Duration of prehospital and in-hospital cardiopulmonary resuscitation and neurological outcome in paediatric out-of-hospital cardiac arrest

Masato Yasuda (D), ^{1,2} Shunsuke Amagasa (D), ¹ Masahiro Kashiura, ³ Hideto Yasuda (D), ³ Satoko Uematsu¹

Handling editor Shammi L Ramlakhan

► Additional supplemental material is published online only. To view, please visit the journal online (https://doi. org/10.1136/emermed-2023-213730)

¹Department of Emergency and Transport Medicine, National Center for Child Health and Development, Setagaya-ku, Tokyo, Japan ²Division of Pediatric Emergency Medicine, Aichi Children's Health and Medical Center. Obu. Aichi, Japan ³Department of Emergency and Critical Care Medicine, Jichi Ika University Saitama Medical Center, Saitama, Saitama, Japan

Correspondence to

Dr Masato Yasuda; masato_yasuda@sk00106. achmc.pref.aichi.jp

Received 25 October 2023 Accepted 2 October 2024 Published Online First 15 October 2024

Check for updates

© Author(s) (or their employer(s)) 2024. No commercial re-use. See rights and permissions. Published by BMJ.

To cite: Yasuda M, Amagasa S. Kashiura M. et al. Emerg Med J 2024;41:742-748

ABSTRACT

Background Because of their young age and lack of known comorbidities, paediatric patients with out-ofhospital cardiac arrest (OHCA) often undergo prolonged cardiopulmonary resuscitation (CPR). We aimed to determine the association between prehospital and inhospital CPR duration and neurological outcomes.

Methods We conducted a retrospective analysis of data from the Japanese Association for Acute Medicine-OHCA Registry for patients <18 years of age with OHCA between June 2014 and December 2019. All patients received prehospital CPR by emergency medical service (EMS). The aetiologies of arrest included traumatic and atraumatic causes. The primary outcome measure was a 1-month neurological outcome of moderate disability or better (Pediatric Cerebral Performance Category 1–3). We calculated the dynamic probability and cumulative proportion of 1-month moderate disability or better neurological outcomes. Dynamic probability calculates patient outcomes during CPR per min. We performed multivariate logistic regression analysis to explore the association between longer CPR duration (as an ordinal variable) and 1-month poorer neurological outcomes. Results Among 1007 eligible children, 252 achieved return of spontaneous circulation and 53 had a 1-month moderate disability or better neurological outcome. The dynamic probability of a 1-month moderate disability or better neurological outcome dropped below 0.01 at 64 min (0.005, 95% CI 0.001 to 0.017). The cumulative proportion of a 1-month moderate disability or better neurological outcome exceeded 0.99 at 68 min (1, 95% CI 1 to 1). With increasing CPR time from CPR initiation by EMS, both crude and adjusted ORs for 1-month neurological outcomes gradually decreased. Conclusion Using a large Japanese database of paediatric OHCA patients, we found that longer CPR duration was associated with a lower likelihood of a 1-month moderate disability or better neurological outcome. Less than 1% of paediatric patients exhibited 1-month moderate disability or better neurological outcomes when total CPR duration is more than 64 min.

INTRODUCTION

Although survival rates for paediatric patients with out-of-hospital cardiac arrest (OHCA) have improved, the overall outcome remains poor.¹⁻³ Physicians may find decisions on when to terminate resuscitation in paediatric OHCA challenging due to limited availability of criteria or evidence to support termination of resuscitation (TOR) decisions.⁴

WHAT IS ALREADY KNOWN ON THIS TOPIC

- ⇒ Prolonged prehospital cardiopulmonary resuscitation (CPR) duration is associated with worse neurological outcomes in paediatric patients with out-of-hospital cardiac arrest (OHCA).
- \Rightarrow The availability of criteria or evidence to support termination of resuscitation decisions was limited in paediatric patients with OHCA.

WHAT THIS STUDY ADDS

- \Rightarrow In this retrospective cohort study using a Japanese registry, longer durations of pre and in-hospital CPR were associated with lower ORs for 1-month neurologic outcomes of moderate disability or better.
- The likelihood of moderate disability or better neurological outcomes at 1 month falls below 1% if CPR continues beyond 64 min.

HOW THIS STUDY MIGHT AFFECT RESEARCH, **PRACTICE OR POLICY**

 \Rightarrow Physicians should consider continuing resuscitation for at least 64 min in paediatric patients with OHCA, if there are no predictors of unfavourable neurological outcomes.

Developing TOR guidelines for paediatric patients with OHCA can be difficult owing to differences in aetiology when compared with adult patients as well as the emotional factors experienced by emergency medical service (EMS) providers, physicians and families.⁴⁻⁶ To help establish paediatric TOR guidelines, it is important to obtain evidence to support decision-making, including the duration of cardiopulmonary resuscitation (CPR) beyond which neurological outcomes decline because resuscitation should not be continued even in children if they cannot be predicted to have an acceptable neurological outcome, generally considered moderate disability or better neurological outcome on the Pediatric Cerebral Performance Category (PCPC) Score.⁶

According to two observational studies using the All-Japan Utstein Registry, a longer prehospital CPR duration was associated with worse neurological outcomes in paediatric patients with OHCA.^{7 8} Goto et al have reported that survival with moderate disability or better neurological



outcome dropped below 1% after 42 min of prehospital CPR.⁷ However, these studies solely focused on prehospital resuscitation data, excluding in-hospital information.

Examining the total duration of resuscitation, including both prehospital CPR and continuation of CPR in the emergency department (ED), is crucial to provide evidence to inform clinicians when resuscitative efforts should cease. Physicians in the ED require adequate knowledge regarding the association between CPR duration (including both prehospital and continued CPR in the ED) and outcomes in paediatric patients with OHCA to reach informed decisions regarding when to end resuscitation efforts.^{9 10}

In the current study, we aimed to examine the association between pre-hospital and in-hospital CPR duration and neurologically moderate disability or better outcomes using data from the Japanese Association for Acute Medicine (JAAM)-OHCA Registry.¹¹

METHODS

Study design

This retrospective cohort study utilised data from the JAAM-OHCA Registry, a nationwide multicentre registry in Japan that prospectively collects both prehospital and in-hospital data of patients with OHCA.¹¹ The ongoing registry includes all patients with OHCA who are transported to the affiliated medical centres. The registry integrates data from the All-Japan Utstein Registry, which collects only prehospital data of patients with OHCA.¹² We used data from collected between June 2014 and December 2019, from the beginning of the registry to the last available date.

Japanese EMS

The Japanese EMS is provided by municipal governments, and each ambulance service team consists of three ambulance crews.¹² All ambulance crews are trained to provide basic life support, following the resuscitation guidelines established by the Japan Resuscitation Council, affiliated with the International Liaison Committee on Resuscitation. At least one crew member is an emergency medical technician trained in advanced life support techniques, including intravenous line insertion, epinephrine administration and the use of semiautomated external defibrillators. All patients with OHCA are transported to hospitals as EMS personnel they are prohibited from terminating resuscitation. Therefore, nearly all patients with OHCA receiving EMS treatment are brought to hospitals.

Participants

This study enrolled paediatric patients aged <18 years old who had experienced OHCA both medial and traumatic. All patients received prehospital CPR by EMS personnel and subsequent treatment by physicians in the ED. Patients were excluded from this study if their data were missing or unreliable, if they achieved return of spontaneous circulation (ROSC) prior to EMS arrival or if they received extracorporeal CPR (ECPR).

Data collection

Pre-hospital medical information was collected from the All-Japan Utstein Registry, including age, sex, witnessed arrest, bystander CPR, time of CPR initiation by EMS providers, initial rhythm, advanced airway management, and epinephrine administration.^{12 13} In-hospital information was collected from electronic medical records and reported by physicians from participating institutions. In-hospital information included time to ROSC, advanced airway management, shock delivery, use of circulatory assist devices, drug administration and targeted temperature management. ROSC was defined as any ROSC. Time to ROSC was defined as the time of the first ROSC after CPR initiation. CPR duration for patients with ROSC was defined as the period from CPR initiation by EMS to ROSC. For patients without ROSC, CPR duration was defined as the period from CPR initiation by EMS to TOR, as reported previously.¹⁴

Outcomes

The primary outcome was 1-month survival with a moderate disability or better neurological outcome after OHCA, assessed using the PCPC Scale, which categorises outcomes as 1 (normal), 2 (mild disability), 3 (moderate disability), 4 (severe disability), 5 (coma or vegetative state) or 6 (brain death).¹⁵ Thus, PCPC scores of \leq 3 were considered as meeting the outcome of moderate disability or better, whereas scores of 4–6 were defined as unfavourable neurological outcomes.^{16–19} The secondary outcome measure was 1-month survival after OHCA.

Statistical analysis

Descriptive statistics were used to summarise patient characteristics and outcomes. Continuous variables are reported as medians and IQRs, while categorical variables are presented as counts and percentages.

The dynamic probability of 1-month moderate disability or better neurological outcomes (DPM(x)) or 1 month survival (DPS(x)) was calculated using the formula in figure 1. Dynamic probability calculates the likelihood of patients achieving outcomes, such as survival or good neurological status, at any given minute during CPR. DPM(x) represents the probability of 1-month moderate disability or better neurological outcomes following CPR initiation by EMS, with CPR duration exceeding x min. Traditionally, futility has been defined as a survival probability of less than 1%; however, the focus has shifted to achieving good neurological and functional outcomes.⁶ Therefore, the

Formulae of dynamic probability DPM(x)=(NM-N(x)).100/N DPS(x)=(NS-N(x)).100/N Formulae of cumulative proportion CPM(x)=N(x).100/NM CPS(x)=N(x).100/NS

Figure 1 Formulae of dynamic probability and cumulative proportion. DPM(x), percentage of 1-month moderate disability or better neurological outcomes who have had>x mins CPR; DPS(x), percentage of 1 month survivors who have had>x mins CPR. CPM(x), cumulative percentage of 1-month moderate disability or better neurological outcomes in patients who had≤x mins of CPR; CPS(x), cumulative percentage of 1-month survivors in patients who had≤x mins of CPR; NM, number of patients with 1-month moderate disability or better neurological outcomes. NS, number of patients with 1-month survival. N(x), number of children who underwent CPR between>0 and x mins. N, number of total patients.

time to a dynamic probability of <0.01 was reported, as in the previous studies.^{7 14}

The cumulative proportion of 1-month moderate disability or better neurological outcomes (CPM(x)) or 1-month survival (CPS(x)) was calculated using the formula listed in figure 1. CPM(x) represents the cumulative percentage of patients achieving 1-month moderate disability or better neurological outcomes after CPR initiation by EMS within 'x' min. The time until the cumulative proportion was >0.99 has been previously reported.^{7 14}

The CIs of the dynamic probability and cumulative proportion were calculated by GraphPad Prism (V.9).

Following the initial analysis, subgroup analyses were planned and conducted. We assessed the association between pre-hospital and in-hospital CPR duration and outcomes, stratified by the time interval from the initiation of CPR by EMS to the arrival at hospital, as well as by the aetiology of arrest, whether traumatic or atraumatic. Further details of the subgroup analyses are given in online supplemental material.

Multivariate logistic regression analysis was performed to investigate the association between longer CPR duration and 1-month poor neurological outcomes or 1-month poor survival. This analysis was conducted using complete case analysis. Crude and adjusted ORs and 95% CIs were calculated using CPR durations as an ordinal variable, categorised as 0–20, 21–40, 41–60 and \geq 61 min. The number of categories was determined based on the outcome size, while the range was set to every 20 min based on the previous study by Goto.⁷ Adjusted ORs for 1-month moderate disability or better neurological outcomes were adjusted to account for the initial shockable rhythm in the prehospital setting.^{20 21} Adjusted ORs for 1-month survival were adjusted to account for the initial shockable rhythm, bystander CPR, witness status, call-to-response, epinephrine administration in the prehospital and age.^{2 20–24}

A generalised additive model, with an adjusted cubic spline, was used to depict the non-linear association between CPR duration and 1-month moderate disability or better neurological outcomes or 1-month survival. The generalised additive model for 1-month moderate disability or better neurological outcomes was adjusted to account for an initial shockable rhythm in the prehospital.^{20 21} The model for 1-month survival was adjusted to account for an initial shockable rhythm, bystander CPR, witness status, call-to-response and epinephrine administration in the pre-hospital.^{2 20–23}

Statistical analyses were performed using EZR (V.1.55, Saitama Medical Center, Jichi Medical University, Saitama, Japan) and R software (V.4.1.3, www.r-project.org).²⁵

Patient and public involvement

Patients were not involved in the design and analysis of this study.

RESULTS

Study population

During the period studied, 1064 children with OHCA were registered in the JAAM-OHCA Registry. Among them, 57 children were not enrolled. Exclusions included 19 children with ECPR, 18 with missing data, 16 with ROSC prior to EMS arrival and 4 with unreliable data. Of the 1007 children included, 252 children achieved ROSC at some point after EMS arrival and among these, 53 (21%) had 1-month PCPC scores of 1-3, indicating moderate disability or better neurological outcomes, and 199 (79%) had scores of 4-6, indicating unfavourable neurological outcomes (figure 2). Among 251 children with traumatic OHCA, 26 (10%) were alive at 1 month and 17 (7%) had 1-month PCPC scores of 1-3. Among 756 children with atraumatic OHCA, 77 (10%) were alive at 1 month and 36 (5%) had 1-month PCPC scores of 1-3. The median time interval from initiated CPR by EMS to arrival at hospital was 16 min (IQR, 11-22 min); 194 children reached the hospital within 10 min, 499 between 11 min and 20 min and 302 arrived in 21 min or longer.

Characteristics and outcomes of the eligible children

Table 1 summarises the characteristics and outcomes of eligiblechildren. The median CPR duration was 31 min (IQR 15–40 min)



Figure 2 Flow chart of the patient selection process. ECPR, extracorporeal cardiopulmonary resuscitation; EMS, emergency medical service; PCPC, Pediatric Cerebral Performance Category; ROSC, return of spontaneous circulation.

 Table 1
 Characteristics and outcomes of children with return of spontaneous circulation after out-of-hospital cardiac arrest

spontaneous aneuration arter sa		
Characteristic, median (IQR) or no (%)	Children with 1-month neurological moderate disability or better outcomes (N=53)	Children with 1-month neurological unfavourable outcomes (N=954)
Pre-hospital		
Age	7 (2-14)	2 (0–13)
Воу	34 (64)	580 (61)
Bystander CPR	32 (60)	553 (58)
Witness	29 (55)	269 (28)
Initial cardiac rhythm		
Total	53 (100)	954 (100)
Ventricular fibrillation	4 (8)	20 (2)
Pulseless ventricular tachycardia	1 (2)	2 (0)
Pulseless electrical activity	15 (28)	153 (16)
Asystole	25 (47)	746 (78)
Others	8 (15)	33 (3)
Pre-hospital defibrillation	6 (11)	47 (5)
Advanced airway management	9 (17)	106 (11)
Epinephrine administration	5 (9)	38 (4)
Aetiology of CA: cardiogenic	9 (17)	296 (31)
ROSC before arrival	13 (25)	31 (3)
In-hospital		
Antiarrhythmic drug administration*	2 (4)	17 (2)
Targeted temperature management	14 (26)	53 (6)
Circulatory assist device	2 (4)	7 (1)
ROSC after arrival	40 (75)	170 (18)
Time intervals		
Call-to-response (min)	7 (6-10)	8 (7-10)
CPR to Arrival (min)†	17 (12–23)	16 (11–22)
CPR duration (min)‡	31 (15–40)	52 (36–68)
Outcomes		
1 month survival	53 (100)	50 (5)
1-month PCPC grade		
Total	53 (100)	954 (100)
PCPC 1	36 (68)	0 (0)
PCPC 2	7 (13)	0 (0)
PCPC 3	10 (19)	0 (0)
PCPC 4	0 (0)	22 (2)
PCPC 5	0 (0)	28 (3)
PCPC 6	0 (0)	904 (95)

*Antiarrhythmic drugs include amiodarone, lidocaine and magnesium.

The median was calculated after excluding unreliable values.

*CPR duration is the combined prehospital and in-hospital CPR duration. CA, cardiac arrest; CPR, cardiopulmonary resuscitation; PCPC, Pediatric Cerebral Performance Category; ROSC, return of spontaneous circulation.

among children with 1-month neurologically moderate disability or better outcomes and 52 min (IQR 36–68 min) among those with 1-month neurologically unfavourable outcomes. Among children with 1-month neurologically moderate disability or better outcomes, 13 (25%) achieved ROSC before hospital arrival, whereas 40 (75%) achieved ROSC after arrival. Among children with 1-month neurologically unfavourable outcomes, 31 (3%) achieved ROSC before hospital arrival and 170 (18%) achieved ROSC after hospital arrival. The distribution of children according to PCPC scores was as follows: PCPC 1: 36 (4%), PCPC 2: 7 (1%), PCPC 3: 10 (1%), PCPC 4: 22 (2%), PCPC 5: 28 (3%), PCPC 6: 904 (90%).

Duration of CPR and outcomes

The longest CPR duration observed in children with a 1-month neurologically moderate disability or better outcome was 68 min. The dynamic probability of a 1-month moderate disability or better neurological outcome fell below 0.01 between 63 min (0.011, 95% CI 0.004 to 0.023) and 64 min (0.005, 95% CI 0.001 to 0.017) (figure 3). The longest CPR duration among the 1-month survivors was 93 min and the PCPC score of this 1-month survivor was 4.

In the subgroup analyses stratified by traumatic or atraumatic arrest, the dynamic probability of a 1-month moderate disability or better neurological outcome fell below 0.01 between 40 min (0.024, 95% CI 0.007 to 0.059) and 48 min (0, 95% CI 0 to 0) in the traumatic group. However, the duration for atraumatic arrest was much longer, falling between 73 min (0.012, 95% CI 0.005 to 0.027) and 75 min (0.009, 95% CI 0.003 to 0.024) (online supplemental figure S1)

Cumulative proportion

The cumulative proportion of a 1-month moderate disability or better neurological outcome exceeded 0.99 between 64 min (0.981, 95% CI 0.969 to 0.988) and 68 min (1, 95% CI 1 to 1) (figure 4). The cumulative proportion of 1-month survival was >0.99 between 68 min (0.981, 95% CI 0.973 to 0.986) and 73 min (0.990, 95% CI 0.985 to 0.994).

The results of other subgroup analyses are provided in online supplemental figure S2-8.

Results of the multiple logistic regression analysis

Compared with those whose CPR lasted 20 min or less, the adjusted ORs of 1 month moderate disability or better neurological outcomes were 0.51 (95% CI 0.26 to 1.02, p=0.055) in patients whose CPR lasted between 21 and 40 min, 0.13 (95% CI 0.06 to 0.32, p<0.001) if the duration was 41–60 min, and 0.04 (95% CI 0.01 to 0.14, p<0.001) if the duration exceeded 61 min. The crude and adjusted ORs of 1-month moderate disability or better neurological outcomes and 1-month survival decreased gradually as CPR duration increased (table 2).

Cubic splines

As CPR duration increased, the odds of achieving 1-month outcomes of neurologically moderate disability or better and 1-month survival decreased (figure 5).

DISCUSSION

Using prospectively reported national registry data, our findings suggest that prolonged CPR duration was associated with a decreased likelihood of 1-month moderate disability or better neurological outcomes and 1-month survival in paediatric patients with OHCA. The total CPR duration, including prehospital CPR and continuing CPR in the ED, at which the probability of a 1-month moderate disability or better neurological outcome fell below 0.01 was determined to be 64 min in this study.

A previous study on paediatric patients with OHCA, using a Japanese registry that included only prehospital CPR data, has reported the probability of a child having a 1-month cerebral performance category (CPC) score of 1 or 2 fell below 0.01 if CPR duration exceeded 42 min.⁷ However, that study only used prehospital CPR duration. In the current study, the CPR

- A. The dynamic probability of 1-month moderate disability or better neurological outcome
- B. The dynamic probability of 1-month survival



Figure 3 The dynamic probability of a 1-month moderate disability or better neurological outcome (A) and 1-month survival (B). Among 1007 eligible children with out-of-hospital cardiac arrest, 53 (5%) had a 1-month moderate disability or better neurological outcome (Pediatric Cerebral Performance Category scores of 1–3) (A) and 103 (10%) were 1-month survivors (B). The dashed line represents the 95% CI.

duration for which the probability of a PCPC score of 1–3 was less than 0.01 was longer than that observed in the previous study included prehospital CPR and continuing CPR in the ED.

Notably, 75% of children with 1-month moderate disability or better neurological outcomes achieved ROSC after arrival at the hospital, with a median time interval of 17 min from CPR to arrival in the current study. As many patients with 1-month moderate disability or better neurological outcome achieved ROSC after hospital arrival, and as the total CPR duration also encompassed a significant amount of duration of CPR performed in the ED, we demonstrate it is insufficient to calculate the CPR duration for a 1-month poor neurological outcome based on prehospital CPR duration alone, as in the previous study.

Since CPC 2, which is often considered the cut-off for CPC in adults, represents a moderate disability, the cut-off for PCPC was set at 3, which also indicates a moderate disability. Additionally, we believe that, despite cardiac arrest, it is important for children to maintain a PCPC of 3, which enables them to perform activities of daily living independently. However, because our study used a cut-off of PCPC3 or lower, it is possible that the CPR duration was longer compared with previous studies using a cut-off of CPC2 or lower. In a study of adult patients with OHCA, which considered both prehospital CPR and continuing CPR in the ED, a 1-month neurological outcome evaluated using CPC was poor when CPR duration exceeded 45 min.¹⁴ This duration was shorter than that observed in the current study, suggesting that physicians may need to perform prolonged resuscitation efforts in paediatric patients with OHCA when compared with that in adult patients.

In subgroup analysis, children with a traumatic aetiology for OHCA had about 30 min shorter CPR duration compared with those with an atraumatic cause for <0.01 probability of a 1-month moderate disability or better neurological outcome. Consistent with the poor prognosis of traumatic OHCA, this study suggests that resuscitation efforts of paediatric patients with traumatic OHCA may be discontinued earlier than in those with atraumatic OHCA. In the subgroup analysis stratified by time interval from CPR to arrival, the shorter this time interval, the shorter the CPR duration that resulted in <1% chance of 1-month moderate disability or better neurological outcome. However, CPR duration after arrival at hospital did not change for any of the groups. The duration of resuscitation required after arrival at a hospital may not change much regardless of the time interval from CPR to arrival.





A. The cumulative proportion of 1-month moderate disability or better neurological outcome

Figure 4 The cumulative proportion of 1-month moderate disability or better neurological outcome (A) and 1-month survival (B). Among 1007 eligible children with out-of-hospital cardiac arrest, 53 (5%) had a 1-month moderate disability or better neurological outcome (Pediatric Cerebral Performance Category scores of 1–3) (A) and 103 (10%) were 1-month survivors (B). The dashed line represents the 95% CI.

	1-month neurologically moderate disability or better outcome (N=53)		ty or better outcome	1-month survival (N=103)		
		Crude OR	Adjusted OR*		Crude OR	Adjusted OR†
CPR duration	N	OR (95% CI) P value		N	OR (95% CI) P value	
0–20 min (N=90)	17	Reference	Reference	34	Reference	Reference
21–40 min (N=240)	24	0.48 (0.24–0.94) p=0.032	0.51 (0.26–1.02) p=0.055	45	0.38 (0.22–0.65) p<0.001	0.48 (0.27–0.85) p=0.012
41–60 min (N=326)	9	0.12 (0.05–0.28) p<0.001	0.13 (0.06–0.32) p<0.001	18	0.10 (0.05–0.18) p<0.001	0.13 (0.06–0.25) p<0.001
61 min or more (N=351)	3	0.04 (0.01–0.13) p<0.001	0.04 (0.01–0.14) p<0.001	6	0.03 (0.01–0.07) p<0.001	0.04 (0.01–0.09) p<0.001

*Adjusted ORs were adjusted to account for the initial shockable rhythm in the pre-hospital setting.

†Adjusted ORs were adjusted to account for various factors during the pre-hospital period, including the initial shockable rhythm, bystander CPR, witness presence, call-toresponse time, and epinephrine administration.

CPR, cardiopulmonary resuscitation.

In our study, a CPR duration \geq 64 min was associated with a probability of a moderate disability or better neurological outcome of less than 0.01. Considering that the patients were children, physicians might need to continue resuscitation for at least 64 min in the absence of any predictors of unfavourable neurological outcomes identified in previous studies (eg, fixed pupils, unwitnessed, underlying terminal disease, traumatic OHCA).^{5 20} The findings of the current study can aid physicians in making informed decisions regarding terminating resuscitation efforts in paediatric patients with OHCA.

Limitations

This study had some limitations. First, owing to the small number of cases, we could not adjust for all confounders. Therefore, there was a possibility that it may have influenced the results of the multivariate analysis. Second, the CPR duration could not be analysed as a continuous variable or categorised into intervals<20 min in the multivariate analysis. We were unable to assess whether the likelihood of a moderate disability or better neurological outcome decreased every minute. Third, the JAAM-OHCA Registry is not a population-based study, and factors such as hospital size and emergency transport time may have influenced the results. Consequently, the CPR duration at which the probability of moderate disability or better neurological outcomes drops below 0.01 could vary due to variation in resuscitation quality. Fourth, this study focused on the CPR duration from CPR initiation by EMS and did not include the CPR duration performed by bystanders. Incorporating bystander CPR duration might have resulted in an even longer appropriate CPR duration. Additionally, the time interval between cardiac arrest and CPR initiation by EMS was not considered. Fifth, the results of this study cannot be extrapolated to individual patients owing to the heterogeneous nature of OHCA, which includes various aetiologies, wide age range, witnessed or not, and initial shockable rhythm. Future studies with larger sample sizes should evaluate the association between CPR duration and neurological outcomes while accounting for various confounding factors.

Conclusions

In this retrospective cohort study on children with OHCA using the JAAM-OHCA Registry, CPR duration may need to be continued for at least 64 min benefits to maximise the number of paediatric cardiac arrest patients who can achieve a neurological outcome of moderate disability or better.



A. 1-month moderate disability or better neurological outcome

B. 1-month survival

Figure 5 Adjusted cubic spline models showing the association between CPR duration and 1-month moderate disability or better neurological outcome (A) or 1-month survival (B). Among 1007 eligible children with out-of-hospital cardiac arrest, 53 (5%) had a 1-month moderate disability or better neurological outcome (Pediatric Cerebral Performance Category scores of 1–3) (A) and 103 (10%) were 1-month survivors (B). The dashed line represents the 95% CI. (A) The model was adjusted to account for initial shockable rhythm in pre-hospital. (B) The model was adjusted to account for initial shockable rhythm, bystander CPR, witness, call-to-response, and epinephrine administration in pre-hospital. CPR, cardiopulmonary resuscitation.

80

Original research

Acknowledgements We would like to thank Editage (www.editage.jp) for English language editing.

Contributors MY and SA conceived the idea of the study. SA, MK and HY developed the statistical analysis plan and conducted statistical analyses. SA, MK and HY contributed to the interpretation of the results. MY drafted the original manuscript. SU supervised the conduct of this study. All authors reviewed the manuscript draft and revised it critically on intellectual content. All authors approved the final version of the manuscript to be published. Guarantor: MY—is responsible for the overall content as guarantor.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval The registry protocol was approved by the Ethics Review Committee of the Responsible Centre, Kyoto University (R1045-5). It was approved by each member of the Institutional Review Board. Participants gave informed consent before taking part.

Provenance and peer review Not commissioned; internally peer-reviewed.

Data availability statement Data may be obtained from a third party and are not publicly available.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

ORCID iDs

Masato Yasuda http://orcid.org/0000-0002-8739-8888 Shunsuke Amagasa http://orcid.org/0000-0002-8371-1507 Hideto Yasuda http://orcid.org/0000-0003-3153-1595

REFERENCES

- 1 Fink EL, Prince DK, Kaltman JR, *et al*. Unchanged pediatric out-of-hospital cardiac arrest incidence and survival rates with regional variation in North America. *Resuscitation* 2016;107:121–8.
- 2 Goto Y, Funada A, Maeda T, et al. Temporal trends in neurologically intact survival after paediatric bystander-witnessed out-of-hospital cardiac arrest: A nationwide population-based observational study. *Resusc Plus* 2021;6:100104.
- 3 Holgersen MG, Jensen TW, Breindahl N, et al. Pediatric out-of-hospital cardiac arrest in Denmark. Scand J Trauma Resusc Emerg Med 2022;30:58.
- 4 Munoz MG, Beyda DH. An Ethical Justification for Termination of Resuscitation Protocols for Pediatric Patients. *Pediatr Emerg Care* 2017;33:505–15.
- 5 American College of Surgeons Committee on T, American College of Emergency Physicians Pediatric Emergency Medicine C, National Association of Ems P, et al. Withholding or Termination of Resuscitation in Pediatric Out-of-Hospital Traumatic Cardiopulmonary Arrest. *Pediatrics* 2014;133:e1104–16.
- 6 Mentzelopoulos SD, Couper K, Voorde P de, et al. European Resuscitation Council Guidelines 2021: Ethics of resuscitation and end of life decisions. *Resuscitation* 2021;161:408–32.

- 7 Goto Y, Funada A, Goto Y. Duration of Prehospital Cardiopulmonary Resuscitation and Favorable Neurological Outcomes for Pediatric Out-of-Hospital Cardiac Arrests: A Nationwide, Population-Based Cohort Study. *Circulation* 2016;134:2046–59.
- 8 Shida H, Matsuyama T, Kiyohara K, et al. Prehospital cardiopulmonary resuscitation duration and neurological outcome after out-of-hospital cardiac arrest among children by location of arrest: a Nationwide cohort study. Scand J Trauma Resusc Emerg Med 2019;27:79.
- 9 Nehme Z, Andrew E, Bernard S, et al. Impact of cardiopulmonary resuscitation duration on survival from paramedic witnessed out-of-hospital cardiac arrests: An observational study. *Resuscitation* 2016;100:25–31.
- 10 Arima T, Nagata O, Sakaida K, et al. Relationship between duration of prehospital resuscitation and favorable prognosis in ventricular fibrillation. Am J Emerg Med 2015;33:677–81.
- 11 Kitamura T, Iwami T, Atsumi T, et al. The profile of Japanese Association for Acute Medicine - out-of-hospital cardiac arrest registry in 2014-2015. Acute Med Surg 2018;5:249–58.
- 12 Kitamura T, Iwami T, Kawamura T, et al. Nationwide public-access defibrillation in Japan. N Engl J Med 2010;362:994–1004.
- 13 Perkins GD, Jacobs IG, Nadkarni VM, *et al.* Cardiac arrest and cardiopulmonary resuscitation outcome reports: update of the Utstein Resuscitation Registry Templates for Out-of-Hospital Cardiac Arrest: a statement for healthcare professionals from a task force of the International Liaison Committee on Resuscitation (American Heart Association, European Resuscitation Council, Australian and New Zealand Council on Resuscitation, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation, Resuscitation Council of Southern Africa, Resuscitation Council of Asia); and the American Heart Association Emergency Cardiovascular Care Committee and the Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation. Circulation 2015;132:1286–300.
- 14 Kashiura M, Hamabe Y, Akashi A, et al. Association between cardiopulmonary resuscitation duration and one-month neurological outcomes for out-of-hospital cardiac arrest: a prospective cohort study. BMC Anesthesiol 2017;17:59.
- 15 Fiser DH. Assessing the outcome of pediatric intensive care. *J Pediatr* 1992;121:68–74.
- 16 Kernan KF, Berger RP, Clark RSB, et al. An exploratory assessment of serum biomarkers of post-cardiac arrest syndrome in children. *Resuscitation* 2021;167:307–16.
- 17 Berg RA, Sutton RM, Reeder RW, et al. Association Between Diastolic Blood Pressure During Pediatric In-Hospital Cardiopulmonary Resuscitation and Survival. *Circulation* 2018;137:1784–95.
- 18 Berg RA, Nadkarni VM, Clark AE, et al. Incidence and Outcomes of Cardiopulmonary Resuscitation in PICUs. Crit Care Med 2016;44:798–808.
- 19 Ortmann L, Prodhan P, Gossett J, et al. Outcomes after in-hospital cardiac arrest in children with cardiac disease: a report from Get With the Guidelines--Resuscitation. *Circulation* 2011;124:2329–37.
- 20 Goto Y, Funada A, Nakatsu-Goto Y. Neurological outcomes in children dead on hospital arrival. *Crit Care* 2015;19:410.
- 21 Goto Y, Maeda T, Nakatsu-Goto Y. Decision tree model for predicting long-term outcomes in children with out-of-hospital cardiac arrest: a nationwide, populationbased observational study. *Crit Care* 2014;18:R133.
- 22 Hansen M, Schmicker RH, Newgard CD, *et al.* Time to Epinephrine Administration and Survival From Nonshockable Out-of-Hospital Cardiac Arrest Among Children and Adults. *Circulation* 2018;137:2032–40.
- 23 Fukuda T, Kondo Y, Hayashida K, et al. Time to epinephrine and survival after paediatric out-of-hospital cardiac arrest. *Eur Heart J Cardiovasc Pharmacother* 2018;4:144–51.
- 24 Nitta M, Iwami T, Kitamura T, et al. Age-specific differences in outcomes after out-ofhospital cardiac arrests. *Pediatrics* 2011;128:e812–20.
- 25 Kanda Y. Investigation of the freely available easy-to-use software "EZR" for medical statistics. *Bone Marrow Transplant* 2013;48:452–8.