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Editorial

Regional cerebral saturation in post-cardiac arrest patients is doomed . . . or is it just a near death experience?

One of the most challenging aspects in the treatment of a post-cardiac arrest patient is the assessment of the extent of brain damage, and its concomitant prognosis. Clinicians are continuously confronted with the optimistic expectations of relatives. Parameters that provide early prognostic information are highly desirable in the post-cardiac arrest setting since they would facilitate communication with relatives and would allow better triage of economically burdensome therapies. Reliable, practical measures of intra- and post-arrest neurologic function have potential to guide treatment geared toward reducing neurological damage and providing a basis for accurate prognostication. A persistent candidate measure to fill this role is cerebral oxygen saturation (rSO_2) monitoring, as assessed by near-infrared spectroscopy (NIRS) technology. It has been mainly used and studied in the perioperative cardiac surgery and paediatric intensive care setting.[1–4] Resulting from the growing body of evidence that optimization of brain oxygenation results in better (neurological) outcomes, expectations for rSO_2 monitoring in the post-cardiac arrest setting were high.[2,4]

Using near-infrared spectroscopy technology, differences between oxygenated and deoxygenated haemoglobin levels are measured and calculated using the modified Beer–Lambert Law. Due to its non-invasiveness, ease of use, lack of need for a pulsatile signal and its ability to provide continuous information about regional oxygenation in the frontal brain lobe, NIRS technology overcomes many limitations of existing monitors in the acute cardiac arrest setting. Still, users need to be aware of the pragmatic issues that are device-dependent (i.e. differences in weight, sensitivity to light interference, and sensor robustness). The sampled blood is 70% venous and 30% arterial, however with interference of sampling of blood of the watershed area. Clinicians should take into account that this 70%–30% ratio is constant in contrast with physiological changes in cerebral blood flow and haemoglobin during the (post-) cardiac arrest phase. But more importantly, clinicians need to bear in mind that, across different NIRS devices, the output (rSO_2) cannot be interchangeably used and interpreted. From this perspective, rSO_2 monitoring should be considered as trend monitoring, especially in the cardiac arrest setting where nor baseline nor optimal rSO_2 levels are known.

In this issue of Resuscitation, Tran et al. report the results of an interesting study in which rSO_2 was measured in 87 in-hospital cardiac arrest (IHCA) patients during the first 48 h after the return of spontaneous circulation (ROSC).[5] The main goal of the study was to investigate whether rSO_2, measured within this time frame, was associated with survival and neurological outcome at hospital discharge. Median rSO_2, measured during the first two hours after cardiac arrest, was significantly higher in patients with a favourable neurological outcome compared to those with an unfavourable neurological outcome (74.7% versus 69.0%, $p = 0.034$). Interestingly, median rSO_2 did not differ across the other compared time intervals between the two outcome groups (i.e. hourly during the first six hours, every six hours between 6–24 h after ROSC and once between 24 and 48 h). Unfortunately, the authors did not take the longitudinal nature of rSO_2 monitoring into account by means of a linear mixed model analysis, and did not correct for multiple comparisons either. In addition to a low sample size, it is also noteworthy that six patients were awake within the first six hours after ROSC. These patients could have biased the results as five out of six were part of the favourable neurological outcome group. It would be interesting to perform a sensitivity analysis. Another important limitation is that neurological outcome was determined at hospital discharge, and not longitudinally assessed. Nonetheless, the fact that patients with a favourable neurological outcome have significantly higher rSO_2 values in the initial two hours following cardiac arrest is intriguing. In two large out-of-hospital cardiac arrest cohorts, no clinically overt differences could be detected in a similar time frame.[6,7] Interestingly, the range of rSO_2 during the first two hours was lower in these OHCA studies (62–66%) as compared to the reported results of Tran et al. (69–75%). This might imply that the initiation of rSO_2 monitoring took place in an earlier phase of the pathophysiological mechanism of cardiac arrest. While Tran et al. most likely captured rSO_2 already in the hyperaemic phase, others were probably measuring rSO_2 in the delayed cerebral hypoperfusion phase, potentially clarifying these differences in absolute rSO_2 values.[6,7]

Over the last decade, numerous studies have been investigating the prognostic significance of NIRS technology in the post-cardiac arrest setting.[6–10] Although the results have been controversial, the margin of the detected differences, if any, remains too small to likely represent a clinically useful outcome differentiation. Although Tran et al. targeted an IHCA population only, it was not surprising that their results strengthened the common belief that rSO_2 monitoring, on its own, is of little clinical relevance in post-CA patients.

Recent studies have demonstrated that rSO_2 correlates with cerebral perfusion pressure.[11] As such, instead of using rSO_2 for outcome prediction, it might be clinically more valuable to use rSO_2 to target a patient-tailored mean arterial pressure (MAP). Cerebral

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autoregulation is known to be absent or right-shifted in approximately one-third of all post-CA patients, thereby questioning whether the recommended MAP target of 65 mmHg is sufficiently high to avoid cerebral hypoperfusion.[12] An observational rSO_2 study showed that MAP should rather be in the range between 85 and 100 mmHg to guarantee optimal cerebral perfusion.[12] Ameloot et al. investigated whether neurological outcome could be improved when MAP levels were targeted within these autoregulatory limits.[13] Although higher MAPs resulted in an improvement of rSO_2, neurological outcome remained unaltered. Independent of the outcome of this study, future (interventional) studies, assessing whether a patient-tailored hemodynamic optimization using an index of autoregulation (COx) would improve neurological outcome after OHCA, are also of interest. However a small study by Hoiland et al. comparing COx to PRx (measuring cerebral autoregulation using the moving correlation coefficient between MAP and intracranial pressure in contrast to MAP and rSO_2 if COx is calculated) to calculate an optimal MAP did not observe an agreement between the two calculated optimal MAP.[14]

Another setting where rSO_2 might play an important role is in the CA setting, i.e. during cardiopulmonary resuscitation (CPR). Multiple studies have shown that increases in rSO_2, but also higher rSO_2 values throughout CPR, are associated with a high probability of attaining ROSC.[15–17] From this perspective, one can consider rSO_2 as a future tool able to assist clinicians in the decision to continue or stop resuscitation efforts. Even further, predicting short and long-term neurological outcome using rSO_2 values measured in the first minutes during CPR remains an intriguing concept and should be adequately studied in the years to come.

In conclusion, rSO_2 monitoring has found its way into post-CA research for several years now, but in this setting it appears to be on a dead track. So far, numerous studies in post-CA patients have failed to show any clinical relevance for the prognostic use of rSO_2 on its own. Combining rSO_2 with other physiological parameters to assess cerebral autoregulation, as well as investigation of its real-time utility during the resuscitation process, might therefore be more valuable alternative lines of investigation.

Conflict of interest

None of the authors have a conflict of interest to declare.

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