Original Article

Cerebral oxygenation monitoring during resuscitation by emergency medical technicians: a prospective multicenter observational study

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Aim: To assess the feasibility and predictive ability of regional cerebral oxygen saturation monitoring during cardiopulmonary resuscitation by emergency medical technicians.

Methods: This prospective observational study included 33 cardiac arrest patients who received cardiopulmonary resuscitation in a prehospital setting. Patients were connected to a near-infrared spectrometer through two disposable probes immediately after entering the ambulance. The monitor, which showed regional cerebral oxygen saturation readings, was obscured by covering it with a sheet of paper. Regional cerebral oxygen saturation was measured continuously until hospital arrival. Outcome variables included the prehospital return of spontaneous circulation, survival to hospital admission, and survival at 90 days.

Results: For patients who survived >90 days after hospital admission (n = 2), the mean regional cerebral oxygen saturation values upon ambulance and hospital arrival were 24% and 60%, respectively; for patients who did not survive (n = 31), the mean regional cerebral oxygen saturation values were 15% and 17%, respectively. Regional cerebral oxygen saturation values increased to a greater extent between ambulance arrival and hospital arrival in patients who survived >90 days (median, 36%; interquartile range, 32–40%) than in those who did not survive (0; 0–6%; P = 0.07). Additionally, regional cerebral oxygen saturation values were not related to the prehospital return of spontaneous circulation or survival to hospital admission.

Conclusion: Regional cerebral oxygen saturation could be monitored during resuscitation by emergency medical technicians, and it can be used during physiological monitor-guided cardiopulmonary resuscitation.

Key words: cardiopulmonary resuscitation, out-of-hospital cardiac arrest, return of spontaneous circulation

INTRODUCTION

THE 2015 AMERICAN Heart Association Guidelines for Cardiopulmonary Resuscitation (CPR) and Emergency Cardiovascular Care emphasize the need for physiological monitoring during CPR for optimal quality.[1] Cerebral perfusion pressure during resuscitation could influence neurological survival during out-of-hospital cardiac arrest (OHCA). A real-time indicator of cerebral perfusion pressure would be useful for estimating the severity of cerebral damage, which would enable prompt post-cardiac arrest care.

Regional cerebral oxygen saturation (rSO_2) is a non-invasive indicator of cerebral perfusion pressure. It can be measured during cardiac arrest using near-infrared spectroscopy (NIRS) and does not require a pulsatile signal.[2] Clinical studies suggest that NIRS can measure rSO_2 during CPR in a real-time, non-invasive, feasible manner.[3–14] Several reports have documented the benefits of rSO_2 monitoring during both in-hospital and out-of-hospital CPR.[3–5,9,10,12,13]

Findings from our previous study showed that the rSO_2 value at hospital arrival predicts neurological outcomes at 90 days after OHCA;[10] however, values before arrival were not monitored. If useful for assessing CPR quality and cerebral damage, prehospital rSO_2 monitoring will allow us to carry out physiological monitor-guided, goal-directed CPR.

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Although several studies have reported doctors monitoring rSO_2 in prehospital settings for OHCA patients,[6–8,11,14] to the best of our knowledge, there have been no reports on rSO_2 monitoring during CPR by emergency medical technicians (EMT).

More than 135 million cardiovascular-related deaths occur each year worldwide.[15] In Japan, 127,018 patients with cardiopulmonary arrest were transported to hospitals in 2017,[16] most of whom were resuscitated by EMT, who were not physicians. The usefulness of rSO_2 monitoring during resuscitation in the prehospital setting requires accurate determination of rSO_2 by such individuals. This study aimed to assess the feasibility and predictive ability of rSO_2 monitoring during CPR by EMT.

METHODS

Study design, population, and ethical considerations

IN THIS OBSERVATIONAL, prospective, multicenter cohort study, the EMT measured prehospital rSO_2 values in OHCA patients between March 2015 and February 2017. Eight ambulances of the Kyoto City Emergency Medical Service (EMS) and two tertiary emergency hospitals in Japan (Kyoto University Hospital and Kyoto Medical Center) participated in this study. The inclusion criterion for patients was OHCA at the time of EMS contact. The exclusion criteria were presence of trauma, accidental hypothermia, age <18 years, and previous completion of the "Do Not Attempt Resuscitation" form.

The study protocol was approved by the Institutional Review Board or Ethics Committee at each participating medical institution (UMIN000026167/E2260).

Emergency medical care

All EMT carried out basic life support on the scene according to current CPR guidelines.[17,18] Patients were transported to the hospital because, in Japan, EMT are not permitted to terminate CPR in the field. Patients who did not achieve return of spontaneous circulation (ROSC) were transported with ongoing CPR. All patients received manual chest compressions, and none received mechanical chest compressions.

Near-infrared spectroscopy

Immediately on entering the ambulance, patients were connected to a near-infrared spectrometer (INVOSTM 5100C; Medtronic Covidien, Boulder, CO, USA) through two disposable probes, bilaterally applied to the patient's forehead by the EMT. The rSO_2 monitor was obscured by covering it with a sheet of paper. The spectrometer emits near-infrared rays at two wavelengths (730 and 805 nm) into the patient's forehead, calculates spatial depth resolution, minimizes superficial signal contamination from the scalp and skull, and detects changes in oxygen saturation in the brain. It utilizes the NIRS technology to measure mixed venous-arterial (70/30) oxygen saturation in the frontal lobes of the cerebral cortex. Limits of detection include a hemoglobin-oxygen saturation of <15% or >95%. Regional cerebral oxygen saturation was measured continuously from the time of ambulance arrival at the scene of the OHCA to the time of patient admission at the hospital or the time of death as confirmed by a physician. Before we started this study, we visited the EMS station and technicians were trained to use the NIRS device and to place the sensor on the patient's forehead for approximately 30 min.

Data collection

Data were collected prospectively using the Utstein Style as a guideline.[19] Baseline patient characteristics and in-hospital data were retrieved from medical records and databases. The data were collected for age, sex, bystander witness, bystander-initiated CPR, presumed cardiogenic arrest, ambulance transport time, prehospital procedure, prehospital ROSC, survival to hospital admission after ROSC, and survival at 90 days as outcome variables. Cardiac arrest was defined as the absence of spontaneous respiration, a palpable pulse, and responsiveness to stimuli. The arrest was presumed to be of cardiac origin unless it was caused by cerebrovascular disease, respiratory disease, external factors (e.g., drug overdose or asphyxia), or any other non-cardiac factors, as determined by a physician.

Outcome

Before the start of this study, the primary outcome was set to Cerebral Performance Categories at 90 days. However, in real-world studies, the recovery rate was lower, and the neurological outcome was worse than that expected. We set the primary outcome as survival at 90 days and the secondary outcomes as prehospital ROSC and survival to hospital admission after ROSC.

Statistical analyses

The Mann–Whitney *U*-test was used for unpaired comparisons, and the χ^2-test and Fisher's exact test were utilized to examine differences between categorical variables. Pearson's correlation coefficient was used to assess the relationship strength between two variables. All statistical tests were two-tailed, and statistical significance was defined as $P < 0.05$, with a trend toward significance if $0.05 < P < 0.1$ and toward non-significance if $P > 0.1$. All statistical analyses were carried out using JMP software version 10.0.0 (SAS Institute, Cary, NC, USA).

RESULTS

Participants and descriptive data

DATA WERE COLLECTED from 114 consecutive patients with OHCA who were transported to two facilities in eight ambulances. Of them, 33 patients were enrolled in the study and 81 were excluded due to protocol violation (the EMT did not use NIRS). Among the included patients, 3/33 attained prehospital ROSC, 8/33 survived to hospital admission after ROSC, and 2/33 were alive 90 days after hospital admission. The baseline characteristics of the study population are listed in Table 1.

Table 1. Demographic data of included cardiac arrest patients who received cardiopulmonary resuscitation in a prehospital setting ($n = 33$)

Characteristic	
Age, years	82 (71–87)
Male sex	23 (70)
Bystander witness	9 (27)
Bystander-initiated CPR	9 (27)
Presumed cardiogenic origin	23 (70)
Ambulance transport time, min	11 (6.5–15)
Prehospital procedures	
Advanced airway devices	11 (33)
Intravenous adrenaline administration	4 (12)
Defibrillation	2 (6)
Prehospital return of spontaneous circulation	3 (9)
Survival to hospital admission	8 (24)
Survival at 90 days	2 (6)
rSO_2 at ambulance arrival (%) [A]	15 (15–23)
Peak rSO_2 (%)	34 (15–70)
Minimum rSO_2 (%)	15 (15–16)
rSO_2 at hospital arrival (%) [B]	15 (15–18)
[B] − [A]	0 (−2–17)

Data are presented as number (%) or median (interquartile range). CPR, cardiopulmonary resuscitation; rSO_2, regional cerebral oxygen saturation.

Outcomes of OHCA patients

For the 33 patients enrolled in this study, the initial and peak mean (interquartile range [IQR]) rSO_2 values in the ambulance were 15% (15–23%) and 34% (15–70%), respectively. The mean (IQR) rSO_2 on hospital arrival was 15% (15–18%) (Table 1). The difference between rSO_2 values during ambulance-administered CPR (i.e., between ambulance arrival and hospital arrival) was 0 (−2–17%). Pearson's correlation coefficient for the association between right- and left-sided rSO_2 was 0.87. In 21 of 33 cases (66%), the lowest rSO_2 (15%) was seen at the start of measurement in the ambulance.

Survival at 90 days

The rSO_2 values significantly increased during ambulance-administered CPR in the two patients who survived >90 days after hospital admission (median, IQR: 36%, 32–40%) than in the 31 patients who did not (0, 0–6%; $P = 0.07$) (Table 2). The initial rSO_2 taken in the ambulance was also higher in patients who survived >90 days (24%, 17–31%) than in those who did not survive (15%, 15–23%; $P = 0.09$), as was the rSO_2 at hospital arrival (60%, 49–71% for survivors; 17%, 15–31% for non-survivors; $P = 0.05$).

Prehospital ROSC

The rSO_2 values increased to a similar extent during ambulance-administered CPR in the three patients who attained prehospital ROSC (0%, −4–32%) and in the 30 patients who did not survive (0%, 0–14%); $P = 0.58$) (Table 2). The rSO_2 values at ambulance and hospital arrival were also unrelated to prehospital ROSC; values for ROSC and no ROSC were 17% (15–22%) and 15% (15–24%; $P = 0.69$), respectively, at ambulance arrival and 18% (15–49%) and 20% (15–40%; $P = 0.97$), respectively, at hospital arrival.

Survival to hospital admission after ROSC

The rSO_2 values increased to a similar extent during ambulance-administered CPR in the eight patients who survived to hospital admission (3%, 0–38%) and in the 25 patients who did not survive (0%, 0–7%; $P = 0.3$). The rSO_2 values at ambulance arrival and hospital arrival were also unrelated to survival to hospital admission; values for patients alive and dead at admission were 16% (15–23%) and 15% (15–24%; $P = 0.63$), respectively, at ambulance arrival and 22% (15–65%) and 18% (15–35%; $P = 0.78$), respectively, at hospital arrival.

DISCUSSION

THIS STUDY SHOWED the feasibility of rSO_2 monitoring through NIRS during the resuscitation of OHCA

Table 2. Effect of regional cerebral oxygen saturation (rSO_2) levels on outcomes in cardiac arrest patients who received cardiopulmonary resuscitation in a prehospital setting

(A)	Survival at 90 days		
	Yes (n = 2)	No (n = 31)	P-value
rSO_2 at ambulance arrival (%) [A]	24 (17–31)	15 (15–23)	0.09**
Peak rSO_2 (%)	70 (66–73)	34 (15–70)	0.18
Minimum rSO_2 (%)	23 (15–31)	15 (15–15)	0.29
rSO_2 at hospital arrival (%) [B]	60 (49–71)	17 (15–31)	0.05**
[B] − [A]	36 (32–40)	0 (0–6)	0.07**

(B)	Prehospital ROSC			Survival to hospital admission after ROSC		
	Yes (n = 3)	No (n = 30)	P-value	Yes (n = 8)	No (n = 25)	P-value
rSO_2 at ambulance arrival (%) [A]	17 (15–22)	15 (15–24)	0.69	16 (15–23)	15 (15–24)	0.63
Peak rSO_2 (%)	50 (15–66)	34 (15–71)	0.85	39 (15 –72)	34 (15–70)	0.98
Minimum rSO_2 (%)	15 (15–15)	15 (15–18)	0.34	15 (15–20)	15 (15–16)	0.98
rSO_2 at hospital arrival (%) [B]	18 (15–49)	20 (15–40)	0.97	22 (15–65)	18 (15–35)	0.78
[B] − [A]	0 (–4–32)	0 (0–14)	0.58	3 (0–38)	0 (0–7)	0.30

Values are presented as median (interquartile range).
**Trend toward significant, $0.05 < P$-value < 0.1. ROSC, return of spontaneous circulation.

patients by an EMT who is not a physician. Our data indicate that prehospital rSO_2 monitoring could be useful for assessing CPR quality and cerebral damage and will enable physiological monitor-guided, goal-directed CPR and stratified post-cardiac arrest critical care.

Newman *et al*. reported no detectable rSO_2 signals in patients with OHCA;[7] however, due to technological improvement in NIRS devices, rSO_2 can now be measured in such patients, even during prehospital resuscitation.[6–8,11,14] In our study, the NIRS monitor was covered by a sheet of paper so that the EMTs were unable to observe the rSO_2 signal. The rSO_2 values for all patients in whom this measurement was attempted were later revealed to the EMT.

Coronary perfusion pressure, arterial relaxation diastolic pressure, central venous oxygen saturation, and end-tidal carbon dioxide ($ETCO_2$) correlate with cardiac output and myocardial blood flow during CPR.[1] Hence, monitoring these parameters would potentially optimize CPR quality. To monitor the first three parameters, arterial lines and/or central venous lines are needed, which is challenging during prehospital CPR. In Japan, EMTs are permitted to insert tracheal tubes only under the direction of a physician.

Previous studies have examined the relationship between $ETCO_2$ and ROSC.[20–22] The $ETCO_2$ concentrations during CPR are primarily dependent on pulmonary blood flow and cardiac output. Failure to maintain $ETCO_2$ concentrations at >10 mmHg during CPR reduces cardiac output and predicts unsuccessful resuscitation.[20,22] Two retrospective observational studies reported worse neurological survival in prehospital OHCA patients receiving any type of advanced airway management, including tracheal intubation, than in those receiving conventional bag valve mask ventilation.[23,24] Prehospital intubation could worsen patient outcomes by impairing the execution of simultaneous basic life support procedures, resulting in ineffective chest compressions.[25]

Near-infrared spectroscopy is a non-invasive technique in which the sensor is placed on the patient's forehead for, on average, approximately 15 s, and it does not interrupt basic or advanced life support procedures.[12] No study reported delays in CPR during sensor application.

Only a few studies have measured cerebral saturation during prehospital CPR;[6–8,11,14] many others measured cerebral oxygen saturation in the hospital environment.[3–5,9,10,12,13] Some studies also suggested that rSO_2 values at hospital arrival help predict neurologic outcomes 1 week after cardiac arrest or at hospital discharge.[10,13] In a study in which rSO_2 was measured during prehospital CPR by a physician, 22 of 53 patients achieved ROSC.[14] In 29 of the 53 patients, the initial rSO_2 level was <15%. With ongoing CPR, the rSO_2 value was higher in the ROSC group than in the no-ROSC group.

In 21 of 33 (66%) cases in our study, the mean rSO_2 value was lowest (15%) at the start of measurement in the ambulance. The initial prehospital rSO_2 value was lower in our study than in a previous study,[11] as was the rate at which ROSC was attained (8/33 patients in our study, 24%).[4,5,8,9,11,13,14] In addition, in 20 cases in our study, rSO_2 values did not increase during CPR. We believe that the included patients in our study were nearing death and hence the rSO_2 levels were not elevated. Due to such differences in the enrolled patients' characteristics, we believe that previous studies showed elevated rSO_2 during CPR in prehospital settings, and that was associated with ROSC. In this study, however, elevated rSO_2 was not significantly associated with ROSC. Furthermore, our study differs from a previous study in terms of prehospital treatment[11]. This might have affected the association between elevated rSO_2 and ROSC.

Limitations

First, as NIRS does not measure cerebral perfusion pressure in the superficial layers of all frontal lobe areas, rSO_2 is not a reliable indicator of the partial pressure of brain tissue oxygen. However, rSO_2 is closely related to oxygen saturation in the jugular bulb, which represents venous oxygenation of the whole brain. Second, unlike the findings in previous studies,[4,5,8,9,11,13,14] the 90-day clinical outcomes in our study were very poor, particularly in patients with cardiac arrest at hospital arrival. Before the start of this study, the primary outcome was set to Cerebral Performance Categories at 90 days, but in real-world studies, the outcome was changed because the survival rate was lower than expected. As potential reasons for our poor outcomes, we note that EMTs in Japan are not permitted to terminate CPR in the field and that most OHCA patients treated by EMTs are transported to emergency hospitals. Therefore, our results might not be generalizable to countries with different practices. Third, the small number of outcome events limited the ability to undertaken multivariable modeling. Fourth, in this study, more than half of the patients were excluded due to protocol violations. We have not collected data of the excluded patients; hence, we could not compare the difference between the included and excluded patients. Finally, as with any observational study design, residual confounding factors could account for some of the associations.

CONCLUSIONS

IN OUR STUDY, increases in rSO_2 during CPR in the ambulance were highest in patients who survived >90 days after hospital admission; this indicates that prehospital rSO_2 monitoring could be useful for assessing CPR quality and cerebral damage, which in turn enables physiological monitor-guided, goal-directed CPR, and stratified post-cardiac arrest critical care.

DISCLOSURE

Approval of the research protocol: The study protocol was approved by the Institutional Review Board or Ethics Committee at each participating medical institution.

Informed consent: The requirement of written informed consent was waived according to Ethical Guidelines for Medical and Health Research Involving Human Subjects.

Registry and the registration no. of the study/trial: UMIN000026167/E2260.

Animal studies: N/A.

Conflict of Interest: K. Nishiyama has conducted an investigator-sponsored study (Covidien, Japan) entitled "Pre-hospital rSO_2 Study" ("Pre-hospital Resuscitation for Sustaining Cerebral Oxidation: Observational Cohort Study").

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