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Review

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

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ABSTRACT

Introduction: Regional cerebral oxygen saturation (rSO2) can be measured non-invasively even at no- or low-flow states. It thus allows assessment of brain oxygenation during CPR. Certain rSO2 values had been associated with return of spontaneous circulation (ROSC) and neurological outcome in the past. Clear-cut thresholds for the prediction of beneficial outcome, however, are still lacking.

Methods: We conducted a database search to extract all available investigations on rSO2 measurement during CPR. Mean, median, and ΔrSO2 values were either taken from the studies or calculated. Thresholds for the outcome "ROSC" and "neurological outcome" were sought.

Results: We retrieved 26 publications for the final review. The averaged mean rSO2 for patients achieving ROSC was 41 ± 12% vs. 30 ± 12% for non-ROSC (p = .009). ROSC was not observed when mean rSO2 remained < 26%. In ROSC patients, ΔrSO2 was 22 ± 16% vs. 7 ± 10% in non-ROSC patients (p = .009). A rSO2 threshold of 36% predicted ROSC with a sensitivity of 67% and specificity of 69% while ΔrSO2 of 7% showed a sensitivity of 100% and a specificity of 86% (AUC = 0.733 and 0.893, respectively). Mean rSO2 of 47 ± 11% was associated with favourable and 38 ± 12% with poor neurological outcome. There was, however, a great overlap between groups due to scarce data.

Conclusion: Higher rSO2 consistently correlated with increased rates of ROSC. The discriminatory power of rSO2 to prognosticate favourable neurological outcome remains unclear. Measuring rSO2 during CPR could potentially facilitate clinical decision-making.

Background

Outcome after cardiac arrest (CA) with CPR is a major health issue. It and has seen only minimal change for the better in the last few years. Management of patients suffering from out-of-hospital cardiac arrest (OHCA) and in-hospital cardiac arrest (IHCA), therefore, leaves room for further enhancement [1–4]. Post-resuscitation ischaemic brain damage and subsequent reperfusion injuries cause further morbidity, depending on the length and the extent of tissue hypoxaemia [5,6]. Accordingly, special techniques and measurement devices to predict neurological outcome after CA have been under investigation in order to be implemented in recommendations and CPR guidelines. One of those prognosticating tools appears to be cerebral oximetry determined by near-infrared spectroscopy (NIRS). It measures regional brain tissue saturation (rSO2) that seems to be a probate marker for regional cerebral tissue oxygenation [7]. This non-invasive device uses red and infrared light emitted via optodes that are uni- or bilaterally attached to the patient's forehead, whereby underlying superficial brain areas are interrogated. It provides a continuous, venous weighted signal, which is independent of pulsatile flow and enables estimation of the balance between oxygen delivery and oxygen consumption. It is even applicable in no-flow states such as CA [8,9]. Several different oximeters are on the market for clinical use that employ different algorithms and incorporate their specific technologies [9]. Some researchers claim that

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measuring rSO2 in the course of CPR facilitated prognostication of return of spontaneous circulation (ROSC) as well as neurological outcome [10,11]. They suggested that rSO2 might be suitable for guidance and for quality improvement during CPR. However, sensitive cut-off levels that correctly predict outcome have not yet been determined [12]. It is also unclear which rSO2 value (initial, mean, highest or the change in rSO2 over the course of CPR) is most informative [13]. Several studies conducted in the field of OHCA and IHCA report rather variable results [6,10–12,14–38]. Although a recent review provided an overview of the topic [13], sensitive thresholds required for prognostication have not been assessed. With this review we tried to overcome these shortcomings. We further included additional data from more recent studies.

Methods & statistics

Objectives

By collecting and analysing published rSO2 data measured during CPR we aimed to determine critical rSO2 thresholds that could be used to predict ROSC and neurological outcome after CPR. We further tried to evaluate the clinical benefit of the use of NIRS during CPR and point towards areas of future research on this topic.

Search conduct

Following a predefined search protocol (search keys were the following expressions “cardiac arrest AND cerebral oximetry”, “cardiac arrest AND cerebral saturation”, “cardiac arrest AND near infrared spectroscopy”, “cardiac arrest AND NIRS”, “resuscitation AND cerebral oximetry”, “resuscitation AND near infrared spectroscopy”, “resuscitation AND NIRS”). The databases *Pubmed/Medline*, *Embase* and *CENTRAL* were searched for eligible articles. The search was conducted in February 2017. In addition, articles from the reference list of retrieved articles or reviews were also screened in order to detect further sources. Duplicates and papers whose title revealed that they are non-eligible were removed.

Selection criteria

All selected publications were either read as a whole or as abstract. All trials reporting on IHCA as well as OHCA cases who were monitored by NIRS were included. Data describing cerebral oxymetry after ROSC was excluded. All measurements such as initial, mean and highest rSO2-values were eliglible for inclusion. Moreover, we included all types of devices used irrespective of the site of measurement (right or left, uni- or bilateral). The average of the right and the left rSO2 value was calculated if both had been given. Only cerebral rSO2 measures were accepted. All publications were screened for outcome data, i.e. ROSC, survival to discharge, favourable neurological outcome described as a cerebral perfomance catergory (CPC) index of 1 or 2. Furthermore, dynamics in cerebral oxygen saturation depicted as delta rSO2-values where either taken from the corresponding trials or calculated. All studies independent of sample size were included.

Data collection and definitions

After assessing every paper’s methodological quality (plausibility of calculations, analysis of methods together with statistics) data was extracted in order to aquire a cumulative pool of rSO2 values. Terms as “cardiac arrest” or “return of spontaneous circulation” were defined according to the updated Utstein Guidelines on uniform reporting upon CA, i.e. as the cessation of cardiac mechanical activity confirmed by the absence of signs of circulation [39]. Only CPC-scores of 1 or 2 qualified as favourable neurological outcome [40]. Initial measurement values were considered to be the first figure obtained after the NIRS-optodes had been placed on the patient’s forehead without further discimination concerning previous duration of CA and CPR. The highest value that could be obtained during the entire data acquisition period was defined as the maximum rSO2 value achieved during CPR. Mean or median values were taken directly from the publication itself using the data available that were provided in the respective tables and figures. In some cases calculated data was taken from previous reviews. This data was marked accordingly. For the calculation of delta rSO2, only values that differed from the initial measurement until detection of ROSC or termination of CPR because of futility were taken into account, excluding all values aquired after ROSC. Averaged values (averaged means and averaged medians) were calculated from repetitive data collected in the corresponding trials. As mean and median values are not directly comparable, they were treated separately. When papers did not give mean or median values, the initial or the highest measurement was taken for the calculation of the averaged mean rSO2 value determined from all available studies. This review is reported consistent with the PRISMA-guidelines for publishing reviews [41].

Statistical analysis

Receiver Operating Characteristic (ROC) – analysis was utilized to show the discriminatory power of specific cut-off levels and thresholds as potential indicators for clinical decision-making. Data was assessed for normal distribution using a Kolmogorov-Smirnov-Test. Normally distributed data was compared with the Student’s *t*-test, non-normally distributed data was compared using the Mann-Whitney-U-test. In order to visually compare the weighted results of those trials that provided mean rSO2 values or from which they could be calculated, a forest plot was composed. A two-tailed p-value of < 0.05 was considered to be statistically significant.

Results

Twenty-six studies all published in English language were included in the final review [6,10,12,14–20,22–27,29–38]. Twenty-three were reviewed in full length and three through their abstracts. The specific characteristics of each included trial are presented in Table 1.

Fig. 1 gives an overview of the search process. Most publications reported mean rSO2 values. The 26 studies represent data from seven Asian and European countries as well as from USA. They therefore encompass different ethnicities. Overall, data from a total of 2620 patients were included, of whom 708 (27%) had ROSC and 51 (2%) a CPC of 1 or 2. Neurologic outcomes were less frequently reported as ROSC. Merely 14 studies (54%) gave detailed results [6,12,14,15,17–19,24,31,32,34–36,38].

Nineteen studies (73%) [10,12,14–16,22–27,29,31,33–38] focused on OHCA, nine (35%) [6,17–20,22,25,30,32] on IHCA, whereas 2 (8%) [22,25] investigated both OHCA and IHCA patients. Fourteen (56%) [12,15,17–19,24–27,33,35–38] stated having used bilateral-, and 10 (40%) [6,10,20,22,23,25,30–32,34] merely unilateral optodes. Two trials [16,29] did not comment. Seven papers (27%) [12,14,18,27,35,36,38] reported only initial rSO2-values, six (23%) [6,10,16,20,30,31] gave only means or medians, and two (8%) [15,26] provided just the highest values that had been determined. Four (15%) [19,22,24,32] reported initial as well as mean/median values, three (12%) [23,25,29] initial and highest values, one (4%) [33] mean/median and highest values, and 2 (8%) [17,34] provided data on all three measurements (see Table 1).

RSO2-values in patients achieving ROSC vs. those not achieving ROSC

In 23 studies (89%) [6,10,15–20,22–27,29–36,38] either the mean or the median rSO2 value of patients achieving ROSC was reported. From this data, the averaged mean rSO2 could be calculated as 41% (± 12) and the averaged median as 42% (± 11). In contrast, in the 21 studies (81%) [6,10,15,16,19,20,22–27,29–36,38] giving information