The prognostic value of cerebral oxygen saturation measurement for assessing prognosis after cardiopulmonary resuscitation

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KEYWORDS
Cardiopulmonary resuscitation; Cerebral oxygen saturation; Prognosis

Abstract

Background: Despite new improvements on cardiopulmonary resuscitation (CPR), brain damage is very often after resuscitation.
Objective: To assess the prognostic value of cerebral oxygen saturation measurement (rSO2) for assessing prognosis on patients after cardiopulmonary resuscitation.
Design: Retrospective analysis.
Measurements and results: We analyzed 25 post-CPR patients (12 female and 13 male). All the patients were cooled to a target temperature of 33–34 °C. The Glasgow Coma Scale (GCS), Corneal Reflexes (CR), Pupillary Reflexes (PR), arterial Base Excess (BE) and rSO2 measurements were taken on admission. The rewarming GCS, CR, PR, BE and rSO2 measurements were made after the patient’s temperature reached 36 °C.
Results: In survivors, the baseline rSO2 value was 67.5 (46–70) and the percent difference between baseline and rewarming rSO2 value was 0.03 (0.014–0.435). In non-survivors, the baseline rSO2 value was 30 (25–65) and the percent difference between baseline and rewarming rSO2 value was 0.031 (–0.08 to –0.20). No statistical difference was detected on percent changes between baseline and rewarming values of rSO2. Statistically significant difference was detected between baseline and rewarming GCS groups (p = 0.004). No statistical difference was detected between GCS, CR, PR, BE and rSO2 to determine the prognosis.
Conclusion: Despite higher values of rSO2 on survivors than non-survivors, we found no statistically considerable difference between groups on baseline and the rewarming rSO2 values. Since
the measurement is simple, and not affected by hypotension and hypothermia, the rSO₂ may be a useful predictor for determining the prognosis after CPR.
Materials and methods

The Regional Ethical Committee approved the study (GOKAEK 2013/191). All new post-CPR patients admitted to the general and surgical ICU who stayed >24 h during a 2-year period (January 1, 2012 to December 31, 2013) were retrospectively enrolled. Our ICUs included 19 beds and the physicians had to have experience in measuring GCS, PR, CR, BE and rSO2.

In our study, we used the term cardiac arrest similar to the definition made by Ito et al., 16 who defined cardiac arrest as the absence of spontaneous respiration, palpable pulse, and responsiveness to stimuli.

Resuscitation time and resuscitation place (the resuscitation places were divided into emergency department and medical departments) were recorded. The illness was categorized to medical cardiac, medical non-cardiac, surgical cardiac and surgical non-cardiac. Comorbidities were also recorded.

Age, gender and APACHE II scores were all recorded on admission.

We used the following responses to calculate the GCS, as described by Teasdale et al. 17: eyes opening response, verbal response, and motor response. CR and PR were described as present or absent. GCS, CR and PR were recorded on admission.

We used the Cobas b221® (Roche, Mannheim, Germany) for arterial blood gases analysis and the arterial Base Excess (BE) was calculated automatically according to the National Committee for clinical laboratory standards recommendations. BE value was recorded on admission.

To measure the rSO2, two sensors were applied bilaterally to the patients’ forehead after the patients’ forehead skin and rSO2 were measured by using the INVOS® (Covidien, USA) device on admission. Lower values were recorded.

In our daily practice, we used hypothermia for all post-CPR patients. All the patients were cooled to 33–34°C by the use of a mattress that uses cold air and ice packs. By cooling, we wanted to reach the target temperature within 4 h and maintain this temperature for 24 h and then follow it with passive rewarming. No sedatives were given to the patients.

After rewarming, GCS, CR, PR, BE and rSO2 measurements were performed and recorded.

During the study, all the patients had a glucose level between 130 and 160 mg.dL−1, central venous pressure 12–13 mmHg and etC02 34–36 mmHg. If necessary, vasoactive or inotropic support was given to patients to maintain a mean arterial blood pressure >65 mmHg.

Patients were followed up until death or ICU discharge. Length of ICU stay and prognosis were recorded and patients were divided into survivors and non-survivors.

Exclusion criteria were as follows: age under 18 years, history of irreversible brain damage and a traumatic origin.

Statistical analysis

Results are expressed as median (min – max) or number. Normality distribution of variables was tested using one sample Kolmogorov–Smirnov test. The groups were compared by Mann Whitney U-test for non-normal distributed data. Categorical variables were compared by using the Fisher’s Chi-square and Mc Nemar test. ROC analysis was performed for GCS baseline and rewarming, BE baseline and rewarming, and rSO2 baseline and rewarming. Sensitivity and specificity were performed for PR baseline and rewarming and CR baseline and rewarming. A p-value < 0.05 was considered as statistically significant. MedCalc V13.3.3 and SPSS 21 statistical softwares were used for statistical analyses.

Results

Thirty-eight patients were admitted to the ICUs during the study period. Only 25 of them were included in the study. Thirteen patients were excluded because of inadequate data like under 18 years old, or they had sedative infusions. Four patients were discharged from the ICUs, while 21 died. The median age of the patients in the survivor group was 65.5 (20–68) years, while it was 68 (22–86) years in the non-survivor group. The ICU stays among the survivors lasted 7 (7–8) days, while non-survivors stayed for 6 (2–61) days. The resuscitation time for survivors was 27.5 (5–30) min, while it was 15 (10–45) min for non-survivors. The APACHE II score for survivors was 23 (7–24), while it was 27 (7–33) for non-survivors. No considerable difference was detected between groups on age, gender, ICU stay, resuscitation time and APACHE II scores (p > 0.005) (Table 1). One patient in survivor group and 15 patients in non-survivor group used vasoactive or inotropic support. The places of resuscitation, the illness categories and comorbidities are shown in Table 1.

The baseline GCS for survivors was 6 (3–15), while it was 3 (3–6) in non-survivors, and no statistically major difference was detected (p = 0.062). The percent changes between baseline and rewarming GCS was found as −1 (−1 to [−1]) in survivors and 0 (0–1) in non-survivors. A statistical difference was detected between the groups (p = 0.004) (Table 2). The baseline BE for survivors was −3.0 (−21.6 to −3.5) and −9.1 (−22 to −2) for non-survivors and no statistically considerable difference was detected (p = 0.235). The percent changes between baseline and rewarming BE for survivors was 1 (1–1) while 0 (−1 to 0) for non-survivors. Statistically considerable difference was detected (p = 0.006) (Table 2). In survivors, the baseline rSO2 value was 67.5 (46–70), and the percent difference between baseline and rewarming rSO2 value was 0.03 (0.014–0.435). In non-survivors, the baseline rSO2 value was 30 (25–65) and the percent difference between baseline and rewarming rSO2 value was 0.031 (−0.08 to .20). Although statistically considerable difference was detected between groups on baseline rSO2 values, no statistical difference was detected on percent changes between baseline and rewarming values of rSO2 (respectively p = 0.003, 0.526) (Table 2).

Among those in the survivor group, three patients had a positive baseline PR, while one had a negative baseline PR. In the non-survivor group, 6 patients had a positive baseline PR while 15 had a negative baseline PR. No statistically considerable difference was detected between groups (p = 0.116). After rewarming, the PR values were as follows: In the survivor group, zero patients had a positive PLR, while four had a negative PR. In the non-survivor group, 6 patients had a positive PR, while 15 had a negative PR.
Table 1  Demographic data.

<table>
<thead>
<tr>
<th></th>
<th>Survivor (n = 4)</th>
<th>Non-survivor (n = 21)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (F/M)</td>
<td>1/3</td>
<td>11/10</td>
<td>0.593</td>
</tr>
<tr>
<td>Age, median (min–max)</td>
<td>65.5 (20–68)</td>
<td>68 (22–86)</td>
<td>0.331</td>
</tr>
<tr>
<td>ICU stay (day), median (min–max)</td>
<td>7 (7–8)</td>
<td>6 (2–61)</td>
<td>0.709</td>
</tr>
<tr>
<td>Resuscitation time (min), median (min–max)</td>
<td>27.5 (5–30)</td>
<td>15 (10–45)</td>
<td>0.497</td>
</tr>
<tr>
<td>Resuscitation places</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emergency department</td>
<td>4</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Medical departments</td>
<td>0</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Illness category</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medical cardiac</td>
<td>2</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Medical non-cardiac</td>
<td>2</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Surgical cardiac</td>
<td>2</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Surgical non-cardiac</td>
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<td>0</td>
<td></td>
</tr>
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<td>Comorbidities</td>
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<tr>
<td>Cerebrovascular diseases</td>
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<td>1</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>2</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>COPD</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Chronic renal disease</td>
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<td>4</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
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<td>7</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>0</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>APACHE II (mean ± SD); median (min–max)</td>
<td>23 (7–24)</td>
<td>27 (7–33)</td>
<td>0.110</td>
</tr>
</tbody>
</table>

Data are presented as median (min–max).

APACHE II, acute physiology and health evaluation; ICU, intensive care unit; COPD, chronic obstructive pulmonary disease.

Table 2  GCS, BE and rSO2 values.

<table>
<thead>
<tr>
<th></th>
<th>Survivor (n = 4); median (min–max)</th>
<th>Non-survivor (n = 21); median (min–max)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline GCS</td>
<td>6 (3–15)</td>
<td>3 (3–6)</td>
<td>0.062</td>
</tr>
<tr>
<td>Difference between baseline and rewarming</td>
<td>−1 (−1–[−1])</td>
<td>0 (0–1)</td>
<td>0.004^a</td>
</tr>
<tr>
<td>Baseline BE</td>
<td>−3.0 (−2.1–6.3)</td>
<td>−9.1 (−22–2)</td>
<td>0.235</td>
</tr>
<tr>
<td>Difference between baseline and rewarming</td>
<td>1 (1–1)</td>
<td>0 (1–0)</td>
<td>0.006</td>
</tr>
<tr>
<td>Baseline rSO2</td>
<td>67.5 (46–70)</td>
<td>30 (25–65)</td>
<td>0.003^a</td>
</tr>
<tr>
<td>Difference between baseline and rewarming</td>
<td>0.031 (−0.08–0.20)</td>
<td>0.03 (0.014–0.435)</td>
<td>0.526</td>
</tr>
</tbody>
</table>

GCS, Glasgow Coma Scale; BE, base excess; rSO2, regional cerebral oxygen saturation.

^a p < 0.005.

Table 3  Corneal and pupillary reflexes.

<table>
<thead>
<tr>
<th></th>
<th>Survivor (n = 4)</th>
<th>Non-survivor (n = 21)</th>
<th>p^a</th>
</tr>
</thead>
<tbody>
<tr>
<td>baseline PR (+/−)</td>
<td>3/1</td>
<td>6/15</td>
<td>0.116</td>
</tr>
<tr>
<td>Rewarming PR (+/−)</td>
<td>0/4^b</td>
<td>6/15^b</td>
<td>0.540</td>
</tr>
<tr>
<td>baseline CR (+/−)</td>
<td>3/1</td>
<td>15/6</td>
<td>0.116</td>
</tr>
<tr>
<td>Rewarming CR (+/−)</td>
<td>0/4^b</td>
<td>6/15^b</td>
<td>0.540</td>
</tr>
</tbody>
</table>

PR, pupillary reflex; CR, corneal reflex; +, present; −, absent.

^a Fisher’s chi-square test.

^b McNemar test.
PR. No statistically considerable difference was detected between groups (p = 0.540). The PR and CR measurements are shown in Table 3. No statistically considerable difference was detected between groups on baseline and rewarming CR (respectively p = 0.186, 0.540). No statistically major difference was detected between percent changes on survivor and non-survivors groups (respectively p = 1.000, 1.000, 1.000, 1.000). The baseline and rewarming measurements of GCS and BE values belonging to the percent changes are calculated, in the survivors group, and for GCS the median (min – max) was –1 (–1 to –1) and for BE the median was 1 (1–1). In the non-survivors group, for GCS, the median (min–max) was 0 (0–1) and for BE, the median (min–max) was 0 (–1 to 0). Statistically considerable difference was detected (respectively p = 0.040, 0.006) (Table 2). In the survivors group, for rSO₂, the median (min–max) was 0.031 (–0.08 to 0.20), and in non-survivors group, for GCS, the median (min–max) was 0.03 (0.014–0.435). Statistically considerable difference was not detected between the groups (p = 0.526).

The Area Under the Curve (AUC) value for baseline GCS was 0.78 with an optimal cut-off point of 5 according to Yaden Index. The sensitivity was found to be 85.7% and the specificity was 75%. The Positive Predictive Value (PPV) was 94.7%, while the Negative Predictive Value (NPV) was found to be 49.9%. No statistically major difference was detected (p = 0.1114). The AUC measurement for the rewarming GCS was 0.958 with an optimal cut-off point of 7 according to Yaden Index. The sensitivity and specificity were found to be 90.4% and 100%. The PPV was 100%, while the NPV was 66.6%. A statistically considerable difference was detected (p < 0.0001) (Table 4). The optimal cut-off point for baseline BE was –7.5 according to Yaden Index with 0.69 as an AUC value. The sensitivity was found to be 76.19% and the specificity was 75%. The PPV was 94.1%, while the NPV was found to be 37.5%. No statistically significant difference was detected (p = 0.390). The AUC value for rewarming BE was 0.976 with an optimal cut-off point of –1.2 according to Yaden Index. The sensitivity was 90.4% while specificity was 100%. The PPV was 100%, while the NPV was found to be 66.7%. Statistically, difference was detected (p < 0.0001) (Table 4). The AUC value for baseline rSO₂ was 0.964. The optimal cut-off point was found to be 41 according to Yaden Index. The sensitivity and specificity were found to be 90.4% and 100%. The PPV was 100%, while the NPV was 66.6%. A statistically significant difference was detected (p < 0.0001). The AUC measurement for the rewarming rSO₂ was 0.976 with an optimal cut-off point of 38 according to Yaden Index. The sensitivity was found to be 90.4% and the specificity was 100%. The PPV and NPV were 100% and 66.6%. A statistically significant difference was detected (p < 0.0001) (Table 4).

The sensitivity for baseline PR and CR was 71.4%, while the specificity was 22% and 25%. The PPV and NPV were 83.3% and 14.3%, respectively (p > 0.05). The sensitivity for rewarming PR and CR was 71.4%, while the specificity was 0 and 100.0%. The PPV were 78.9% and 100.0%, and the NPV were 0.0% and 40.0% (p = 0.508) (Table 4).

On comparison of all tests with each other no statistically considerable difference was detected (respectively; p = 0.754, 0.508, 0.754).

**Discussion**

We aimed to evaluate the prognostic value of cerebral oxygen saturation measurement to assess prognoses after CPR. Despite higher values of rSO₂ on survivors than non-survivors, we found no statistically considerable difference between groups on baseline and the rewarming rSO₂ values. Also, no difference was detected between other tests.

Ito et al. defined cardiac arrest as the absence of spontaneous respiration, palpable pulse, and responsiveness to stimuli, and we also used this definition in our study. Despite improvements on resuscitation and ICU protocols, the rate of survival was low. Peberdy et al. carried out a study on 14,720 cardiac arrest patients and reported that 17% survived hospital discharge. Another study by Greer et al. demonstrated a good outcome of 9.9% survival among patients. In our study, we found a 16% survival rate.

Therapeutic hypothermia is one of the treatment methods for patients surviving cardiac arrest. Therapeutic hypothermia was defined as cooling of the patient to 32–34 °C for 12–24 h. Different studies reported the advantages and disadvantages of therapeutic hypothermia. Due to the uncertain recommendations on therapeutic hypothermia, we routinely used it for our patients in our intensive care.

Outcome prediction is an important component of the management of post-CPR patients. Monitoring GCS is a very useful method and is frequently used in ICUs; moreover, hospital staff members are well trained in calculating GCS scores. Several previous studies reported the usage of GCS as a prognostic factor in post-CPR critically ill patients. Schefold et al. designed a study to analyze the usefulness of GCS for outcome prediction in survivors of cardiac arrest treated with therapeutic hypothermia. They found that GCS scores were significantly higher in patients with a good outcome compared with those with an unfavorable outcome. The authors reported that a score of >3 on the motor component pointed good outcomes with a specificity of 100% on the first day. Mullie et al. suggested that the GCS-based rule can be helpful in predicting outcomes in patients resuscitated after out-of-hospital cardiac arrest. In another study, Bouwes et al. found that the motor scores 72 h after CPR were not valuable when it came to determining the prognosis after CPR. In a review by Wijdicks et al., the GCS was divided into a motor part and brainstem reflexes, and the authors found that the prognosis was poor with absent PR or CR or absent or extensor motor responses 3 days after cardiac arrest. In our study, we calculated the GCS twice. The median baseline GCS for survivors was 6 (3–15), while it was 3 (3–6) in non-survivors. The percent differences between baseline and rewarming values for GCS were –1 (–1 to –1) in survivors and 0 (0–1) in non-survivors.

CR and PR have also been widely used. A study made by Greer et al. demonstrated that PR may be absent immediately after post-arrest and may subsequently recover. The authors concluded that the absence of PR and CR on day 3 remained highly valuable for predicting poor outcomes. Moreover, Bouwes et al. reported similar results and concluded that absent pupillary light responses and CR 72 h after CPR were reliable predictors of poor outcomes. The same authors determined that motor scores 72 h after CPR was
The authors concluded that the possible explanation of their observation might be an overrating of the motor score. Maia et al. enrolled 26 patients in their study and reported that absent PLR and absent CR showed no false-positives in predicting poor outcomes. In our study, in the survivor group, 3 patients had a positive baseline PLR while one had a negative baseline PLR. In the non-survivor group, 6 patients had a positive baseline PLR, while 15 had a negative baseline PLR. No statistically considerable difference was detected between groups. After rewarming, the PLR values were as follows: In the survivor group, zero patients had a positive PLR, while four had a negative PLR. In the non-survivor group, 6 patients had a positive PLR, while 15 had a negative PLR. No statistical major difference was detected between groups. Moreover, no statistically significant difference was detected between groups on baseline and rewarming CR.

Monitoring of arterial base excess is used for assessing outcome after CPR. In their study, Takasu et al. measured arterial base excess after CPR on 87 patients. They reported significantly high BE values in the survivors group and concluded that BE could distinguish survivors from non-survivors, but BE was not found as a predictor for mortality in resuscitated patients. The authors concluded that BE values were well correlated with resuscitation time. In our study, we found higher BE values in survivors in baseline and rewarming periods.

The measurement of the saturation of the brain is a recent method, and previous studies have reported that a decline in the value of rSO₂ is a significant predictor for postoperative cognitive dysfunction and prolonged ICU and hospital stays. The advantage of this method is that the device is not affected by hypothermia or hypotension. Measurements are collected using near infrared spectroscopy. Murkin et al. monitored brain oxygen saturation during coronary bypass surgery on 200 patients and reported that patients who had major organ morbidity or mortality had lower rSO₂ values. Moreover, the authors reported that length of hospital stay and ICU stay with respect to postoperative complications were longer with lower rSO₂ values. They concluded that in maneuvers during coronary revascularization surgery, pump flow is often decreased and caused a profound decrease in rSO₂. The goal of another study made by Slater et al. was to determine if maintenance of cerebral perfusion with the use of cerebral oximetry monitoring had an impact on early postoperative outcomes. The authors demonstrate that intraoperative rSO₂ desaturation is significantly associated with demonstrable neurocognitive decline in a prospectively randomized coronary artery bypass grafting population.

The clinical value of rSO₂ was already demonstrated in previous studies. Ito et al. investigated the association between rSO₂ and neurological outcomes in patients with out-of-hospital cardiac arrest. The authors enrolled 92 patients in their study and found that the overall rate of good neurological outcome was 14%. They classified their patients into three categories and found that 0% of patients with rSO₂ < 25%, 22.2% of patients with an rSO₂ of 25–40%, and 40% of patients with rSO₂ > 40% had good neurological outcomes. The authors concluded that rSO₂ on hospital arrival may be a predictive factor for assessing neurological outcome. In another study made by Storm et al. the authors aimed to investigate the prognostic value of rSO₂ on cardiac arrest patients, and they found significantly higher rSO₂ values on survivors than non-survivors. They also found that the rSO₂ range largely overlaps between outcome groups, and concluded that the rSO₂ values have limited potential to predict poor outcome. They concluded that normal ranges of rSO₂ is based on a stable cerebral physiology, but the effects of the impairment of the blood–brain barrier caused by global hypoxia due to cardiac arrest on rSO₂ dynamics remains unclear. In our study, we found that the baseline rSO₂ value was 67.5 (46–70) and the difference between baseline and rewarming rSO₂ value was 0.031 (–0.08 to 0.20) in survivors. In non-survivors, the baseline rSO₂ value was 30 (25–65) and the difference between baseline and rewarming rSO₂ value was 0.03 (0.014–0.435). Although statistically considerable difference was detected between groups on baseline rSO₂ values, no statistical difference was detected on percent changes between baseline and rewarming values of rSO₂ (respectively p = 0.003, 0.526).

In conclusion, the rSO₂ measurement is simple, and not affected by hypotension or hypothermia; thus, the rSO₂ may be a useful predictor for determining the prognosis after CPR.

### Conflicts of interest

The authors declare no conflicts of interest.
References


