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EDITORIAL

Cerebral oximetry in cardiac arrest: a potential role but with limitations

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In patients with cardiac arrest (CA) cerebral oximetry has emerged as a real-time indicator of oxygen delivery to the brain which could be used to optimise cerebral oxygenation during and after cardiopulmonary resuscitation (CPR) (Table 1). Near-infrared spectroscopy (NIRS) emits infrared light (700–950 nm wavelength), which is not absorbed significantly by melanin in the skin and enables non-invasive monitoring of the regional haemoglobin oxygen saturation in the brain (rSO_2). NIRS electrodes are placed on the scalp above the frontal cortex and the sampling volume is located about 2 cm underneath the skull [1]. Since about 70% of the sampled blood is venous, normal rSO_2 is approximately 60–80%. Unlike arterial pulse oximetry, rSO_2 can still be measured when blood flow is nonpulsatile or even absent, enabling NIRS to be used during CA. Unlike the electroencephalogram, NIRS is not susceptible to motion artefact generated by CPR.

Use of cerebral oximetry during cardiac arrest

Higher rSO_2 values during CPR are associated with significantly higher rates of return of spontaneous circulation (ROSC). In a review of 26 observational studies (1995–2016), the averaged mean rSO_2 in patients achieving ROSC was 41 ± 12% vs. 30 ± 12% for those without ROSC ($p = 0.009$) [2]. However, there was wide overlap of rSO_2 values between the two groups. Among 183 in-hospital CA (IHCA) patients [3], a 25% rSO_2 cut-off predicted no ROSC with 100 [94–100]% specificity, while a 65% rSO_2 cut-off predicted ROSC with 99 [95–100]% specificity. However, these values corresponded to the extremes of the distribution, so that the relevant sensitivities were low (13 [8–21]% and 21 [12–33]%, respectively).

During CPR, rSO_2 trends appear to be better predictors of ROSC than mean values or values recorded at single time points. In a study on 329 out-of-hospital CA (OHCA) [4] rSO_2 increased steadily during resuscitation in both ROSC and non-ROSC patients, but the increase was twice as high in the ROSC group [median 17% (IQR 6–29) vs. 8% (IQR 2–13); $p < 0.001$]. After adjustment for major confounders, a greater than 15% increase in rSO_2 during CPR was the best predictor of ROSC (odds ratio [OR] 4.88 [2.79–8.54]).

As has been observed for end-tidal carbon dioxide ($ETCO_2$), an abrupt increase in rSO_2 values during CPR indicates that ROSC has occurred [5]. In a study on 53 OHCA patients, 22 (42%) had ROSC after a mean of 22.5 min of CPR; when ROSC occurred, the median rSO_2 increased from 22.5% [16–35] to 51% [39–55] in 3 min [6]. A potential advantage of rSO_2 compared with $ETCO_2$ for monitoring during CPR is that detection of the rSO_2 signal does not require advanced airway management.

In a study on IHCA [3], time with $rSO_2 > 50\%$ during CPR best predicted favourable neurological outcome after resuscitation (cerebral performance category 1–2), suggesting that rSO_2 may reflect the quality of cerebral oxygenation and perfusion during CPR. In another study, among 92 OHCA patients who arrived at the emergency department with ongoing CPR, the rate of neurological recovery was 50% in those with $rSO_2 > 40\%$, 22% in those with rSO_2 26–40%, and 0% in those with rSO_2 25% or less [7].

Cerebral oximetry in post-resuscitation care

Optimising cerebral oxygenation and perfusion is one of the mainstays of post-resuscitation care. Autoregulation of cerebral blood flow (CBF) is lost in about one third of comatose CA survivors [8], while in others the

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Table 1 Cerebral oximetry (rSO_2) in cardiac arrest

Potential applications	Results/advantages	Limitations
Monitoring brain oxygenation	NIRS measures the regional oxygen saturation (rSO_2) by analysing the intensity of infrared light backscattered from tissue located about 2 cm underneath a probe placed on the frontal scalp rSO_2 can be detected even when flow is nonpulsatile or absent, as in cardiac arrest	There is a significant risk of contamination of the NIRS signal by extracerebral sources [1, 13]
Prediction of ROSC during CPR	In a systematic review of 26 studies [2], the averaged mean rSO_2 in patients with ROSC was 41 ± 12% vs. 30 ± 12% for those without ROSC ($p = 0.009$) In a study on 183 IHCA [3], a ≥ 65% rSO_2 cut-off had 99 [95–100]% specificity for ROSC, while a ≤ 25% rSO_2 cut-off had 100 [94–100]% specificity for no ROSC In a study on 329 OHCA, a 15% increase of rSO_2 during CPR was the best predictor of ROSC (OR 4.88 [2.79–8.54])	There was a wide overlap of averaged rSO_2 values between ROSC and no-ROSC studies High specificities only at the extremes of the distribution. The relevant sensitivities were low (21 [12–33]% and 13 [8–21]%, respectively)
Targeting MAP to optimise cerebral perfusion after resuscitation	Optimal MAP is defined as the one which minimises the correlation coefficient (COX) between MAP and rSO_2 (optimal autoregulation) Observational evidence [8, 9, 11] showed that deviation from optimal MAP is associated with worse neurological outcome or lower survival in both children and adults	There are no interventional studies showing that targeting a specific MAP improves neurological outcome after CPR The relationships between rSO_2, CBF and neurological outcome are not fully understood and deserve further investigation

CBF cerebral blood flow, *CPR* cardiopulmonary resuscitation, *IHCA* in-hospital cardiac arrest, *MAP* mean arterial pressure, *OHCA* out-of-hospital cardiac arrest, *ROSC* return of spontaneous circulation, *rSO_2* regional oxygen saturation of the brain

zone of autoregulation is narrowed and right-shifted [9] so that CBF is maintained consistent and independent from mean arterial pressure (MAP) only within a narrower and higher MAP range. In clinical studies the optimal MAP has been identified as that where the correlation coefficient between rSO_2 and MAP (termed as COX) is minimal in the individual patient [9]. In children resuscitated from CA, deviations from optimal MAP have been associated with worse neurological outcome [8, 10]. In a study on 51 resuscitated comatose adults [9], the time spent below the optimal MAP was associated with a lower likelihood of survival (OR 0.97 [0.96–0.99], $p = 0.02$).

Cerebrovascular reactivity to CO_2 is generally preserved after CA and manipulating arterial partial pressure of carbon dioxide ($PaCO_2$) may be used in order to optimise CBF and brain oxygenation. In the recent COMACARE randomised pilot trial [11], a high-normal (5.8–6.0 kPa) $PaCO_2$ was associated with higher rSO_2 than low-normal (4.5–4.7 kPa) $PaCO_2$ in comatose resuscitated patients. A larger randomised trial (NCT03114033) comparing mild hypercarbia (6.7–7.3 kPa) with normocarbia after CA is currently ongoing.

Current limitations and future perspectives

The association between higher rSO_2 values during CPR and the rates of ROSC or neurological recovery suggests that rSO_2 could be used as a physiological target to optimise CPR quality. However, the nature of this association is not completely clear. In fact, since NIRS signals can be contaminated from extracerebral circulation [12], rSO_2 values during CPR may reflect whole-body rather than brain perfusion. In addition, patients who achieve ROSC usually show higher rSO_2 values from the beginning of the resuscitation attempt [2], so that it is not clear whether a higher rSO_2 in these patients reflects more effective CPR or, instead, other favourable factors, such as witnessed status or a shorter no-flow time.

Although lower nadir rSO_2 levels have been associated with worse neurological outcome in resuscitated comatose patients [13], observational studies did not show an association between mean rSO_2 in the early post-resuscitation phase and neurological outcome. In the COMACARE trial, changes in mean rSO_2 were not associated with differences in the levels of neuron-specific enolase, a marker of neuronal ischaemia. However, rSO_2 values were within normal values in all study groups. A limitation of this and other investigational models, such as the ones based on COX, is that the relationship between rSO_2 and CBF is not well known, although a recent study has shown that rSO_2 is positively correlated with cerebral perfusion pressure evaluated noninvasively using transcranial Doppler [14]. Further research is required to determine if cerebral oximetry is of real value in resuscitation, but based on current evidence it is not ready for routine clinical use.

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Compliance with ethical standards

Conflicts of interest
Sandroni: none to declare. Parnia: none to declare. Nolan: Editor-in-Chief of *Resuscitation*.

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