

## Review Article

# Non-Invasive Regional Cerebral Oxygen Saturation (rSO<sub>2</sub>) and Postoperative Neurological Dysfunction

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## Introduction

Regional Cerebral oxygen saturation (rSO<sub>2</sub>) is the one non-invasive monitoring technique for bedside cerebral oxygen saturation, which has the advantages of real-time, sensitivity, rapidity, and persistence. It is the most widely used method for monitoring cerebral oxygen saturation at present. The application of near-infrared spectroscopy to the monitoring of rSO<sub>2</sub> was reported for the first time in 1977 by Jobsis [1]. In recent years, there has been a significant increase in the use of rSO<sub>2</sub> during perioperative period, especially in cardiac [2], aortic [3], carotid surgery [4-5], thoracic [6-8], resuscitation [9-10], neonatal [11], and geriatric surgery [12]. In recent years, with the increasing use of rSO<sub>2</sub> in clinical practice, a large number of literatures show that maintain a certain range of rSO<sub>2</sub> can shorten the length of tracheal extubation, stay in intensive care unit and in hospital [2,14-15]. Finally, it can improve the prognosis of patients, reduce the occurrence of postoperative neurological dysfunction and reduce the mortality of patients [16-18].

## The Principle and Detection Method of rSO<sub>2</sub>

Continuous noninvasive monitoring of regional cerebral oxygen saturation (rSO<sub>2</sub>) was carried out by Near-Infrared Spectroscopy (NIRS) technique. The principle of NIRS monitoring system is that near infrared light (wavelength range 700-950 nm) that transmitted and absorbed through tissues [19]. Near infrared light can penetrate the scalp, skull and brain tissue to detect brain rSO<sub>2</sub>. Based on Lambert Beer Law and light scattering theory, chromophore biomolecules have different optical densities in near infrared spectra, and their concentration can be determined in the range of relative absorption wavelength [20-22]. By measure the difference of optical absorption coefficient between reduced hemoglobin and oxygenated hemoglobin that is the most commonly used chromophore [23]. Then calculating the absorption spectrum ratio, the concentration of local two kinds of hemoglobin can be obtained. In the brain, the arterial blood volume is about 20%, capillary blood volume is about 5%, and the remaining 75% is venous blood volume, so in fact, rSO<sub>2</sub> is similar to cerebral venous oxygen saturation [24]. Finally, the weighted average value of blood oxygen saturation of the three blood vessels was used to reflect

the changes of oxygen supply and consumption balance in the brain [24]. Near-infrared light cannot pass through the entire head, both near-infrared light sources and detection devices are located on the same side of the brain, a few centimeters apart, so that rSO<sub>2</sub> actually detects the cortex of the brain.

## Threshold and Availability of rSO<sub>2</sub>

The normal range of rSO<sub>2</sub> in healthy adult volunteers was (71.2±3.9) % under the normal air condition [25]. Most studies suggest that the normal range of average rSO<sub>2</sub> value is 55%~75%, but there is a large variation among individuals [11]. Hirofumi believe that rSO<sub>2</sub> decrease to 55% means there is a risk of neurological complications after surgery and clinicians need to intervene accordingly [26]. Shmigeskii also found that if the rSO<sub>2</sub> value is less than 55%, the probability of cerebral ischemia and hypoxia is high, which suggests that anesthesiologists should make appropriate treatment and rescue measures as soon as possible [27]. The current research tends to use relative values to represent the range of rSO<sub>2</sub>. Samra continuously monitored rSO<sub>2</sub> in CEA patients and found that rSO<sub>2</sub> was 20% lower than the baseline value and could predict postoperative neurological dysfunction. The sensitivity and specificity were 80% and 82% respectively [28]. A study of 70 patients with cardiac operation under cardiopulmonary bypass found that rSO<sub>2</sub> decreased by 10% (6% to 15%), suggesting insufficient cerebral perfusion and requiring intervention [29]. A recent study of 50 beach chair patients undergoing shoulder surgery showed an 18% decrease in cerebral oxygen saturation during the perioperative period. The maximum decrease of rSO<sub>2</sub> from the baseline was 32%, and the average duration was more than 3 min will lead to the bad outcome in the patients. Kobayashi and Colak suggested that the decrease of rSO<sub>2</sub> from the initial value of 20% to 30% or as low as 40% to 50% absolute value was abnormal and was related to the lack of oxygen supply in the brain [30-31]. In one 594 patients study with carotid stenosis of more than 70% were assigned to shunt based on changes in rSO<sub>2</sub> levels, the relative decrease of rSO<sub>2</sub> was more reliable than the absolute decline to detect brain low oxygen supply [32]. During CEA surgery under general anesthesia, the monitoring of rSO<sub>2</sub> the reliability was 95.38%, the sensitivity was 100%, and the specificity was 95.36%. A brief relative decline in rSO<sub>2</sub> to 20% baseline is allowed for 2 min to automatic adjustment of fluctuations. Another algorithms for rSO<sub>2</sub>, the duration of rSO<sub>2</sub> AUC score 50% area [50%-(rSO<sub>2</sub>- 50%)]\* duration time is used as the index [33]. Although rSO<sub>2</sub>-directed ischemic thresholds have not been verified, clinical research and management processes often use absolute rSO<sub>2</sub> values of less than 50% or a 20% decline from baseline as the trigger point for initiating improvements in cerebral oxygenation [34]. Slater et al came to a similar conclusion that patients with rSO<sub>2</sub> reduction score 13000s during CABG were more likely to have cognitive impairment after CABG, and the risk of prolonged hospitalization increased nearly threefold [33]. Although rSO<sub>2</sub>-directed thresholds for ischemia have not been verified, clinical

research and management processes often use absolute  $rSO_2$  values of less than 50% or a 20% decline from baseline as the trigger point for initiating elevate cerebral oxygenation.

### Advantages and Influencing Factors of $rSO_2$

Unlike noninvasive arterial blood pressure monitoring,  $rSO_2$  which represents regional oxygen supply and oxygen consumption balance does not rely on the measurement of blood flow pulsation [35-37]. Therefore, even in the special cases of hypotension, weak pulse and circulatory arrest, continuous monitoring of cerebral oxygen metabolism and oxygen consumption can be carried out to evaluate the oxygenation status of brain tissue. The signal of monitoring cerebral oxygen saturation mainly comes from venous blood, so  $rSO_2$  is not affected by hypothermic arterial vasoconstriction. Furthermore, unlike Electroencephalogram (EEG) and autologous evoked potentials (SEPs),  $rSO_2$  did not change because of any sedation and analgesic medicine intervention [38-39]. All in all, a series of studies have shown that continuous monitoring of  $rSO_2$  during operation to predict cerebral ischemia is reliable and sensitive and can enable clinicians to timely detect the occurrence of intraoperative cerebral ischemia and hypoxia and make timely intervention. Although  $rSO_2$  is widely used in clinic, it is also affected by some physiological variables, including blood pH, arterial oxygen saturation ( $PaO_2$ ), arterial  $CO_2$  partial pressure ( $PaCO_2$ ), hemoglobine concentration, cerebral blood flow (CBF), cerebral blood volume (CBV), cerebral oxygen metabolism rate (COMR) [40, 37-38]. The skull thickness, skin pigments and the position of the probe also have a weak effect for  $rSO_2$  [39]. There was a negative correlation between  $rSO_2$  and age, and a positive correlation between  $rSO_2$  and hemoglobine concentration. One of the major challenges of  $rSO_2$  accuracy is acute brain injury from intracranial hematoma, cerebral edema or subarachnoid hemorrhage, which may invalidate based on  $rSO_2$  related algorithms.

### $rSO_2$ and Post-Operative Cognitive Dysfunction (POCD)

Post-Operative Cognitive Dysfunction (POCD) is a common complication after anesthesia and operation. The clinical manifestations are memory deficit, cognitive dysfunction, changes in personality and social integration ability, etc. In severe cases these patients may evolved to Alzheimer's disease. The incidence of POCD after cardiac surgery in elderly patients can be as high as 19% within 24 hours post-operation, especially in abdominal surgery may increase to 40%. The incidence of POCD can be as high as 50%~70% one week and 30% ~50% after 2 months, seriously decrease the quality of life and long-term survival of patients [40]. At present, the pathogenesis of POCD is still unclear, which may involve many factors, including embolism, hypoperfusion, hypoxia, inflammatory reaction, advanced age, cerebrovascular disease and so on [41-42]. However, these factors are ultimately related to cerebral ischemia and imbalance of oxygen supply and consumption in the whole or the part of the brain. The patients underwent cardiac surgery and CPB were monitored by  $rSO_2$ . The value of  $rSO_2$  was maintained above 80% of the baseline or 55% of the absolute value of the  $rSO_2$  by interventions during the operation. Cognitive function was assessed by a series of scales such as trailing test (TMT) before and 5 days after operation. The results showed that the incidence of POCD was 43%, which was not significantly different from the incidence of POCD

in previous observational studies, and the analysis of the operating characteristic curve AUC of subjects showed that the  $rSO_2$  value <65% showed a sensitivity of 86.7% and a specificity of 65% in predicting POCD occurrence, respectively [43]. According to Monk studies, the incidence of postoperative cognitive impairment in elderly patients is closely related to the frequent occurrence of low  $rSO_2$  during operation, and these patients stay in hospital for a relatively long time. Compared with the patients without ASEM and MMSE, the patients with damaged ASEM and MMSE had a greater decrease in  $rSO_2$  value during operation. Multivariate regression analysis showed that 40% decrease of  $rSO_2$  was an independent risk factor for ASEM and MMSE damage [44]. Another multivariate regression analysis showed that  $rSO_2$  AUC >3000% significantly increased the risk of POCD in the early postoperative period and increased the risk of prolonged hospitalization nearly threefold. A randomized trial was carried out on the elderly patients undergoing major abdominal surgery. The intervention group received continuous monitoring of  $rSO_2$  during the operation, make the  $rSO_2$  >75% of the baseline, interventions were taken by raising  $FiO_2$ ,  $EtCO_2$  and blood pressure. The results showed that there was a significant difference between the intervention group and the control group in the average value of  $rSO_2$ . Slater get the coincidence result under CABG patients [45]. Casati found every four patients undergoing abdominal surgery in a healthy elderly population experienced intraoperative low  $rSO_2$ , which is associated with a decline in early cognitive levels [46-47]. The MMSE score of the control group was significantly lower than that of the intervention group on the 7<sup>th</sup> day after operation, and the resuscitation time and hospitalization time in the post-anesthesia monitoring room were significantly longer than those in the intervention group. In de Tournay Jette study, the patients with  $rSO_2$  <50%, were 7.69 times more likely to develop POCD a week after surgery than those without  $rSO_2$  <50% [48].

### $rSO_2$ and Delirium and Stroke

A large number of literatures have shown that  $rSO_2$  monitoring can reduce the incidence of delirium after cardiac surgery and shorten the length of stay in hospital [49]. A recent systematic review has concluded that only low-level evidence suggests that intraoperative decreased cerebral oxygenation is associated with postoperative stroke [39].  $rSO_2$  monitoring can reduce the incidence of stroke after CEA surgery [50]. Reducing the risk of cerebral ischemia and anoxia patients undergoing beach chair surgery have a higher risk of hypotension related cerebral ischemia after anesthesia, so it is important to monitor cerebral oxygen saturation during perioperative period in this kind of operation. Morimoto found the delirium rate positive correlated with age and basic of  $rSO_2$  [51]. Continuous monitoring of  $rSO_2$  during operation can effectively prevent perioperative death and stroke associated with carotid endarterectomy CEA. The current research found, in terms of perfusion parameters, postoperative  $rSO_2$  was lower in the delirium than the non-delirium group (65±10% vs. 74±5%), but the delta- $rSO_2$  (the difference between means post-operative and intra-operative) was associated with post-operative delirium. Treatment with Oxygen concentration, liquid resucetation based on the  $SO_2$  will reduce the delirium [52]. Some study indicated that cerebral aortic blood flow changes significantly correlated with  $rSO_2$  and reduced its value 13% as the beginning of cerebral infarction [53].

## Conclusion

The  $rSO_2$  a continuous, noninvasive, sensitive and specific method for detect cerebral oxygen saturation guide the prevention and reduction of cerebral ischemia and hypoxia injury in real time and play a guiding role in anesthetic management during operation. It is one of the core tasks of perioperative anesthesia management to maintain the balance of cerebral oxygen supply and demand to ensure the metabolism of brain tissue. Monitoring regional cerebral oxygen saturation using near infrared spectroscopy can detect the balance between cerebral oxygen supply and demand, cerebral perfusion and cerebral blood flow as early as possible, and judge the degree of cerebral ischemia and hypoxia, the change of cerebral function.  $rSO_2$  is helpful timely adjustment of anesthesia plan, finally reduce the occurrence of postoperative neurological dysfunction, shorten the period of hospitalization, and improve the quality of life of patients.

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