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ORIGINAL RESEARCH

Initial five and ten-minute regional cerebral oxygen saturation as a predictor of the futility of resuscitation for out-of-hospital cardiac arrest

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Abstract

This study aimed to investigate the usefulness of cerebral regional oxygen saturation (rSO2) during the initial 5 and 10 minutes of cardiopulmonary resuscitation (CPR) compared with an initial rSO2 and mean rSO2 during entire CPR to predict the futility of resuscitation for patients without of-hospital-cardiac arrest (OHCA). This was a prospective study involving 52 adult patients presenting in OHCA and whose cerebral rSO2 values were measured until either CPR was terminated or sustained return of spontaneous circulation (ROSC) was achieved. Receiver operating characteristics analyses were used to evaluate which time and type of measurement is better to predict non-ROSC. The area under the curve (AUC) of each rSO2 value according to measurement time (overall, initial 5 minutes and 10 minutes) were the highest value of 0.743, 0.724, and 0.739, mean values of 0.724, 0.677 and 0.701 and ΔrSO2 (Changes in values of regional cerebral oxygen) value of 0.722, 0.734 and 0.724, respectively, while all of the initial values had a poor AUC ($<$0.7) and also were not statistically significant. The optimal cut-off value of each rSO2 values during overall, initial 5 minutes and 10 minutes were the highest value of 26% (sensitivity, 53.9%; specificity, 92.3%), 24% (sensitivity, 56.4%; specificity, 92.3%), and 30% (sensitivity, 61.5%; specificity, 84.6%), mean value of 15.2%, 15.3% and 16%, respectively. None of the patients with a persistent rSO2 $\leq$18% during the overall period achieved ROSC. Initial 5 minutes and 10 minutes cerebral rSO2 values an out-of-hospital-cardiac arrest (OHCA) are a better predictor in deciding the futility of CPR, compared to initial and overall measurements.

Keywords

Out-of-hospital cardiac arrest; Cardiopulmonary resuscitation; Cerebral oximetry; Near-infrared spectroscopy; Futility of CPR

1. Introduction

The decision to terminate resuscitative efforts during refractory cardiac arrest (CA) can be difficult and continues to be debated in the medical literature. In countries with restrictive policies for cardiopulmonary resuscitation (CPR) termination such as Korea and Japan, more accurate guidelines are needed [1, 2]. Although clinical guidelines for termination of resuscitation (TOR) have been developed and validated [3, 4], their implementation in different countries and emergency medical systems (EMS) is still difficult and a multimodal approach is necessary.

Most hemodynamic monitoring tools currently in use do not reliably detect the presence of a pulsatile flow during CA and cannot provide reliable information. Furthermore, brain monitoring tools that can measure cerebral perfusion and oxygenation such as transcranial doppler ultrasonography, and jugular bulb saturation cannot be used in out-of-hospital cardiac arrest conditions [5].

Cerebral near-infrared spectroscopy (NIRS) can provide continuous, non-invasive, and real-time cerebral regional oxygen saturation (rSO2), which is easily accessible. These changes in NIRS reflect changes in cerebral perfusion and oxygen tension during CA, which correlates with coronary perfusion pressure (CPP) [6].

Recent studies have demonstrated that rSO2 has the potential to predict outcomes such as the return of spontaneous circulation (ROSC) and neurological outcomes during CA [7]. In these studies, the most commonly used rSO2 values for prediction were the initial static value measured on hospital arrival and the mean value. However, the initial static cerebral rSO2 is not sufficient to predict futility due to the possibility of technical error [8], its lower specificity and variable thresholds [9, 10], and a broad range of rSO2 values at the time of death [11]. Moreover, rSO2 is mainly used to determine instantaneous changes; changes over the course of a CA may

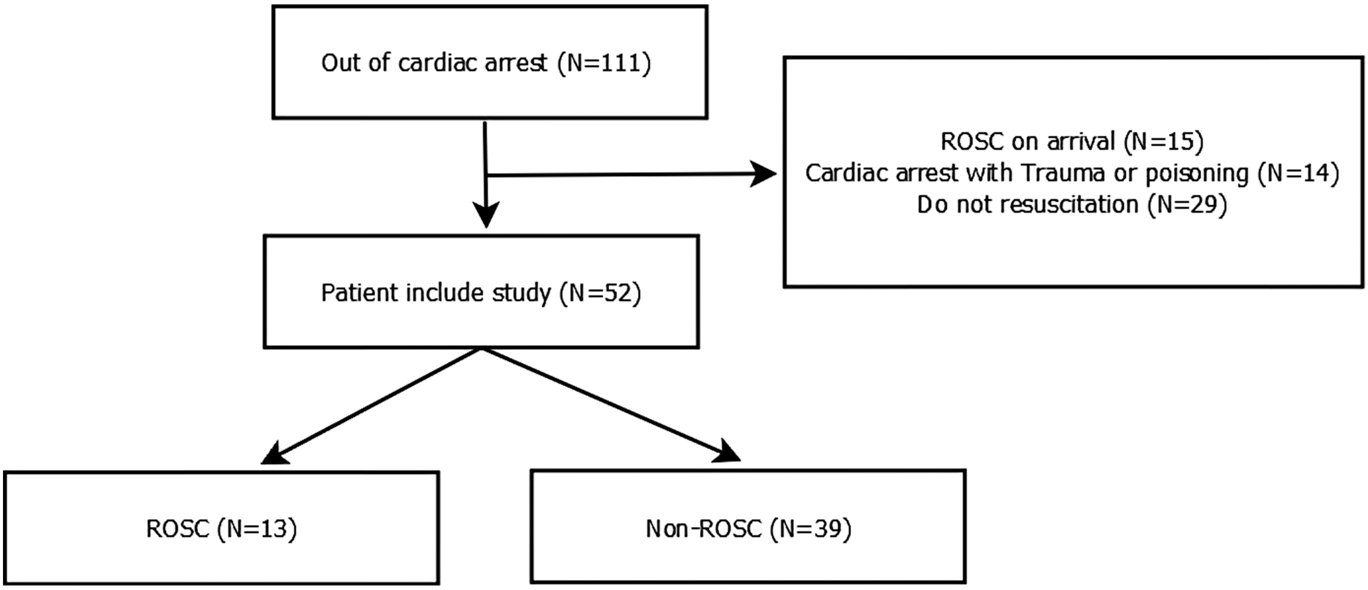

FIGURE 1. Flow diagram of including patients. ROSC, Return of spontaneous circulation.

be a more important prognostic indicator [12, 13]. Some studies have suggested that measurements made throughout the resuscitation may be better to evaluate outcomes rather than a single measurement, which does not reflect the improvements seen during CPR [14]. Although the mean rSO2 value could better reflect these changes and is a better predictor than the initial value [7], they might not be as easily accessible during the early CPR period. Therefore, the best practices for the use of cerebral rSO2 as a futility indicator of OHCA have not yet been established. And further research is needed to evaluate which time points and types of measurements provide the best information during CPR to determine futility.

This study aimed to investigate the usefulness of rSO2 measurements during the initial 5 and 10 minutes of CPR compared with an initial measurement on hospital arrival and overall measurements during CPR to predict the futility of CPR in patients with OHCA.

2. Methods

2.1 Study design

This was a single-center, prospective, observational study conducted at an urban tertiary care academic medical center. This hospital with 1300 inpatient beds annually admits approximately 100,000 patients into the emergency department. This study was conducted in the emergency department from May 2015 to October 2015. The study population included adult patients with OHCA who were transported to the emergency department directly from the scene of the CA. Exclusion criteria included cardiac arrest caused by trauma or poisoning, patients who had already achieved ROSC on hospital arrival, and patients who had previously completed a "do not attempt resuscitation" form (Fig. 1).

2.2 Data collection

The data was collected on a prospective registry form using Utstein-style prehospital EMS records and hospital medical records. In the prehospital period, an emergency medical technician (EMT) performed CPR and analyzed electrocardiography using an automatic external defibrillator which performed defibrillation when indicated. All EMTs completed professional training on CPR. Professional training curriculum included supraglottic airway usage, performing high-quality CPR, and injection of epinephrine. During the hospital period, chest compressions were performed by a physician or EMT. Emergency physicians secured airways and analyzes the electrocardiogram. The prehospital EMS records included information such as the witness and bystander CPR status, and the initial cardiac rhythm. The hospital medical records included information such as patient sex, age, blood pH, lactate level, and whether ROSC was achieved. Sustained ROSC was defined as ROSC without repetitive cardiopulmonary arrest for 20 consecutive minutes.

2.3 Near-infrared spectroscopy measurement

A near-infrared spectroscopy (NIRS) device (INVOS 5100C; Covidien, Boulder, CO, USA) was used which contained two probes for attachment to the forehead. Each probe consists of an adhesive strip housing a single near-infrared light transmitter and two sensors. The limits of detection for the device include a hemoglobin-oxygen saturation of $<15\%$ or $>95\%$ and a cortical tissue depth of >2 cm. The NIRS was attached above the muscles in the forehead in less than a minute after arrival in the emergency room. Cerebral rSO2 values were recorded continuously until either CPR was terminated or sustained ROSC was achieved. Both lower and higher cerebral rSO2 values obtained from the 2 probes were recorded. If only 1 of 2 cerebral rSO2 values were recorded, it was recorded as both the lower and the higher value. When the measured values were different in the left and right probes, the lower measured value showed a higher predictive power [15]. Therefore, the lower values were used for prognosis with the exception of the initial value. The rSO2 values were blinded to the

TABLE 1. Baseline characteristics of the study population.

Characteristics	[g]ROSC (N = 13)	Non-ROSC (N = 39)	p-value
Male, n (%)	11 (84.6)	23 (59.0)	0.18
Age (year), median (IQR)	55 (48–67)	72 (57–77)	0.02
Witnessed, n (%)	11 (84.6)	17 (43.6)	0.01
Bystander [a]CPR, n (%)	8 (61.5)	19 (48.7)	0.42
Shockable initial rhythm, n (%)	4 (30.8)	3 (7.7)	0.06
Meet the rule of [b]TOR, n (%)	2 (15.4)	11 (28.2)	0.48
Arrest to [c]BLS (min), median ([d]IQR)	7 (1–11)	7 (3–10)	0.47
Arrest to [e]ACLS (min), median (IQR)	28 (21–34.5)	25 (20–30)	0.56
Arrest to arrival (min), median (IQR)	26 (12–31.5)	28 (22–36)	0.18
[f]ABGA, median (IQR)			
pH	6.92 (6.8–7.07)	6.9 (6.8–7.02)	0.96
[h]PCO_2 (mmHg)	75 (66.5–114)	78 (61–96)	0.37
[i]PO_2 (mmHg)	9 (4–14.5)	15 (7–36)	0.15
[j]HCO_3 (mEq/L)	11.4 (0–14.65)	8.8 (0–12.2)	0.71
Lactate (mmol/L)	10.5 (7.7–11.05)	11.6 (9–14.7)	0.11

[a]CPR, Cardiopulmonary resuscitation; [b]TOR, Termination of resuscitation; [c]BLS, Basic life-support; [d]IQR, Interquartile range; [e]ACLS, Advanced cardiac life-support; [f]ABGA, Arterial blood gas analysis; [g]ROSC, Return of spontaneous circulation; [h]PCO_2, Partial pressure of carbon dioxide; [i]PO_2, Partial pressure of oxygen; [j]HCO_3, bicarbonate ion.

attending emergency physicians and were not used in any treatment protocol or to make therapeutic decisions. Data were downloaded using the manufacturer's instructions. To determine the optimal time and rSO2 value for predicting the futility of resuscitation, the following parameters were analyzed: (1) higher, lower, and mean rSO2 at the initial time (2) the highest, lowest, and mean rSO2 values that were measured during initial 5 and 10 minutes, (3) the highest, lowest and mean rSO2 values that were measured during the overall CPR period.

2.4 Statistical analyses

For each patient, continuous rSO2 measurements were analyzed and expressed as the mean, median, highest, and lowest value of the recordings taken during the entire period, and the initial 5 and 10 minutes of resuscitation. The primary outcome was sustained ROSC. Continuous variables were presented as the median with interquartile range (IQR). Categorical variables were presented as the frequency with percentage. The Mann-Whitney U test was used to compare differences between groups when the dependent variable was continuous. A chi-square test was used to examine the association between categorical variables. The predictive power of each rSO2 value was assessed using the area under the curve (AUC) of the receiver operator characteristic (ROC) curve. An AUC value of 0.9–1.0 indicate excellent, 0.8–0.89 good, 0.7–0.79 moderate, 0.6–0.69 poor and 0.5–0.59 not useful. Calibration was assessed using the Hosmer-lemeshow goodness-of-fit test and $p > 0.05$ was considered well-calibrated. A p-value less than 0.05 was considered statistically significant. Statistical analysis was performed using SPSS version 18.0 (SPSS, Chicago, IL, USA) and MedCalc program version 12.7.7.0 (MedCalc Software, Mariakerke, Belgium).

3. Results

3.1 Baseline characteristics

During the study period, a total of 52 adult OHCA patients were consecutively enrolled in this study. Baseline characteristics related to CA are shown in Table 1. Overall, 13 patients achieved ROSC (ROSC group), whereas 39 patients did not achieve ROSC (non-ROSC group). Non-ROSC groups were significantly older (55 *vs.* 72 years, $p = 0.02$) and less likely to have their event witnessed (84.6% *vs.* 43.6%, $p = 0.01$) than ROSC groups. There were no significant differences in the sex, bystander CPR, initial cardiac rhythm, presumed cause of CA, time from arrest to hospital, basic life-support (BLS) and advanced life-support (ACLS), and values of initial arterial blood gas analysis (ABGA) between the two groups. There was no difference in the duration of resuscitation between ROSC and non-ROSC groups (21 (19.5–31) *vs.* 21 (15–30) minutes, $p > 0.05$).

3.2 Comparison of cerebral rSO2 between ROSC and non-ROSC groups

Table 2 shows the comparison of each cerebral rSO2 value during resuscitation between ROSC and non-ROSC groups. Non-ROSC groups had significantly lower highest value (67% *vs.* 25%, $p = 0.009$), mean value (24.7% *vs.* 15.3%, $p = 0.02$), and difference (Δhighest-lowest value) between highest and lowest value (42% *vs.* 10%, $p = 0.02$) measured during the overall CPR period. Non-ROSC groups had significantly

TABLE 2. Comparison of regional cerebral oxygen saturation between ROSC and non-ROSC groups.

[a]rSO2 value (%)	ROSC (N = 13)	Non-ROSC (N = 39)	*p*-value
Overall (%), median ([b]IQR)			
Lowest	15 (15–15)	15 (15–15)	0.35
Highest	67 (37.5–73.5)	25 (15–65)	0.009
Mean	24.9 (18.43–39.12)	15.3 (15–27.35)	0.02
Initial 0 min (%), median (IQR)			
Lower	19 (15–59.5)	15 (15–22)	0.09
Higher	34 (15–66)	15 (15–28)	0.05
Mean	29.5 (15–60.75)	15 (15–24)	0.06
Initial 5 min (%), median (IQR)			
Lowest	15 (15–19.5)	15 (15–15)	0.66
Highest	52 (30.5–69)	23 (15–50)	0.01
Mean	20.4 (17.59–45.18)	15.3 (15–27.35)	0.05
Initial 10 min (%), median (IQR)			
Lowest	15 (15–22)	15 (15–15)	0.18
Highest	57 (31–69)	20 (15–49)	0.009
Mean	25.1 (20.39–40.36)	15.6 (15–29.1)	0.03
[c]ΔrSO2 (%), median (IQR)			
Highest–lowest, overall	42 (22.5–55.5)	10 (0–50)	0.02
Highest–lowest, initial 5 min	28 (15.5–49)	7 (0–22)	0.01
Highest–lowest, initial 10 min	31 (14–45.5)	3 (0.0–34.0)	0.01

[a]rSO2, regional cerebral saturation; [b]IQR, Interquartile range; [c]ΔrSO2, Highest value minus lowest value.

lower highest values (52% *vs*. 23%, $p = 0.01$, 57 *vs*. 20, $p = 0.009$) and Δhighest-lowest value (28% *vs*. 7%, $p = 0.01$, 31% *vs*. 3%, $p = 0.01$) measured during the initial 5 and 10 minutes of resuscitation, respectively. Mean values during only the initial 10 minutes of resuscitation had a significant difference between the two groups. There were some differences in the initial lower value (19% *vs*. 15%, $p = 0.09$), highest value (34% *vs*. 15%, $p = 0.05$), mean value (29.5% *vs*. 15%, $p = 0.06$) between the two groups, but this was not statistically significant.

3.3 ROC analyses of cerebral rSO2 in predicting non-ROSC

Table 3 and Figs. 2,3 show the ROC analyses of cerebral rSO2 values according to each measurement time for predicting non-ROSC. The AUC of each rSO2 value according to measurement time (overall, initial 5 minutes and 10 minutes) were the highest value of 0.743, 0.724, and 7.39, mean value of 0.724, 0.677 and 0.701 and Δhighest-lowest value of 0.722, 0.734 and 0.724, respectively while all of the initial values and lowest value had a poor AUC (<0.7) and low specificity and also were not statistically significant.

The optimal cut-off value (COV) of each rSO2 values during overall, initial 5 minutes and 10 minutes were the highest value of 26% (sensitivity, 53.9%; specificity, 92.3%), 24% (sensitivity, 56.4%; specificity, 92.3%), and 30% (sensitivity, 61.5%; specificity, 84.6%), mean value of 15.2% (sensitivity, 43.6%; specificity, 100%), 15.3% (sensitivity, 51.3%; specificity, 92.3%) and 16% (sensitivity, 53.9%; specificity, 92.3%), Δhighest-lowest value of 11%, 9% and 10%, respectively The “100%-specific” COV of overall-highest rSO2 for prediction of non-ROSC was 18%, and sensitivity, negative predictive value were 35.9% and 34.2%, respectively (Fig. 3A). When specificity was set at 92.3%, COV of the highest rSO2 during the initial 10 minutes was 20% (Fig. 3C). However, all Initial rSO2 values were not an appropriate predictor and statistically not significant.

4. Discussion

In this study, we found that the highest and mean rSO2 values during the initial 5, 10 minutes, and overall resuscitation period were significantly associated with non-ROSC and revealed high specificity, whereas the initial value was not. The predictive power of rSO2 values during the initial 5, 10 minutes were similar to those during the overall resuscitation period. Furthermore, none of the patients with a persistent value of rSO2 ≤18% during the overall period achieved ROSC.

To date, there is no accurate tool to aid physicians in deciding how long to prolong resuscitation efforts. The decision is often made solely on clinical judgment. Recently, cerebral oximetry, a non-invasive and real-time monitoring tool, has been used to determine cerebral perfusion in various clinical scenarios [16, 17]. It can be easily used, even in the CA setting

TABLE 3. ROC analysis of rSO2 values according to time point of measurements in predicting non-ROSC.

	[a]AUC (95% CI)	[b]COV (%)	[c]Sens (%)	[d]Spec (%)	[e]PPV (%)	[f]NPV (%)	*p*-value
Overall							
Lowest	0.544 (0.400–0.683)	22	100	15.4	78	100	0.65
Highest	0.743 (0.603–0.854)	26	53.9	92.3	95.5	40	<0.001
		18	35.9	100	100	34.2	
Mean	0.724 (0.582–0.839)	15.2	43.6	100	100	37.1	0.002
0 min							
Lower	0.639 (0.494–0.768)	33	89.7	38.5	81.4	55.6	0.13
Higher	0.668 (0.523–0.792)	32	82.1	53.9	84.2	50.0	0.07
Mean	0.665 (0.520–0.790)	29	82.1	53.9	84.2	50	0.08
5 min							
Lowest	0.530 (0.386–0.669)	28	100	15.4	78	100	0.69
Highest	0.738 (0.597–0.850)	24	56.4	92.3	95.7	41.4	0.002
Mean	0.677 (0.533–0.800)	15.3	51.3	92.3	95.2	38.7	0.03
10 min							
Lowest	0.586 (0.441–0.721)	16	87.2	30.8	79.1	44.4	0.26
Highest	0.739 (0.598–0.851)	30	61.5	84.6	92.3	42.3	0.002
		20	51.3	92.3	95.2	38.7	
Mean	0.701 (0.558-0.820)	16	53.9	92.3	95.5	40.0	0.01
ΔrSO2							
Overall	0.722 (0.580–0.837)	11	53.9	92.3	95.5	40	0.002
Initial 5 min	0.734 (0.593–0.847)	9	56.4	92.3	95.7	41.4	0.002
Initial 10 min	0.724 (0.582–0.839)	10	64.1	84.6	92.6	44.0	0.003

[a]AUC, Area under curve; [b]COV, Cut off value; [c]Sens, Sensitivity; [d]Spec, Specificity; [e]PPV, Positive predictive value; [f]NPV, Negative predictive value.

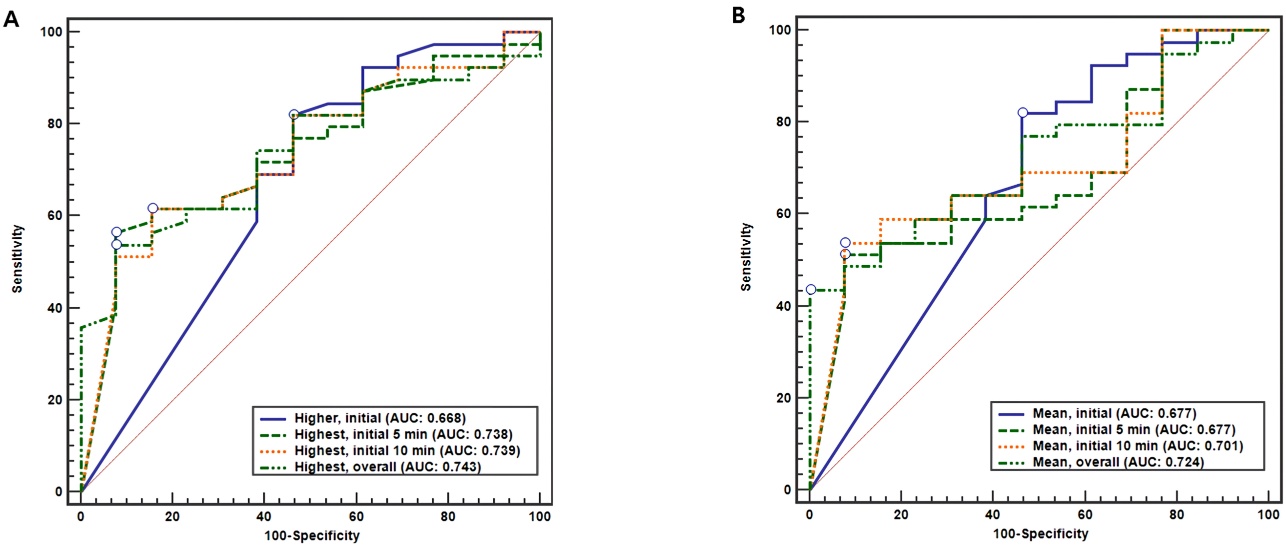

FIGURE 2. The area under the receiver operating curve of regional cerebral oxygen saturation to predict non-ROSC. A: Highest rSO2 values, B: Mean rSO2 values.

where there is no pulsatile flow, and has been shown to accurately correlate cerebral blood oxygenation with myocardial perfusion [7, 18].

Therefore, there is now an increased number of studies evaluating the utility of cerebral oximetry as a monitoring tool for the prediction of prognosis during CA. It has been demon-

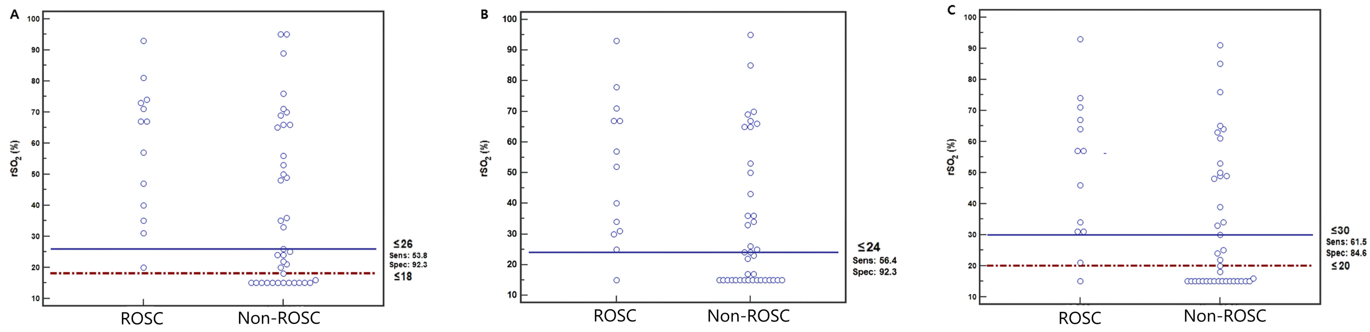

FIGURE 3. The Interactive dot diagram of the highest rSO2 values between ROSC and non-ROSC. A: Highest rSO2 values during overall period of CPR. The optimal cut off value for prediction of non-ROSC was 26% (sensitivity: 53.9%, specificity: 92.3%) and the dot line at 18% depicts cut-off value with the specificity of 100%, B: Highest rSO2 values during the initial 5 minutes of CPR. The optimal cut off value for prediction of non-ROSC was 24% (sensitivity: 56.4%, specificity: 92.3%), C: Highest rSO2 values during the initial 10 minutes of CPR. The optimal cut off value for prediction of non-ROSC was 30% (sensitivity: 61.5%, specificity:84.6%) and the dot line at 20% depicts cut-off value with the specificity of 92.3%.

strated that the cerebral rSO2 value is significantly associated with ROSC, neurological outcome, and even the quality of CPR in CA patients [12, 19, 20]. However, the optimal time point, type of measurement, and threshold are still unclear. Furthermore, there have been a limited number of studies using cerebral rSO2 to predict the futility of resuscitation [10].

In previous studies, various types of measurements (initial, mean, highest, or the change during overall CPR) have been used to predict ROSC or futility, but, it is unclear which rSO2 value is most predictive. Except for the initial value, the role of those values that measure overall CPR to predict futility in the early period of CPR is unknown. An initial single measurement can be incorrect due to technical error or ambient light interference in the chaotic environment of a CA [8]. A study which enrolled a small population demonstrated that the absolute rSO2 value at the moment of death varied considerably (3~46%) indicating that there is no clear cut-off rSO2 value to predict outcomes, and that the changes in rSO2 are more important rather than one absolute value during CA [11], and that changes over time may be a better marker to predict outcomes rather than a single measurement which is unlikely to reflect the response to CPR. This is supported by the results of our studies and those of others showing that elevations in cerebral rSO2 during CPR led to ROSC whereas persistently low rSO2 (<18%) did not achieve ROSC [12, 13]. And that there is no significant association between initial rSO2 value and non-ROSC [21].

Previous studies have shown that blood perfusion is at its peak after about 40–45 seconds of chest compressions [22], and that rSO2 is sensitive to hemodynamic changes and changes in cardiac rhythm. In OHCA, immediately after the patient arrives to the hospital, cardiac compressions are often interrupted, and measurements of initial rSO2 may underestimate cerebral perfusion.

In a recent meta-analysis of 20 observational studies, mean values were found to have a better association with ROSC than initial values, and that ROSC was unlikely to be achieved with a mean cut-off value of rSO2 <30% [7]. Mean values in most previous studies have been measured during the overall or last 5 minutes CPR period, and their COV was 23~30% with a low specificity [7, 12, 23]. The COV of mean values (15~16%) in our study showed lower all-time points than previous studies but showed higher specificity greater than 90%. This difference may due to the patient's characteristics such as a lower initial shockable rhythm, longer downtimes compared with previous studies, and the usage of lower values among the two probes. The new finding from our study was that mean, highest, and Δhighest-lowest values during the initial 5 and 10 minutes showed similar predictability and high specificity compared with values during the overall period. Therefore, the initial single rSO2 value might be an inadequate indicator in predicting the futility of CPR and the overall-mean rSO2 value could be a surrogate marker that can replace the initial value. However, the mean values might not be as easily accessible during CPR and may only be measured after CPR has ended. Therefore, it is difficult for clinicians to use these values to decide whether to continue CPR in the early period. Although there has been a study of the rSO2 values during the last 5 minutes, there has not been a study about rSO2 values during the early resuscitation period such as the initial 5~10 minutes. Therefore, this study focused on evaluating methods to make an earlier decision for terminating resuscitation efforts. We hypothesized that the initial 5 minutes or 10 minutes rSO2 is a better marker for predicting the futility in the early period because this is a better reflection of the early response of cerebral perfusion to resuscitation efforts during this early period.

Previous studies investigating the futility of CPR have been limited and have shown various cutoff values to accurately predict futility following CA. Fukuda's study suggested initial values at the time of hospital arrival as indicators of futility [10]. It resulted in COVs of 26% and 19% with specificity of 56.3% and 62.5% and PPV of 87.0% and 87.8% in prediction of non-ROSC, respectively. A multicenter study by Parnia [12] *et al* reported that persistent rSO2 <25% despite all interventions strongly favors the inability to achieve ROSC/survival or a good neurological outcome [23]. Recently, two review studies suggested mean values of rSO2 <23% and 30% were found to be unlikely to achieve ROSC [7, 14].

In order to use cerebral rSO2 values as a criterion for the termination of resuscitation, it is necessary for the specificity and PPV to approach 100%. Nevertheless, previous studies including Fukuda's study showed high sensitivity but low specificity, whereas the highest rSO2 and ΔrSO2 values during the initial 5 minutes and overall period of our results demonstrated high specificity of 92.3% to 100% and a PPV of 95.5% to100% with COV of the highest rSO2 of 24% and 26% and ΔrSO2 of 9% and 11%, respectively.

Our study, suggests that the Initial 5 minutes or 10 minutes rSO2 value (≤24% or 30%) may be useful as an early indicator to achieve successful CPR while overall rSO2 may be useful in deciding termination of CPR when rSO2 is not rising to a specific value (≤26% or 18%) despite sufficient resuscitative efforts. However, the AUC and diagnostic performance were not sufficiently high, and the termination of resuscitation should not be determined based solely on these cerebral rSO2 values. It may be necessary to use these values in combination with other indicators to predict non-ROSC.

According to an article published in 2020 [24], we are not able to find a clear statistical cutoff value for predicting neurological prognosis following CPR using near-infrared spectroscopy measurements. This study suggests how changes in the value of rSO2, the value of rSO2, and a combination of values at a given time point can be used to predict the outcome of CPR following a CA. In a future randomized control study, these values will be helpful in attempting to predict ROSC.

This study has several limitations. First, the sample size was too small to provide statistical significance. Moreover, this study did not perform a multivariate analysis and therefore we cannot exclude the effects of several confounders related to CA prognosis. Larger studies with other indicators to predict futility are necessary to confirm our findings. Second, the higher rate of non-ventricular fibrillation and non-witnessed arrest compared to previous studies and the usage of different devices with different calibration and algorithms in each study may result in a selection bias and thus may not be applicable to other settings. Third, since the quality of CPR of the prehospital stage could not be evaluated accurately, it was difficult to reflect the patient's condition in the initial period. Furthermore, only the presence of ROSC was confirmed, and the long-term neurological prognosis was insufficient. More future research is needed, including findings on neurological prognosis. However, this study focused on early decision-making rather than long-term neurological prognosis prediction. Lastly, a previous meta-analysis study revealed too much heterogeneity within the highest measurement studies. To the best of our knowledge, this is the first study that evaluated initial 5 and 10 minutes rSO2 as predictors of the futility of CPR. Despite these limitations, it is meant to suggest new guidelines that can help to reduce unnecessary resuscitation following OHCA.

5. Conclusion

Initial 5 and 10 minutes cerebral rSO2 values in OHCA might have the potential to be an indicator in deciding termination of CPR efforts. However, cerebral oxygen saturation alone to judge the futility of resuscitation is not sufficient. Thus, cerebral rSO2 should be used in combination as one marker in the multimodal approach. Moreover, future research should focus on seeking the optimal threshold and more specific methods that reflect changes and trends of rSO2 during CPR.

AVAILABILITY OF DATA AND MATERIALS

The data presented in this study are available on reasonable request from the corresponding author.

AUTHOR CONTRIBUTIONS

JHJ—contributed to the planning, development, and editing of the manuscript, including reading and approving the final manuscript, JHW, JSC—contributed to the development and editing of the manuscript, including reading and approving the final manuscript, HJY, JYC—contributed to the development and editing of the manuscript, including reading and approving the final manuscript, YSL, WSC—contributed to the planning, development, and editing of the manuscript, including reading and approving the final manuscript; all authors have read and approved the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Approval for the study was obtained from the Institutional Review Board of the Gachon Gil medical center (GBIRB2015-108). Review Board approved waiver of informed consent.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

[1] KimTH, Shin SD, Kim YJ, Kim CH, Kim JE. The scene time interval and basic life support termination of resuscitation rule in adult out-of-hospital cardiac arrest. The Journal of Korean Medical Science. 2015; 30: 104–109.

[2] Kajino K, Iwami T, Daya M, Nishiuchi T, Hayashi Y, Kitamura T, *et al*. Impact of transport to critical care medical centers on outcomes after out-of-hospital cardiac arrest. Resuscitation. 2010; 81: 549–554.

[3] Morrison LJ, Visentin LM, Kiss A, Theriault R, Eby D, Vermeulen M, *et al*. Validation of a rule for termination of resuscitation in out-of-hospital cardiac arrest. New England Journal of Medicine. 2006; 355: 478–487.

[4] Goto Y, Maeda T, Goto YN. Termination-of-resuscitation rule for emergency department physicians treating out-of-hospital cardiac arrest patients: an observational cohort study. Critical Care. 2013; 17: R235.

[5] Genbrugge C, Dens J, Meex I, Boer W, Eertmans W, Sabbe M, *et al*. Regional cerebral oximetry during cardiopulmonary resuscitation: useful or useless? The Journal of Emergency Medicine. 2016; 50: 198–207.

[6] Friess SH, Sutton RM, French B, Bhalala U, Maltese MR, Naim MY, *et al*. Hemodynamic directed CPR improves cerebral perfusion pressure and brain tissue oxygenation. Resuscitation. 2014; 85: 1298–1303.
[7] Cournoyer A, Iseppon M, Chauny JM, Denault A, Cossette S, Notebaert É. Near-infrared spectroscopy monitoring during cardiac arrest: a systematic review and meta-analysis. Academic Emergency Medicine. 2016; 23: 851–862.
[8] Zaouter C, Arbeid E. Influence of ambient light on cerebral oximeters. British Journal of Anaesthesia. 2010; 105: 873–874.
[9] Ito N, Nanto S, Nagao K, Hatanaka T, Kai T. Regional cerebral oxygen saturation predicts poor neurological outcome in patients with out-of-hospital cardiac arrest. Resuscitation. 2010; 81: 1736–1737.
[10] Fukuda T, Ohashi N, Nishida M, Gunshin M, Doi K, Matsubara T, *et al*. Application of cerebral oxygen saturation to the prediction of the futility of resuscitation for out-of-hospital cardiopulmonary arrest patients: a single-center, prospective, observational study: can cerebral regional oxygen saturation predict the futility of CPR? The American Journal of Emergency Medicine. 2014; 32: 747–751.
[11] Genbrugge C, Eertmans W, Jans F, Boer W, Dens J, De Deyne C. Regional cerebral saturation monitoring during withdrawal of life support until death. Resuscitation. 2017; 121: 147–150.
[12] Parnia S, Nasir A, Shah C, Patel R, Mani A, Richman P. A feasibility study evaluating the role of cerebral oximetry in predicting the return of spontaneous circulation in cardiac arrest. Resuscitation. 2012; 83: 982–985.
[13] Genbrugge C, Meex I, Boer W, Jans F, Heylen R, Ferdinande B, *et al*. Increase in cerebral oxygenation during advanced life support in out-of-hospital patients is associated with the return of spontaneous circulation. Critical Care. 2015; 19: 112.
[14] Schnaubelt S, Sulzgruber P, Menger J, Skhirtladze-Dworschak K, Sterz F, Dworschak M. Regional cerebral oxygen saturation during cardiopulmonary resuscitation as a predictor of return of spontaneous circulation and favorable neurological outcome—a review of the current literature. Resuscitation. 2018; 125: 39–47.
[15] Nishiyama K, Ito N, Orita T, Hayashida K, Arimoto H, Abe M, *et al*. Characteristics of regional cerebral oxygen saturation levels in patients with out-of-hospital cardiac arrest with or without return of spontaneous circulation: a prospective observational multicentre study. Resuscitation. 2015; 96: 16–22.
[16] Moerman A, Wouters P. Near-infrared spectroscopy (NIRS) monitoring in contemporary anesthesia and critical care. Acta Anaesthesiologica Belgica. 2010; 61:185–194.
[17] Brady K, Joshi B, Zweifel C, Smielewski P, Czosnyka M, Easley RB, *et al*. Real-time continuous monitoring of cerebral blood flow autoregulation using near-infrared spectroscopy in patients undergoing cardiopulmonary bypass. Stroke. 2010; 41: 1951–1956.
[18] Sanfilippo F, Serena G, Corredor C, Benedetto U, Maybauer MO, Al-Subaie N, *et al*. Cerebral oximetry and return of spontaneous circulation after cardiac arrest: a systematic review and meta-analysis. Resuscitation. 2015; 94: 67–72.
[19] Yagi T, Nagao K, Kawamorita T, Soga T, Ishii M, Chiba N, *et al*. Detection of ROSC in patients with cardiac arrest during chest compression using nirs: a pilot study. Advances in Experimental Medicine and Biology. 2016; 876: 151–157.
[20] Meex I, De Deyne C, Dens J, Scheyltjens S, Lathouwers K, Boer W, *et al*. Feasibility of absolute cerebral tissue oxygen saturation during cardiopulmonary resuscitation. Critical Care. 2013; 17: R36.
[21] Ahn A, Nasir A, Malik H, D'Orazi F, Parnia S. A pilot study examining the role of regional cerebral oxygen saturation monitoring as a marker of return of spontaneous circulation in shockable (VF/VT) and non-shockable (PEA/Asystole) causes of cardiac arrest. Resuscitation. 2013; 84: 1713–1716.
[22] Berg RA, Sanders AB, Kern KB, Hilwig RW, Heidenreich JW, Porter ME, *et al*. Adverse hemodynamic effects of interrupting chest compressions for rescue breathing during cardiopulmonary resuscitation for ventricular fibrillation cardiac arrest. Circulation. 2001; 104: 2465–2470.
[23] Parnia S, Yang J, Nguyen R, Ahn A, Zhu J, Inigo-Santiago L, *et al*. Cerebral Oximetry during Cardiac Arrest: a multicenter study of neurologic outcomes and survival. Critical Care Medicine. 2016; 44: 1663–1674.
[24] Takegawa R, Hayashida K, Rolston DM, Li T, Miyara SJ, Ohnishi M, *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. Frontiers in Medicine. 2020; 7: 587930.

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