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Clinical paper

Effectiveness of near-infrared spectroscopy-guided continuous chest compression resuscitation without rhythm check in patients with out-of-hospital cardiac arrest: The prospective multicenter TripleCPR 16 study

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Abbreviations: A-AD, Stanford type-A aortic dissection, CA, cardiac arrest, CI, confidence interval, CC, chest compression, CPA, cardiopulmonary arrest, CPR, cardiopulmonary resuscitation, DNAR, do not attempt resuscitation, ECMO, extracorporeal membrane oxygenation, EMS, emergency medical service, IPTW, inverse probability of treatment weighting, NIRS, near-infrared spectroscopy OHCA, out-of-hospital cardiac arrest, OR, odds ratio, ROSC, return of spontaneous circulation, rSO_2, regional cerebral oxygen saturation, SAE, serious adverse events

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Abstract

Background: The proportion of adult patients with return of spontaneous circulation (ROSC) following out-of-hospital cardiac arrest (OHCA) remains unchanged since 2012. A better resuscitation strategy is needed. This study evaluated the eectiveness of a regional cerebral oxygen saturation (rSO_2)-guided resuscitation protocol without rhythm check based on our previous study.
Methods: Because defibrillation is the definitive therapy that should be performed without delay for shockable rhythm, the study subjects were OHCA patients with non-shockable rhythm on hospital arrival at three emergency departments. They were divided into three groups based on their baseline rSO_2 value (%): ≥50, ≥40 to <50, or <40. Continuous chest compression without rhythm checks was performed for 16 minutes or until a maximum increase in rSO_2 of 10%, 20%, or 35% was achieved in each group, respectively. This intervention cohort was compared with a historical control cohort regarding the probability of ROSC using inverse probability of treatment weighting (IPTW) with propensity score.
Results: The control and intervention cohorts respectively included 86 and 225 patients. The rate of ROSC was not significantly dierent between the groups (adjusted OR 0.91 [95% CI, 0.64–1.29], P = 0.60), but no serious adverse events occurred. Sensitivity analyses 1 and 2 showed a significant dierence or positive tendency for higher probability of ROSC (adjusted OR 1.63 [95% CI, 1.22–2.17], P < 0.001) (adjusted OR 1.25 [95% CI, 0.95–1.63], P = 0.11).
Conclusions: This trial suggested that a new cardiopulmonary resuscitation protocol with dierent rhythm check timing could be created using the rSO_2 value.
Clinical trial number: UMIN000025684.
Keywords: Continuous chest compression, Cardiopulmonary resuscitation, Cerebral oximetry, Heart arrest, Near-infrared spectroscopy, Regional cerebral oxygen saturation, Return of spontaneous circulation, Timing of rhythm check

Introduction

Neurological and cognitive sequelae after out-of-hospital cardiac arrest (OHCA) remain a major public health challenge worldwide. The proportion of adult patients with return of spontaneous circulation (ROSC) following OHCA attended by emergency medical services (EMS) personnel has remained essentially unchanged since 2012.[1,2] Thus, better resuscitation strategies must be established to further increase the probability of achieving ROSC and a favourable neurological outcome in patients suffering OHCA.

Current guidelines recommend a rhythm check every 2 min, but there is no direct evidence for using this particular time interval.[3–6] The guidelines also emphasise minimising the interruptions in chest compression (CC) and performing high-quality CPR.[4,7] Given the reports suggesting adverse effects during interruptions of CC,[8,9] treatment strategies should be considered that reduce interruptions even more. Therefore, we focused on whether the rhythm check should be performed every 2 min.

Several recent studies have highlighted the usefulness of regional cerebral oxygen saturation (rSO_2) measured by near-infrared spectroscopy (NIRS) for brain monitoring during cardiopulmonary resuscitation (CPR) in patients with OHCA.[10–13] We previously showed that continuous assessment of rSO_2 during CPR could predict ROSC.[14] That study presented a non-linear multivariate logistic curve in which the maximum amount of increase in rSO_2 value over the initial 16 min after hospital arrival was the best predictor of ROSC, indicating that a higher increase in rSO_2 resulted in a higher rate of ROSC. This suggests that a customised CPR protocol using rSO_2 might provide better advanced life support algorithms. As the possibility of ROSC is low with poor elevation of rSO_2, we hypothesised that a CPR algorithm without rhythm check in combination with rSO_2 monitoring would provide a better beneficial strategy when compared to a rhythm check every 2 min in terms of detecting ROSC. The purpose of this study was to evaluate whether a CPR algorithm without a rhythm check every 2 min but with rSO_2 monitoring can lead to improvement of the rate of ROSC in patients with OHCA.

Methods

Patient eligibility and participating hospitals

This prospective, multicentre, intervention study was conducted from January 2017 to July 2019 at three university hospitals in Japan. Patients aged 16 years and older with OHCA and a non-shockable rhythm on hospital arrival (i.e. the initial rhythm) were included, given that defibrillation is the definitive treatment in patients with a shockable rhythm. Exclusion criteria were pregnant women and patients with traumatic cardiac arrest (CA) as they could suffer from head injury and could receive open-chest CPR. Patients requiring interventions such as pericardiocentesis or pericardial fenestration for cardiac tamponade were also excluded because mechanical CC could not be safely performed, resulting in a deviation from the study protocol. The participating hospitals included two advanced critical care centres, Osaka University Hospital and Kansai Medical University Hospital, and one critical care centre, Kansai Medical University Medical Center, located in the northern region of Osaka, one of the largest cities in Japan. The Ethics Committee of each hospital approved this study. The local institutional review board waived the need for informed consent because all subjects were in cardiopulmonary arrest (CPA).

EMS in Japan and rSO_2 monitoring by NIRS during CPR

The TOS-QQ® (TOSTEC Co., Ltd., Tokyo, Japan) brain oximeter[15] was used in this study. Details of EMS and rSO_2 monitoring are shown in the Supplementary Methods.

Continuous CC resuscitation algorithm with rSO_2 assessment

During the study period, eligible patients received the designated CPR algorithm, named TripleCPR, which includes continuous CC in combination with rSO_2 monitoring (Fig. 1).

rSO_2 guided resuscitation protocol

If the patient met the inclusion criteria, a brain NIRS oximeter was attached to the patient's forehead within 1 min after hospital arrival,

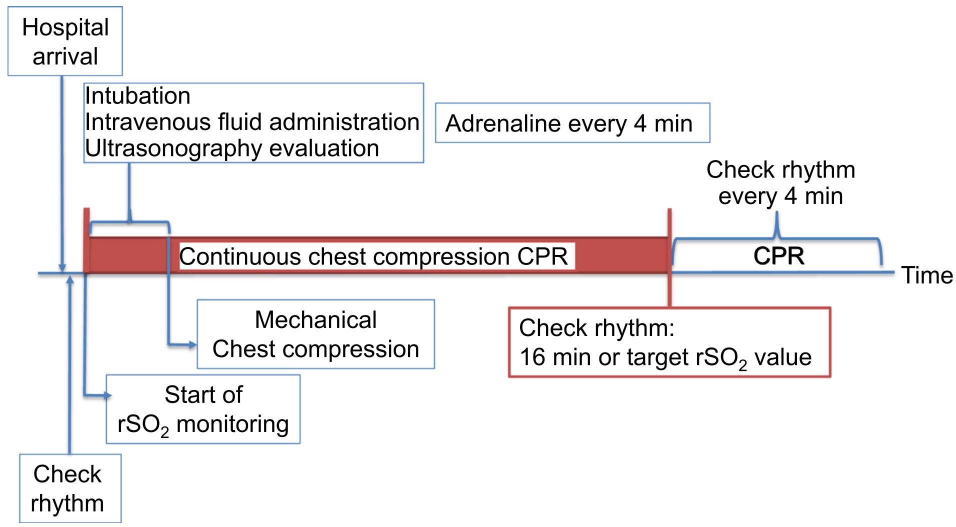

Fig. 1 – Protocol of the TripleCPR 16 study. When patients aged 16 and over with OHCA showed a non-shockable rhythm on hospital arrival, they were enrolled in this study. rSO_2 monitoring was initiated, and chest compressions were continued for 16 min or until the target rSO_2 value was achieved. Chest compression was discontinued temporarily while checking the position of the tracheal intubation tube, and ultrasonography was simultaneously performed. Thereafter, chest compression was changed from manual to mechanical. Adrenaline was administered every 4 min. OHCA, out-of-hospital cardiac arrest; CPR, cardiopulmonary resuscitation; rSO_2, regional cerebral oxygen saturation.

and the study protocol was initiated when monitoring of the rSO_2 value began. Based on the average value over the initial 1 min of monitoring (baseline rSO_2), CC was performed continuously for 16 min or until the targeted rSO_2 value was achieved. Specifically, for baseline rSO_2 values of ≥50%, ≥40% to <50%, or <40%, CC was continued for 16 min or until a maximum increase in rSO_2 value of 10%, 20%, or 35%, respectively, was achieved (Table 1). After rSO_2 monitoring began, the second rhythm check after hospital arrival was performed when the target value was reached or 16 min had passed. If ROSC was not achieved, mechanical CC was restarted, and rhythm checks were subsequently performed every 4 min. If a shockable rhythm was recognised on the second rhythm check, defibrillation was performed, and thereafter, a rhythm check was performed every 2 min. ROSC was defined as a palpable carotid pulse. Termination of CPR was at the discretion of the attending physician.

Continuous CC and general resuscitation protocol

Immediately after hospital arrival, manual CC was restarted. After starting the rSO_2-guided algorithm, if the patient was not already intubated, tracheal intubation was performed in tandem with manual CC. After confirming intubation tube position by auscultation and end-tidal carbon dioxide ($EtCO_2$) monitoring, manual CC was converted to mechanical CC with an AutoPulse® (ZOLL, Chelmsford, MA, USA) or Clover 3000® (KOHKEN Medical, Tokyo, Japan) device. If the patient was already intubated, mechanical CC was initiated after checking intubation tube position. During auscultation, CC was temporarily discontinued to allow checking of ventilatory sounds. Adrenaline was administered every 4 min.

At one participating hospital (Osaka University Hospital), a head-to-pelvis computed tomography scan was routinely performed in all patients to examine the cause of CA regardless of achieving ROSC. The other components described above followed the International Consensus on Science with Treatment Recommendations 2015 (CoSTR).[16,17]

Data collection and outcomes

Patients' clinical data (age, sex, medical history), pre- and in-hospital characteristics (witnessed arrest, bystander CPR, initial electrocardiogram rhythm, amount of adrenaline administration, number of defibrillations, presence of ROSC, cause of CPA), time course (onset time of CPA, time to ROSC, total CPA time, time to reaching the target value), hospital stay, in-hospital treatment, serious adverse events (SAE) associated with CPR, and cerebral rSO_2 data (baseline value, rSO_2 value, and amount of maximum rise in rSO_2 at ROSC or 16 min) were collected.

The primary outcome was the rate of ROSC. SAE were evaluated as a secondary outcome to assess the feasibility of continuous CC without the rhythm check every 2 min. Rib and sternum fractures,

Table 1 – The protocol for the continuous chest compression based on baseline rSO_2 value.

Baseline value (%) (mean value for 1 minute)	Duration of continuous chest compression
≥ 50	for 16 minutes or until by increase in rSO_2 value by 10%
≥ 40 to <50	for 16 minutes or until by increase in rSO_2 value by 20%
< 40	for 16 minutes or until by increase in rSO_2 value by 35%

pneumothorax, mediastinal emphysema, and airway and alveolar haemorrhage that are likely to occur during standard CPR were defined as adverse events, and SAE were defined as organ damage accompanied by haemorrhage requiring haemostatic treatment, which was evaluated by computed tomography scan or ultrasound before leaving the emergency room.

Statistical analysis

The TripleCPR cohort was compared to a historical control cohort of 86 non-traumatic OHCA patients aged ≥16 years old with non-shockable rhythm on hospital arrival who were transported to Osaka University Hospital from December 2012 to December 2015 (Supplementary Fig. 1).[14] Patients in the control cohort were resuscitated and treated according to the CoSTR 2010 guideline and received the same protocol in terms of converting manual CC to mechanical CC after hospital arrival as that in the current study but a rhythm check every 2 min.

The inverse probability of treatment weighting (IPTW) method was used to adjust for baseline differences between cohorts. First, multivariable logistic regression was used to estimate the propensity score for each patient based on the number of adrenaline doses and defibrillations, age, sex, bystander CPR, witnessed arrest, initial rhythm, and baseline rSO_2 value. Missing values were imputed with a multiple imputation method generating 5 sets of imputed datasets based on aregImpute (www.rdocumentation.org/packages/Hmisc/versions/4.4-2/topics/aregImpute) with all explanatory variables and the response variable. The coefficients in the above regression obtained from all 5 datasets were pooled by taking the average; then the pooled coefficients were applied to the 5th imputed dataset to calculate propensity scores. Second, to assess whether there was a difference in the achievement of ROSC between the two cohorts, the outcome regression was performed with a multivariable logistic regression with weighting of each observation with the IPTW where the Huber-White sandwich estimator (for estimation of variance) was used to consider data clustering by the weighting. The following covariates were considered in the outcome regression: indicators of the cohort, bystander CPR, witnessed arrest, and the continuous variable of baseline rSO_2 value. Moreover, a restricted cubic spline was applied to model the effect of the baseline rSO_2 value (Supplementary Table 1).

To remove biases due to a differential rate of Stanford type-A aortic dissection (A-AD) between the two cohorts, we performed sensitivity analyses restricting both cohorts to patients in Osaka University Hospital because A-AD data were only measured in that hospital. Two methods were used in the sensitivity analyses: (1) restricting the cohorts used in the IPTW analysis to those without A-AD and (2) adjusting for the differential distribution of A-AD through the IPTW analysis by adding the A-AD variable to the logistic regression model for the main analysis to compute the propensity score.

Sensitivity analysis 1 may be suitable considering that among all patients diagnosed as having A-AD, their ROSC rate was very low at 7.7% (2/26 patients), and sensitivity analysis 2 may be better to produce an analytical result more generalizable for the whole cohort. The restriction method may be better because the increase in rSO_2 values over 16 min in the A-AD patients was not plausible (median [interquartile range]: 0.6% [−2.5, 2.3]) in the TripleCPR cohort.

Baseline characteristics are summarised using medians and interquartile ranges for continuous variables and as frequencies and percentages for categorical variables. All statistical analyses were carried out with a two-sided significance level of 5% and performed using R software version 3.6.3 (www.r-project.org).

Results

During the study period, 444 patients with OHCA arrived at the participating hospitals. The following patients were excluded according to the exclusion criteria: those not meeting the inclusion criteria, those whose data could not be collected successfully, and those with protocol deviation. Finally, 225 patients with OHCA comprised the TripleCPR cohort (Fig. 2).

Table 2 shows the patient characteristics of both cohorts. In the TripleCPR cohort, the median age was 77 years old, 129 (57%) patients were males, 94 (42%) CA were witnessed, 123 (55%) patients received bystander CPR, 156 (69%) had asystole as their initial rhythm, and the median baseline rSO_2 value was 42.7%. There was no significant difference in any of the baseline variables except for prehospital adrenaline administration (0 [0–0] vs 0 [0–1] mg, $P = 0.003$) between the two groups. The ROSC rates were 34 (39.5%) and 76 (33.8%) in the control and TripleCPR cohorts, respectively. No SAE occurred in either cohort. In sensitivity analysis 1 and 2, there were no significant differences in the baseline characteristics except for bystander CPR status ($P = 0.02$ and 0.03, respectively). After IPTW, these cohorts were more balanced (Supplementary Fig. 2). Only age and A-AD fell outside a standardised difference of 0.10; thus, the TripleCPR and control groups were largely comparable.

The IPTW model showed no significant difference in the achievement of ROSC between the two groups (adjusted OR, 0.91 [95% CI, 0.64 to 1.29], $P = 0.60$) (Table 3). In sensitivity analysis 1, the difference was significant (adjusted OR, 1.63 [95% CI, 1.22 to 2.17], $P < 0.001$). In sensitivity analysis 2, TripleCPR showed a positive tendency for a higher probability of ROSC, but the difference was not significant (adjusted OR, 1.25 [95% CI, 0.95 to 1.63], $P = 0.11$) (Table 3). Estimated coefficients are shown in Supplementary Table 1 and Supplementary Fig. 3.

Discussion

Main findings

The rSO_2-guided resuscitation protocol was created on the basis of our previous study,[14] which reported that the maximum amount of rise in rSO_2 value over 16 min was the best predictor of ROSC. The study patients with OHCA and a non-shockable rhythm were divided into three groups according to their baseline rSO_2 value. Each group received continuous CC for 16 min or until achievement of the target rSO_2 value without a rhythm check every 2 min. The probability of ROSC was compared with a historical control cohort in which rhythm had been checked every 2 min. The findings of the present study did not show a significant difference compared with those of the historical cohort. However, given that A-AD is a possible confounder in the main analysis, we performed sensitivity analyses. Sensitivity analysis 1 showed a significant difference, indicating that the TripleCPR protocol is useful to achieve ROSC in OHCA patients without A-AD. Sensitivity analysis 2, which evaluated all patients for whom the effect of A-AD was adjusted because, in general, the cause of CA when starting CPR is unknown, showed a positive

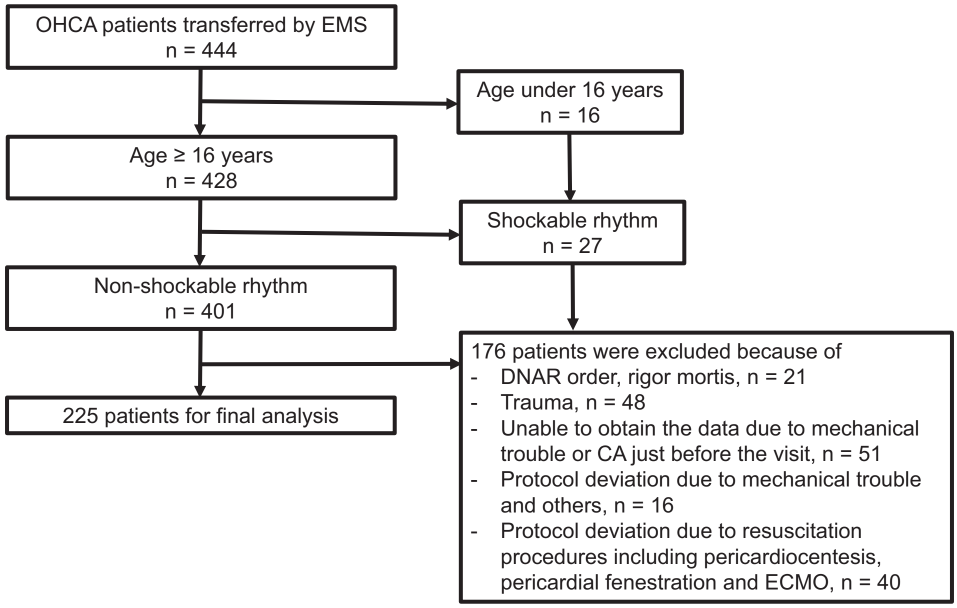

Fig. 2 – Patient flowchart of out-of-hospital cardiac arrest. OHCA, out-of-hospital cardiac arrest; EMS, emergency medical service; DNAR, do not attempt resuscitation; CA, cardiac arrest; ECMO, extracorporeal membrane oxygenation.

tendency for higher probability of ROSC, but the difference was not significant. The results of the sensitivity analyses suggested that the main analysis was affected by the difference in distribution of A-AD. Given that significant differences may not have been detected due to insufficient sample size or different distributions in each group, a further large-scale, prospective study will be required to assess the utility of a new CPR protocol using the rSO_2 value as an index of ROSC, while excluding those patients with certain specific causes of CA to stratify the likelihood of ROSC.

Detection of ROSC by NIRS and future direction

A poor increase in rSO_2 could suggest that the cause of the CA is a disorder making the achievement of ROSC difficult or impossible and could also indicate the point at which further resuscitation efforts can be considered futile. In a recent systematic review and meta-analysis, Schnaubelt et al. showed that both mean rSO_2 and ΔrSO_2 (i.e. the difference from the initial measurement until detection of ROSC or termination of CPR) were higher in the ROSC group than those in the non-ROSC group and that ROSC was not observed when mean rSO_2 remained below 26%.[12] CoSTR 2020 also summarised that a trend of rising rSO_2 may be a more reliable predictive factor for ROSC.[18] Thus, a protocol using the rSO_2 value as the index of ROSC is reasonable and would realise NIRS-guided resuscitative strategies that omit a rhythm check every 2 min. Notably, it would be useful to simplify the resuscitation protocol in prehospital settings in which EMS personnel cannot resuscitate patients in a calm environment due to the transfer situation. Further, Grunau et al. reported that intra-arrest transport to hospital compared with continued on-scene resuscitation among OHCA patients was associated with lower probability of survival to hospital discharge.[19] A disorder such as A-AD, with pathophysiology that shuts down cerebral blood flow, would not increase the rSO_2 value. NIRS-guided resuscitation may be used when determining transport of a patient, with EMS personnel selecting to continue resuscitation at the scene in case the patient's rSO_2 level rises.

Mechanical CC devices in continuous CC

The recommendation of a rhythm check every 2 min is supported by indirect evidence that rescuer fatigue occurs by about 2 min.[7] The use of mechanical CC may be a solution, but the injuries associated with this method may affect CC quality. Segal et al. tested the changes in chest compliance before and after 5 min of mechanical CC in 9 human cadavers who had not received CPR before the study. These data showed that chest compliance increased significantly over time, suggesting that adjustments in compression and decompression forces may be needed to optimise CPR over time.[20] It has been pointed out that increased chest wall compliance, such as that due to rib fracture, affects spontaneous chest wall recoil, which leads to incomplete chest wall recoil.[21,22] We used a piston-type mechanical CC device without a suction cup (Clover 3000®) or load-distributing band (AutoPulse®) in the present study. The reason for no significant difference in ROSC in the primary analysis may have been that insufficient recoil due to increased chest wall compliance led to fewer benefits. It may be necessary to lift the chest wall during the decompression phase, as is done by the LUCAS® device.

Study limitations

This study has several limitations. This was a non-blinded study that included only patients with non-shockable rhythms, and neurological prognosis was not evaluated. Further research on OHCA in additional subgroups (e.g. those with shockable rhythm) is warranted. Second, we used a historical control cohort, and this should be kept in mind when interpreting the results, including the existence of unexpected biases. Furthermore, omitting the rhythm check every 2 min may have caused the resuscitation team not to detect conversion to a potentially shockable rhythm. At the discretion of the attending

Table 2 – Baseline patients characteristics.

	All eligible patients					Patients in Sensitivity analysis 1				Patients in Sensitivity analysis 2			
Variable	Level	Control (N=86)	TripleCPR (N=225)	p	Missing (%)	Control (N=82)	TripleCPR (N=141)	p	Missing (%)	Control (N=86)	TripleCPR (N=167)	p	Missing (%)
Age, years (median [IQR])		76 [68, 84]	77 [70, 83]	0.96	0	76 [69, 84]	76 [67, 83]	0.50	0	76 [68, 84]	77 [68, 84]	0.91	0
Male % (freq)		66 (57)	57 (129)	0.19	0	67 (55)	60 (85)	0.39	0	66 (57)	55 (92)	0.11	0
Witness % (freq)		43 (37)	42 (94)	0.94	0	43 (35)	40 (57)	0.85	0	43 (37)	43 (72)	1.00	0
Bystander CPR % (freq)		42 (36)	55 (123)	0.06	0	42 (34)	58 (82)	0.02	0	42 (36)	58 (96)	0.03	0
Prehospital Adrenaline (median [IQR]) (mg)		0 [0, 0]	0 [0, 1]	0.003	1	0 [0, 0]	0 [0, 0]	0.16	1	0 [0, 0]	0 [0, 0]	0.07	1
Adrenaline administration mg, % (freq)	0	87 (74)	70 (158)			86 (70)	79 (111)			87 (74)	77 (129)		
	1	2 (2)	7 (16)			3 (2)	5 (7)			2 (2)	5 (9)		
	2	4 (3)	8 (17)			4 (3)	4 (6)			4 (3)	6 (10)		
	3	4 (3)	7 (16)			4 (3)	6 (9)			4 (3)	5 (9)		
	4	0 (0)	4 (8)			0 (0)	1 (1)			0 (0)	1 (1)		
	5	4 (3)	2 (5)			4 (3)	3 (4)			4 (3)	2 (4)		
	6	0 (0)	1 (3)			0 (0)	1 (2)			0 (0)	2 (3)		
	7	0 (0)	1 (2)			0 (0)	1 (1)			0 (0)	1 (2)		
Prehospital Defibrillation (median [IQR]) (freq)		0 [0, 0]	0 [0, 0]	0.92	1	0 [0, 0]	0 [0, 0]	0.85	1	0 [0, 0]	0 [0, 0]	0.69	1
Number of Defibrillation, % (freq)	0	92 (78)	92 (206)			91 (74)	91 (128)			92 (78)	90 (151)		
	1	4 (3)	2 (4)			4 (3)	2 (3)			4 (3)	2 (3)		
	2	2 (2)	4 (8)			3 (2)	4 (5)			2 (2)	4 (7)		
	3	2 (2)	3 (6)			3 (2)	3 (4)			2 (2)	3 (5)		
	4	0 (0)	0 (1)			0 (0)	1 (1)			0 (0)	1 (1)		
Initial rhythm on hospital arrival % (freq)	PEA	29 (25)	31 (69)	0.89	0	29 (24)	31 (43)	0.97	0	29 (25)	32 (53)	0.77	0
	Asystole	71 (61)	69 (156)			71 (58)	70 (98)			71 (61)	68 (114)		
Baseline rSO_2 value (median [IQR])		45.1 [37.1, 50.0]	42.7 [37.9, 48.4]	0.42	0	45.2 [38.1, 50.2]	44.2 [40.0, 49.4]	0.55	0	45.1 [37.1, 50.0]	43.7 [39.5, 49.3]	0.52	0
rSO_2 initial type % (freq)	Init < 40	38 (33)	36 (82)			37 (30)	25 (35)			38 (33)	27 (45)		
	$40 \leq$ Init <50	36 (31)	45 (101)			37 (30)	53 (75)			36 (31)	53 (88)		
	Init $\geq$ 50	26 (22)	19 (42)			27 (22)	22 (31)			26 (22)	20 (34)		
Stanford type-A aortic dissection % (freq)		5 (4)	16 (26)			0 (0)	0 (0)			5 (4)	16 (26)		

IQR, Interquartile range; freq, frequency; CPR, cardiopulmonary resuscitation; PEA, pulseless electrical activity; rSO_2, regional cerebral oxygen saturation; Init, initial; Missing, percentage of missing data.

Table 3 – Logistic regression analyses for ROSC between CPR strategies.

Method	Odds Ratio Estimate	Lower	Upper	P-value
Primary analysis; All eligible patients				
TripleCPR vs. historical cohort	0.91	0.64	1.29	0.60
Sensitivity analysis 1; excluded A-AD				
TripleCPR vs. historical cohort	1.63	1.22	2.17	<0.001
Sensitivity analysis 2; included A-AD				
TripleCPR vs. historical cohort	1.25	0.95	1.63	0.11

ROSC, return of spontaneous circulation; CPR, cardiopulmonary resuscitation; A-AD, stanford type-A aortic dissection.

physician, two patients were defibrillated at the second rhythm check due to the determination of fine ventricular fibrillation. However, the rhythms appeared to be asystole, and they were difficult to judge. Recent commercially available devices can analyse the rhythm during ongoing CC,[23–27] but their effectiveness needs to be fully evaluated in prospective clinical trials even with mechanical CC. These technologies would resolve the above problem and could lead to improved research involving patients with a shockable rhythm. Finally, based on our previous research,[14,13] we set the target rSO_2 value to that at which approximately 87.5% of CA patients are expected to achieve ROSC in each group. However, had we set the increase in rSO_2 to a lower amount or a rhythm check interval shorter than 16 min, we might have detected additional patients with ROSC earlier. Additionally, a rhythm check at 4-min intervals was used to extend the continuous CC time in patients with a non-shockable rhythm after 16 min. However, the target rSO_2 value and time interval we set in this study protocol may not have been the best, and further study will be needed.

Conclusion

We performed CPR using rSO_2 as an index of ROSC and omitted the rhythm check every 2 min. There was no significant difference in the odds ratio of ROSC compared with the conventional protocol, but organ damage accompanied by haemorrhage requiring haemostatic treatment did not occur. Although it will be necessary to reconsider the optimal cut-off value for rSO_2 to detect ROSC, this novel trial suggested the potential for creating a CPR protocol that does not require a rhythm check every 2 min.

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Declaration of Competing Interest

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

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Author statement

All of the authors have made a substantial contribution to all of the following: the conception and design of the study, or acquisition of data, or analysis and interpretation of data; drafting the article or revising it critically for important intellectual content; and final approval of the version to be submitted.

This article does not overlap with previous publications, has not been published previously, and is not under consideration for publication elsewhere.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.resuscitation.2021.09.006.

REFERENCES

1. Merchant RM, Topjian AA, Panchal AR, et al. Part 1: Executive Summary: 2020 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation 2020;142(16_suppl_2). https://doi.org/10.1161/CIR.0000000000000918.
2. Virani SS, Alonso A, Benjamin EJ, et al. Heart Disease and Stroke Statistics-2020 Update: A Report From the American Heart Association. Circulation 2020;141:e139–596.
3. Nolan JP, Maconochie I, Soar J, et al. Executive Summary 2020 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. Resuscitation 2020;156:A1–A22.
4. Olasveengen TM, Mancini ME, Perkins GD, et al. Adult Basic Life Support: International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. Resuscitation 2020;156:A35–79.
5. Wik L, Hansen TB, Fylling F, et al. Delaying defibrillation to give basic cardiopulmonary resuscitation to patients with out-of-hospital ventricular fibrillation: a randomized trial. JAMA 2003;289:1389. https://doi.org/10.1001/jama.289.11.1389.

6. Baker PW, Conway J, Cotton C, et al. Defibrillation or cardiopulmonary resuscitation first for patients with out-of-hospital cardiac arrests found by paramedics to be in ventricular fibrillation? A randomised control trial. Resuscitation 2008;79:424–31.
7. Perkins GD, Travers AH, Berg RA, et al. Part 3: Adult basic life support and automated external defibrillation: 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations. Resuscitation 2015;95:e43–69.
8. Berg RA, Sanders AB, Kern KB, et al. Adverse hemodynamic effects of interrupting chest compressions for rescue breathing during cardiopulmonary resuscitation for ventricular fibrillation cardiac arrest. Circulation 2001;104:2465–70.
9. Meex I, De Deyne C, Dens JO, et al. Feasibility of absolute cerebral tissue oxygen saturation during cardiopulmonary resuscitation. Crit Care 2013;17(2):R36. https://doi.org/10.1186/cc12546.
10. Sanfilippo F, Serena G, Corredor C, et al. Cerebral oximetry and return of spontaneous circulation after cardiac arrest: a systematic review and meta-analysis. Resuscitation 2015;94:67–72.
11. Cournoyer A, Iseppon M, Chauny J-M, et al. Near-infrared spectroscopy monitoring during cardiac arrest: a systematic review and meta-analysis. Acad Emerg Med 2016;23:851–62.
12. Schnaubelt S, Sulzgruber P, Menger J, et al. Regional cerebral oxygen saturation during cardiopulmonary resuscitation as a predictor of return of spontaneous circulation and favourable neurological outcome - A review of the current literature. Resuscitation 2018;125:39–47.
13. Takegawa R, Hayashida K, Rolston DM, et al. Near-infrared spectroscopy assessments of regional cerebral oxygen saturation for the prediction of clinical outcomes in patients with cardiac arrest: a review of clinical impact, evolution, and future directions. Front Med (Lausanne) 2020;7. https://doi.org/10.3389/fmed.2020.58793010.3389/fmed.2020.587930.s001.
14. Takegawa R, Shiozaki T, Ogawa Y, et al. Usefulness of cerebral rSO_2 monitoring during CPR to predict the probability of return of spontaneous circulation. Resuscitation 2019;139:201–7.
15. Takegawa R, Hayashida K, Choudhary R, Rolston DM, Becker L. Brain monitoring using near-infrared spectroscopy to predict outcome after cardiac arrest: a novel phenotype in a rat model of cardiac arrest. J Intensive Care 2021;9:4.
16. Hazinski MF, Nolan JP, Aickin R, et al. Part 1: Executive Summary: 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. Circulation 2015;132(16 Suppl 1):S2–S39.
17. Callaway CW, Soar J, Aibiki M, et al. Part 4: Advanced Life Support: 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. Circulation 2015;132:S84–S145.
18. Maconochie IK, Aickin R, Hazinski MF, et al. Pediatric Life Support: 2020 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. Resuscitation 2020;156:A120–55.
19. Grunau B, Kime N, Leroux B, et al. Association of intra-arrest transport vs continued on-scene resuscitation with survival to hospital discharge among patients with out-of-hospital cardiac arrest. JAMA 2020;324:1058. https://doi.org/10.1001/jama.2020.14185.
20. Segal N, Robinson AE, Berger PS, et al. Chest compliance is altered by static compression and decompression as revealed by changes in anteroposterior chest height during CPR using the ResQPUMP in a human cadaver model. Resuscitation 2017;116:56–9.
21. Frascone RJ. The risk versus benefit of LUCAS: is it worth it? Anesthesiology 2014;120:797–8.
22. Oh JH. Effects of cardiopulmonary resuscitation time on chest wall compliance in patients with cardiac arrest. Resuscitation 2017;117:e1. https://doi.org/10.1016/j.resuscitation.2017.05.010.
23. Zoll Company. X Series Operator's Guide. (Accessed 12 June 2021, at https://www.accessdata.fda.gov/cdrh_docs/pdf16/P160022C.pdf)
24. NIHON KOHDEN. TEC-5600 Series. (Accessed 12 June 2021, at https://ae.nihonkohden.com/sites/default/files/u21/t7846_TEC5600_En_S.pdf)
25. Stryker. cprINSIGHT Analysis Technology. (Accessed 12 June 2021, at https://www.strykeremergencycare.com/globalassets/assets/hosted-docs/cprinsight-analysis-technology-whitepaper-1.pdf)
26. Tan Q, Freeman GA, Geheb F, Bisera J. Electrocardiographic analysis during uninterrupted cardiopulmonary resuscitation. Crit Care Med 2008;36(Suppl):S409–12.
27. de Graaf C, Beesems SG, Oud S, Stickney RE, Piraino DW, Chapman FW, Koster RW. Analyzing the heart rhythm during chest compressions: Performance and clinical value of a new AED algorithm. Resuscitation 2021;162:320–8.