshold to accept the balance of potential benefits and harms. The reason why we used the duration as 45 minutes in this study is because it is part of the SAVE-J study criteria, and many clinicians in Japan may have used it as a reference to consider the ECPR candidate. Accordingly, it should be noted that a duration of 45 minutes from emergency call initiation to hospital arrival is not a definitive cut-off but one of the references to consider the ECPR candidate.

Limitations

This study has several limitations. First, although the clinical data of this registry were doubly checked by clinicians and data administrators of this research committee, there may be insufficient records

Please cite this article as: Y. Okada, T. Irisawa, T. Yamada et al., Clinical outcomes among out-of-hospital cardiac arrest patients treated by extracorporeal cardiopulmonary resuscitation: The CRITICAL study in Osaka, Resuscitation, https://doi.org/10.1016/j.resuscitation.2022.06.007

and missing data in the actual resuscitation scenario. This may be a risk of measurement bias. Second, the sample size of this study was limited; thus, it might not have adequate power to detect clinically important differences. Third, complete clinical details, such as clinical course after the admission or details of ECPR procedures, were not collected in the CRITICAL study database. Fourth, the implementation of ECPR was determined by each physician or according to each institution's protocol. Thus, there may be a risk of selection bias. Fifth, this study only descriptively indicated the outcome; thus, caution should be exercised when interpreting the results, with great attention being paid to the confounders. Finally, this study assessed data derived from critical care centres in Osaka, Japan; the generalisability of these findings to other settings was unclear.

Conclusions

This study descriptively indicated that approximately 60% of patients treated by ECPR met the three criteria (initial shockable, time to the hospital within 45 minutes, and age <75) and these patients achieved better neurological outcomes than patients who did not meet the criteria. The three criteria would be valuable for making clinical decisions and planning further research about the effects of ECPR.

Ethical approval

This study was conducted according to the Declaration of Helsinki. The Ethics Committee of Kyoto University and each participating institution approved this study protocol and the retrospective analysis, and the need for written informed consent was waived (approval ID: R1045).

Availability of data and materials

The datasets and/or analyses in this study are not publicly available because the ethics committee did not permit it.

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.

Funding

This study was supported by a scientific research grant from the JSPS KAKENHI of Japan (22H03313 to Iwami and 22 K09139 to Kitamura).

CRediT authorship contribution statement

Yohei Okada: Conceptualization, Writing – original draft, Visualization. **Taro Irisawa:** Investigation, Data curation. **Tomoki Yamada:** Investigation, Data curation. **Kazuhisa Yoshiya:** Investigation, Data curation. **Changhwi Park:** Investigation, Data curation. **Tetsuro Nishimura:** Investigation, Data curation. **Takuya Ishibe:** Investigation, Data curation. **Hitoshi Kobata:** Investigation, Data curation. **Takeyuki Kiguchi:** Investigation, Data curation. **Masafumi Kishimoto:** Investigation, Data curation. **Sung-Ho Kim:** Investigation, Data curation. **Yusuke Ito:** Investigation, Data curation. **Taku Sogabe:** Investigation, Data curation. **Takaya Morooka:** Investigation, Data curation. **Haruko Sakamoto:** Investigation, Data curation. **Keitaro Suzuki:** Investigation, Data curation. **Atsunori Onoe:** Investigation, Data curation. **Tasuku Matsuyama:** Investigation, Data curation. **Daisuke Kobayashi:** Writing – review & editing. **Norihiro Nishioka:** Investigation, Data curation. **Satoshi Matsui:** Investigation, Data curation. **Satoshi Yoshimura:** Investigation, Data curation. **Shunsuke Kimata:** Investigation, Data curation. **Shunsuke Kawai:** Investigation, Data curation. **Yuto Makino:** Investigation, Data curation. **Kosuke Kiyohara:** Data curation. **Ling Zha:** Data curation. **Tetsuhisa Kitamura:** Validation, Data curation, Writing – review & editing, Funding acquisition. **Taku Iwami:** Writing – review & editing, Supervision, Funding acquisition.

Acknowledgements

We are deeply grateful to all EMS personnel for collecting Utstein data and to Ms. Ikuko Nakamura and Yumiko Murai for supporting the CRITICAL study. We thank our colleagues from Osaka University Centre of Medical Data Science and Advanced Clinical Epidemiology Investigator's Research Project for providing their insight and expertise for our research.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.resuscitation.2022.06.007.

Author details

[a]Department of Preventive Services, School of Public Health/Graduate School of Medicine, Kyoto University, Kyoto, Japan [b]Department of Emergency Medicine and Critical Care, Japanese Red Cross Society Kyoto Daini Hospital, Kyoto, Japan [c]Department of Traumatology and Acute Critical Medicine, Osaka University Graduate School of Medicine, Suita, Japan [d]Emergency and Critical Care Medical Center, Osaka Police Hospital, Osaka, Japan [e]Department of Emergency and Critical Care Medicine, Kansai Medical University, Takii Hospital, Moriguchi, Japan [f]Department of Emergency Medicine, Tane General Hospital, Osaka, Japan [g]Department of Critical Care Medicine, Osaka City University, Osaka, Japan [h]Department of Emergency and Critical Care Medicine, Kindai University, Faculty of Medicine, Osaka-Sayama, Japan [i]Osaka Mishima Emergency Critical Care Center, Takatsuki, Japan [j]Critical Care and Trauma Center, Osaka General Medical Center, Osaka, Japan [k]Osaka Prefectural Nakakawachi Medical Center of Acute Medicine, Higashi-Osaka, Japan [l]Senshu Trauma and Critical Care Center, Osaka, Japan [m]Senri Critical Care Medical Center, Saiseikai Senri Hospital, Suita, Japan [n]Traumatology and Critical Care Medical Center, National Hospital Organization Osaka National Hospital, Osaka, Japan [o]Emergency and Critical Care Medical Center, Osaka City General Hospital, Osaka, Japan [p]Department of Pediatrics, Osaka Red Cross Hospital, Osaka,

Japan [q]*Emergency and Critical Care Medical Center, Kishiwada Tokushukai Hospital, Osaka, Japan* [r]*Department of Emergency and Critical Care Medicine, Kansai Medical University, Hirakata, Osaka, Japan* [s]*Department of Emergency Medicine, Kyoto Prefectural University of Medicine, Kyoto, Japan* [t]*Division of Environmental Medicine and Population Sciences, Department of Social and Environmental Medicine, Graduate School of Medicine, Osaka University, Osaka, Japan* [u]*Department of Food Science, Faculty of Home Economics, Otsuma Women's University, Tokyo, Japan*

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;396:1807–16.
2. 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.
3. Dennis M, Zmudzki F, Burns B, et al. Cost effectiveness and quality of life analysis of extracorporeal cardiopulmonary resuscitation (ECPR) for refractory cardiac arrest Impact of first documented rhythm on cost-effectiveness of extracorporeal cardiopulmonary resuscitation Cost-utility of extracorporeal cardiopulmonary resuscitation in patients with cardiac arrest. Resuscitation. 139. Ireland: Crown 2019. Published by Elsevier B.V 2019 Elsevier B.V; 2019. p. 49–56.
4. Kawashima T, Uehara H, Miyagi N, et al. Impact of first documented rhythm on cost-effectiveness of extracorporeal cardiopulmonary resuscitation. Resuscitation. 140. Ireland: 2019 Elsevier B.V; 2019. p. 74–80.
5. Perkins GD, Graesner JT, Semeraro F, et al. European Resuscitation Council Guidelines 2021: Executive summary. Resuscitation 2021;161:1–60.
6. 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-S468.
7. Sakamoto T, Asai Y, Nagao K, et al. Multicenter non-randomized prospective cohort study of extracorporeal cardiopulmonary resuscitation for out-of hospital cardiac arrest: Study of Advanced Life Support for Ventricular Fibrillation with Extracorporeal Circulation in Japan (SAVE-J). Am Heart Assoc 2011.
8. Kitamura T, Iwami T, Kawamura T, Nagao K, Tanaka H, Hiraide A. Nationwide public-access defibrillation in Japan. N Engl J Med. 362. United States: 2010 Massachusetts Medical Society; 2010. p. 994-1004.
9. Kitamura T, Kiyohara K, Sakai T, et al. Public-Access Defibrillation and Out-of-Hospital Cardiac Arrest in Japan. N Engl J Med 2016;375:1649–59.
10. 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 Councils of Southern Africa). Circulation. 1United States2004. p. 3385–97.
11. Yamada T, Kitamura T, Hayakawa K, et al. Rationale, design, and profile of Comprehensive Registry of In-Hospital Intensive Care for OHCA Survival (CRITICAL) study in Osaka, Japan. J Intensive Care 2016;4:10.
12. Communications MoIAa. Statistics Bureau. Available from: https://www.stat.go.jp/english/.
13. Fire and Disaster Management Agency of the Ministry of Internal Affairs and Communications website. Available from: http://www.fdma.go.jp/neuter/topics/fieldList9_3.html.
14. 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. 132. United States; 2015. p. S436–43.
15. von Elm E, Altman DG, Egger M, et al. The strengthening the reporting of observational studies in epidemiology (strobe) statement: Guidelines for reporting observational studies. Ann Intern Med 2007;147:573–7.
16. Okada Y, Kiguchi T, Irisawa T, et al. Association between low pH and unfavorable neurological outcome among out-of-hospital cardiac arrest patients treated by extracorporeal CPR: a prospective observational cohort study in Japan. J Intensive Care 2020;8:34.
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;83:1011–8.
18. Matsuyama T, Irisawa T, Yamada T, et al. Impact of Low-Flow Duration on Favorable Neurological Outcomes of Extracorporeal Cardiopulmonary Resuscitation After Out-of-Hospital Cardiac Arrest: A Multicenter Prospective Study. Circulation 2020;141:1031–3.
19. 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 2021.
20. 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.
21. Okada Y, Kiguchi T, Irisawa T, et al. Development 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-e.
22. Haas NL, Coute RA, Hsu CH, Cranford JA, Neumar RW. Descriptive analysis of extracorporeal cardiopulmonary resuscitation following out-of-hospital cardiac arrest-An ELSO registry study. Resuscitation 2017;119:56–62.
23. Nakajima M, Kaszynski RH, Goto H, et al. Current trends and outcomes of extracorporeal cardiopulmonary resuscitation for out-of-hospital cardiac arrest in Japan: A nationwide observational study. Resusc Plus 2020;4:100048.
24. Lunz D, Calabrò L, Belliato M, Contri E, Broman LM, Scandroglio AM, et al. Extracorporeal membrane oxygenation for refractory cardiac arrest: a retrospective multicenter study. Intensive Care Med. 46. United States; 2020. p. 973–82.