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Clinical Paper

Regional cerebral oxygen saturation after cardiac arrest in 60 patients—A prospective outcome study

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ABSTRACT

Introduction: Non-invasive near-infrared spectroscopy (NIRS) offers the possibility to determine regional cerebral oxygen saturation (rSO_2) in patients with cardiac arrest. Limited data from recent studies indicate a potential for early prediction of neurological outcome.
Methods: Sixty cardiac arrest patients were prospectively enrolled, 22 in-hospital cardiac arrest (IHCA) and 38 out-of-hospital cardiac arrest (OHCA) patients respectively. NIRS of frontal brain was started after return of spontaneous circulation (ROSC) during admission to ICU and was continued until normothermia. Outcome was determined at ICU discharge by the Pittsburgh Cerebral Performance Category (CPC) and 6 months after cardiac arrest.
Results: A good outcome (CPC 1–2) was achieved in 23 (38%) patients, while 37 (62%) had a poor outcome (CPC 3–5). Patients with good outcome had significantly higher rSO_2 levels (CPC 1–2: rSO_2 68%; CPC 3–5: rSO_2 58%; $p < 0.01$). For good and poor outcome median rSO_2 within the first 24 h period was 66% and 59% respectively and for the following 16 h period 68% and 59% ($p < 0.01$). Outcome prediction by area of rSO_2 below a critical threshold of $rsO_2 = 50\%$ within the first 40 h yielded 70% specificity and 86% sensitivity for poor outcome.
Conclusion: On average, rSO_2 within the first 40 h after ROSC is significantly lower in patients with poor outcome, but rSO_2 ranges largely overlap between outcome groups. Our data indicate limited potential for prediction of poor outcome by frontal brain rSO_2 measurements.

1. Introduction

Prediction of neurological outcome in patients after cardiac arrest by biomarkers, clinical neurological examination and electrophysiological testing can be difficult and may partly be affected by targeted temperature management.[1–6] To enhance the power of early prognostication an integrated multimarker and clinical examination approach has been recommended in a recently published large review.[7] This approach combined with novel techniques and new biomarkers might increase the precision of prognostication.[8,9] In general, post-hypoxic brain damage after cardiac arrest could be associated with changes in regional oxygen saturation (rSO_2) of brain tissue following changes in oxygen consumption ($CMRO_2$), cerebral blood flow (CBF) or cerebral blood volume (CBV). Both hyperoxygenation due to reduced cerebral oxygen consumption as well as hypooxygenation due to reduced cerebral blood flow could indicate hypoxic ischemic encephalopathy. Therefore, additional information for reliable outcome prediction may be gained by using continuous bedside near-infrared spectroscopy (NIRS) monitoring of frontal brain regional oxygen saturation.

The aim of our study was to improve the knowledge on changes in regional cerebral oxygen saturation after cardiac arrest and to evaluate continuous real-time, non-invasive cerebral oxygenation monitoring by NIRS for outcome prediction.

2. Material and methods

The local ethics committee of the Charité-Universitätsmedizin Berlin approved the study protocol and the study was registered

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(www.clinicaltrials.gov: NCT01531426). For all survivors a healthcare proxy was contacted to give written informed consent as all cardiac arrest survivors were unconscious on admission. Patients were enrolled between January 2012 and January 2013. Patients were included into the study during admission to ICU after cardiac arrest ($n = 38$ OHCA; $n = 22$ IHCA) without general exclusion criteria.

2.1. Post-resuscitation protocol

All patients received cardiac arrest treatment according to our local standard and post-resuscitation care according to current guidelines. The local standard operating procedure (SOP) provides hypothermia for 24 h at 33 °C followed by a controlled rewarming at a rate of 0.25 °C/h to all patients remaining comatose. Hypothermia was performed with a computer controlled feedback surface-cooling device (Arctic Sun 2000; C.R. BARD; Colorado; USA). In cases of a presumed cardiac cause a coronary angiography was generally performed immediately or a brain computed tomography in an unknown cause of arrest or presumed primary intracranial hemorrhage. In addition mean arterial pressure >65 mmHg, normocapnia, normoventilation and normoglycaemia were targeted. Arterial blood gas analysis was performed as part of routine diagnostics at regular intervals after arrival on the ICU.

2.2. NIRS monitoring

Cerebral oximetry was performed with the INVOS monitor (INVOS 5100 C; Covidien; Mansfield, USA). NIRS was started during admission and continued until the end of rewarming (approximately 40 h; 24 h hypothermia followed by 16 h controlled rewarming at 0.25 °/h). The two surface sensors were placed on the forehead for detection of bilateral frontal cerebral oxygen saturation. The monitoring device used detects the absorption of light at wavelengths of 724 nm and 810 nm and calculates regional hemoglobin oxygen saturation (rSO_2). For analysis of the recorded spectroscopy data the software package provided by COVIDIEN was used (INVOS Analytics Tool, Version 1.2). For single time point analysis the mean rSO_2 of right and left sensor was calculated. For a continuous analysis of rSO_2 over time, the area of the rSO_2 curve below a preset rSO_2 threshold was calculated. For example, if rSO_2 remains constantly at 50% for 40 h, the area under the pre-defined rSO_2 threshold of 60% is 10% × 40 h revealing a result of 400%*h. This cumulative dual dimension parameter thus reflects both duration and severity of desaturation.[10,11] To avoid confusion with the area under the curve obtained from ROC analysis, in the following we refer to this parameter as cumulative subthreshold rSO_2 with the dimension of h*%. Forehead and upper part of the body positioning was standardized at 30 degrees in all patients during the whole period of treatment. In 8/60 patients rSO_2 values were not available for all time points due to death or other reasons (1 patient low battery; 1 patient disconnected sensor cable).

2.3. Outcome assessment

For neurological assessment we routinely perform electroencephalography (EEG), determine somatosensory evoked potentials (SEP) and neuron specific enolase (NSE) in addition to repeated clinical examination by a highly experienced neurologist. Final outcome was assessed at discharge and in a 6-month follow-up by the Pittsburgh Cerebral Performance Category (CPC), good outcome was defined as CPC 1–2 and poor outcome as CPC 3–5. For 6-month follow-up mortality was assessed by the German residents registry and CPC follow-up by contacting the patient.

2.4. Statistical analysis

Statistical analysis was performed using SPSS (IBM SPSS Version 20) and Stata (Stata 13; StataCorp LP). Data are given as median and interquartile range (25–75; IQR) or absolute numbers and percent. For comparison of rSO_2 between patients with good and poor outcome a non-parametric longitudinal analysis was performed. A Spearmann correlation was calculated between NIRS values and time to ROSC. A significance level of $\alpha = 0.05$ was used. To define a possible outcome related threshold of rSO_2 a ROC analysis was performed. The cumulative subthreshold rSO_2 below a pre-defined rSO_2 limit (40, 45, 50, 55 and 60%) over the 40 h of NIRS monitoring was calculated for each patient and these values were related to outcome in a ROC analysis.

3. Results

A good outcome (CPC 1–2) was achieved in 23/60 (38%) patients, while 37/60 (62%) had a poor outcome (CPC 3–5). A coronary angiography after admission was performed in 35/60 patients after cardiac arrest and presumed myocardial infarction. Finally 30/35 patients were diagnosed with a coronary heart disease, a further 10 patients had a primary arrhythmia as cause of arrest.

3.1. Baseline characteristics

Baseline characteristics of all survivors are given in Table 1. There was a significant difference between good and poor outcome with respect to time to ROSC, location of arrest, proportion of patients with cardiac cause of arrest, epinephrine dose, ventilator time and length of stay. Total hemoglobin was slightly lower in patients with poor outcome (11.2 versus 13.0 g/dl, $p = 0.02$, Table 1). There was no statistically significant difference between good and poor outcome concerning arterial blood pCO_2, SO_2, and pO_2 at any time point but a significant difference for FiO_2 after 12 h (Table 1).

3.2. rSO_2 after ROSC

Patients with good outcome had persistently significantly higher median rSO_2 levels after cardiac arrest for almost all timepoints (CPC 1–2 median rSO_2 68%; CPC 3–5 median rSO_2 58%; $p < 0.01$; Fig. 1 and Table 2). However, rSO_2 levels largely overlapped between outcome groups but remained largely stable during the hypothermia period (Fig. 1). Detailed results for rSO_2 at different time points are given in Fig. 1 and Table 2. For good and poor outcome median average rSO_2 within the first 24 h period during hypothermia was 66% and 59% respectively and for the following 16 h period of rewarming (24–40 h after cardiac arrest) 68% and 59% (supplementary figure). Separate results for right and left sensor at different time points are given in Table 3, showing only small differences between both sensors. There was no significant correlation between time to ROSC and rSO_2 at any time (Spearmann correlation $r < 0.1$ at all time points).

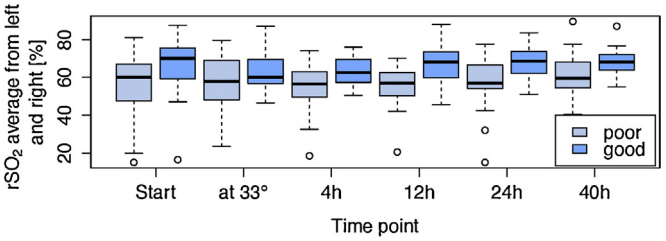

Fig. 1. rSO_2 levels at different time points are given as median and interquartile range (25–75) for good and poor outcome. CPC: cerebral performance category.

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