

# The Relationship between Prolonged Cerebral Oxygen Desaturation and Postoperative Outcome in Patients Undergoing Coronary Artery Bypass Grafting

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## ABSTRACT

58 patients who underwent on-pump coronary artery bypass graft surgery were evaluated for changes in regional cerebral oxygen saturation ( $rSO_2$ ) measured by near infrared spectroscopy (NIRS). If  $rSO_2$  during the operation fell to more than 20% under the baseline, standardized interventions were undertaken to maintain  $rSO_2$ . Despite those interventions, in some cases we observed inability to maintain  $rSO_2$  above this threshold. Therefore we divided patients in two subgroups: 1. without prolonged  $rSO_2$  desaturation; 2. with prolonged  $rSO_2$  desaturation (area under the curve >150 min% for  $rSO_2$ <20% of baseline and >50 min% for  $rSO_2$ <50% of absolute value). The data were analyzed to determine whether there were major differences in outcome of these two groups. 18 out of 58 patients (31%) had prolonged  $rSO_2$  desaturation during operation. There was significantly higher number of diabetic patients in group with prolonged  $rSO_2$  desaturation ( $p=0.02$ ). Intraoperative data revealed significantly more blood consumption during cardiopulmonary bypass ( $p=0.007$ ) and the need for inotropes ( $p=0.04$ ) in desaturation group. Three patients in prolonged desaturation group and no one in another group had stroke, coma or stupor ( $p=0.03$ ). Logistic regression analysis revealed diabetes mellitus and age as predictors for prolonged  $rSO_2$  desaturation. We concluded that prolonged intraoperative  $rSO_2$  desaturation is significantly associated with worse neurological outcome in patients – nonresponders to standardized interventions for prevention of  $rSO_2$  desaturation.

**Key words:** cerebral oximetry, near-infrared spectroscopy, on-pump coronary artery bypass, neurologic outcome

## Introduction

Neurological injury in patients undergoing coronary revascularization remains one of the major causes of morbidity after cardiac surgery. The incidence of cerebral injury is still high (up to 6.1%) because the number of aged patients with numerous comorbidities has significantly increased in cardiosurgical population. Several etiologic factors have been proposed including embolisation, hypoxic insult, compromised cerebral blood flow and systemic inflammatory response, but also previous unrecognized neurological abnormality<sup>1–3</sup>.

There is a need for cerebral monitoring during cardiac surgery with the aim to reduce postoperative neurological complications<sup>4–6</sup>. Transcranial near-infrared spectroscopy (NIRS) provides continuous noninvasive measurement of regional cerebral oxygen saturation ( $rSO_2$ ) in small local area of cortex. It is influenced by the actual oxygen supply and demand balance and serves as a sensitive indicator of global cerebral hypoperfusion<sup>7,8</sup>. Numerous studies reported that cerebral desaturation during cardiac surgery is associated with early neurological dys-

function and other postoperative adverse events. Intraoperative monitoring of cerebral oxygenation with NIRS and maintaining of balance in oxygen supply-demand can reduce postoperative neurologic and systemic complications<sup>9–14</sup>.

The aim of the study was to examine usefulness of intraoperative cerebral oxymetry monitoring and efficacy of interventions performed to maintain regional rSO<sub>2</sub> above the baseline value by determining a relationship between intraoperative cerebral oxygen desaturation and adverse postoperative events.

## Patients and Methods

### Study population

The data were obtained from University Hospital Center Zagreb and the study was approved by the hospital Ethical committee. The total number of 58 patients, who underwent on-pump coronary artery bypass graft surgery (CABG) and signed informed consent, was included in the study. These patients were recruited between June 2009 and February 2010. Patients with significant carotid artery stenosis, previous stroke or head injury, seizure, psychiatric illness, decompensate heart failure (NYHA III/IV), emergency cardiac surgery, off-pump CABG, and severely impaired renal or liver function were excluded from the study.

### Operation protocol

The same anesthesia protocol was applied to all patients and included premedication with intramuscular morphine 0.1 mg/kg and induction with midazolam 0.1 mg/kg, hypnomidate 0.2 mg/kg, sufentanyl 1 mcg/kg and pancuronium 0.1 mg/kg. After tracheal intubation anesthesia was maintained with sufentanyl-continuous infusion of 0.8 mcg/kg/h, propofol-5 mg/kg/h (only during cardiopulmonary bypass), sevoflurane 0.5–2 minimal alveolar concentration (MAC) and pancuronium 2 mg if necessary. Minute ventilation was adjusted to maintain arterial CO<sub>2</sub> partial pressure (PaCO<sub>2</sub>) between 4.5 and 6 kPa and FiO<sub>2</sub> of 0.5. Measurements of cardiac index and other hemodynamic parameters were provided using Swan-Ganz catheter from the beginning of the operation until 24 hours after arrival in ICU. Inotropic agents were used to maintain a cardiac index  $\geq 2.0$  L/min/m<sup>2</sup> and a systolic blood pressure  $\geq 90$  mmHg after preload was adjusted according to hemodynamic parameters obtained by Swan-Ganz catheter and transesophageal ultrasound. The first inotrop of choice was dobutamin. No other monitoring of neurologic function was used. BIS monitoring was not used.

After heparinization (400 i.j./kg) cardiopulmonary bypass (CPB) was established with a moderate hemodilution and systemic hypothermia (28–32 °C). Heart was protected with blood cardioplegia (Croatian Institute for Transfusion Medicine, Zagreb) during cross-clamping of aorta. Generally a single clamp technique was used. Standard flow rates of 2–2.5 L/minute/m<sup>2</sup> were main-

tained with hematocrit above 22%, mean arterial pressure over 60 mmHg, partial pressure of carbon dioxide between 4.5 and 6 kPa by alpha-stat management<sup>15</sup>.

The following parameters were recorded during operation: number of grafts, cardiopulmonary bypass time (CPB time), aortic cross-clamping time (ACC time), duration of operation, cardiac index (CI) before and after cardiopulmonary bypass, the amount of blood given during and after cardiopulmonary bypass, number of patients who needed inotropic support and parameters about rSO<sub>2</sub>.

### Cerebral oxymetry

All patients were monitored using the INVOS system (INVOS 5100C; Somanetics Corp, Troy, MI, USA). The INVOS system is based on near-infrared spectroscopy (NIRS) for noninvasive and continuous measurement of changes in cerebral oxygen saturation. Before induction in anesthesia the probes for INVOS cerebral oxygen monitoring were attached bilaterally on the patient's forehead overlying the frontal-temporal region. The light in the near infrared range penetrates the skin, skull and deeper cerebral tissues. Two values were measured with two detectors at different distances (3 cm and 4 cm) from the light source. The signals common to both measurements (from extracranial tissue) are eliminated and oxygen saturation of blood in the cerebral cortex beneath the sensors is displayed. NIRS doesn't need pulsatile flow so it can be used during cardiopulmonary bypass.

Probes were attached in awoken patients who breathe 6 L/min of oxygen by nasal catheter. Several minutes after the probes were attached the baseline regional cerebral oxygenation (rSO<sub>2</sub>) value was determined for each side of the brain. During the entire surgery rSO<sub>2</sub> values were displayed on a screen and recorded on the USB memory stick. If the rSO<sub>2</sub> decreased to more than 20% of baseline during the operation, we responded with standardized interventions to maintain rSO<sub>2</sub> above the baseline value. These interventions (after checking head and perfusion cannulae position) included maximizing of cerebral oxygen delivery (increasing of oxygen concentration – FiO<sub>2</sub>, arterial CO<sub>2</sub> partial pressure – PaCO<sub>2</sub>, mean arterial pressure, cardiac output or pump flow and hematocrit) or reduction in cerebral oxygen consumption (raising of anesthetic depth and reduction of temperature)<sup>16</sup>. If systemic oxygen saturation fell we increased the fraction of inspired oxygen (FiO<sub>2</sub>). We try to maintain mean arterial pressure within 15% of baseline using vasopressors as required. Arterial CO<sub>2</sub> partial pressure (PaCO<sub>2</sub>) has strong impact on cerebral blood flow. Hypocapnia causes decrease and hypercapnia increase in cerebral blood flow and rSO<sub>2</sub>, so one of the common interventions was normalization of hypocapnia or increasing of PaCO<sub>2</sub> to higher normal values. rSO<sub>2</sub> desaturation associated with hematocrit reduction to  $< 22\%$  was the indication for transfusion. We undertook certain steps (preload and afterload management, inotropes) to increase cardiac output or to increase pump flow rate to correct rSO<sub>2</sub> desaturation. We avoided hyperthermia after rewar-

ming during cardiopulmonary bypass because it would be associated with increase in cerebral metabolic rate of oxygen (CMRO<sub>2</sub>) and with rSO<sub>2</sub> reduction. The rewarming rate during cardiopulmonary bypass was slow, and it took approximately half an hour. One of the measures to improve rSO<sub>2</sub> was deepening of anesthesia to reduce CMRO<sub>2</sub>.

The order of performed interventions was at the anesthesiologist's discretion according to estimation of decline degree of each parameter from acceptable range. Usually the parameter with the worst decline from normal was first modified.

After the surgery, areas under the curve (AUC) were calculated for desaturations; more than 20% of baseline value (rSO<sub>2</sub> AUC<20% baseline), more than 50% (rSO<sub>2</sub> AUC<50% absolute) and more than 40% of absolute value (rSO<sub>2</sub> AUC<40% absolute). Areas under the curve account for both depth and duration of desaturation below these thresholds so they are expressed as min% values. We divided patients for analysis in two subgroups: 1. without prolonged cerebral desaturation; 2. with prolonged cerebral desaturation. Prolonged desaturation was defined as rSO<sub>2</sub> AUC<20% baseline of more than 150 min% or rSO<sub>2</sub> AUC<50% absolute of more than 50 min%, based on the Murkin<sup>12</sup> and Slater<sup>14</sup> studies. The data were analyzed to determine whether there were major differences in outcome of both groups.

#### Postoperative management and patients' outcome

During postoperative period all complications were recorded. ECGs were obtained before CABG, immediately after arrival in ICU and each postoperative day in ICU. Patients were monitored by telemetry during their postoperative hospital stay and the incidence of new atrial fibrillation from ICU admission until hospital discharge was recorded. Troponin T levels were measured immediately after surgery and on the first and second postoperative day. The presence of neurological deficit such as coma, stupor, stroke or delirium was observed<sup>17</sup>. Coma is defined as a profound state of unconsciousness without response to verbal call, pain or any other stimulus. Stupor is defined as a state of unconsciousness from which patient can be aroused only by vigorous physical stimulation. Stroke is defined as a syndrome characterized by the acute onset of a neurologic deficit that persists for at least 24 hours and reflects focal involvement of the central nervous system. Delirium or encephalopathy is characterized by confusion, agitation, disorientation, decreased alertness, sleep disturbances, memory deficit or seizure but without an obvious focal neurological deficit.

Ventilatory time was recorded in hours from the admission to ICU until the moment of extubation. Respiratory insufficiency is defined as a need for prolonged mechanical ventilation for more than 48 hours. Infection is defined as a clinically manifested and microbiologically confirmed infection which required antibiotics therapy. Patients who developed acute renal insufficiency and needed dialysis treatment were detected. The length of stay in the ICU was defined as time from ICU arrival un-

til transfer to the floor. Before transfer, patients had to be extubated with stable vital signs and without any inotropic support. Patients in our institution usually spend up to seven days in the hospital after surgery. The need for prolonged hospitalization of more than seven days was recorded. Criteria for discharge included stable cardiac rhythm, temperature < 37 °C, a well healed incision, and oxygen saturation >90 % on the room air.

Logistic value of EuroSCORE was calculated for all patients. EuroSCORE is a simple, objective and up-to-date scoring system for assessment of heart surgery, based on one of the largest, most complete and accurate databases in European cardiac surgery<sup>18</sup>.

SAPS II (Simplified Acute Physiology Score) values were calculated in the moment of entrance and discharge from ICU. SAPS II is a severity of disease classification system for patients admitted to intensive care units<sup>19</sup>.

All patients older than 65 years and diabetic patients older than 60 years were routinely preoperatively screened for evidence of carotid artery disease.

#### Statistical analysis

Descriptive statistics were calculated for all analyzed variables. Continuous data are presented as mean±standard deviation ( $\bar{X}\pm SD$ ). Categorical variables are presented as frequencies numbers and percentages. For all analysis type I error of 5% was considered statistically significant. Categorical data were analyzed using the  $\chi^2$ -test or Fisher's exact test. For continuous variables, comparison between groups was performed using a t-test or non parametric Mann-Whitney U test as appropriate. Multivariate (stepwise procedure) logistic regression was used to reveal predictors of prolonged rSO<sub>2</sub> desaturation. All statistical analyses were performed using Statistica 7.1 and SAS 8.2 software.

#### Results

The pattern of rSO<sub>2</sub> changes during the operation was similar. During the period before CPB, rSO<sub>2</sub> desaturation rarely occurred. Most cases of desaturation were observed during CPB; immediately after initiation of CPB, after aortic cross-clamp and releasing of the clamp and during rewarming. After the termination of CPB, rSO<sub>2</sub> usually increased to preoperative values.

18 out of 58 patients had prolonged rSO<sub>2</sub> desaturation during procedure. Considering preoperative data, it is important to notice that there were significantly more patients with diabetes mellitus (p=0.02) in group with prolonged desaturation (Table 1). Patients in desaturation group were older (Figure 1) and had higher EuroSCORE values but this was not statistically significant.

The analyses of intraoperative parameters show that the use of blood during CPB (p=0.007) and the need for inotropes (p=0.04) were significantly higher in desaturation group (Table 2).

Although baseline rSO<sub>2</sub> values were lower in desaturation group, that parameter has not reached statisti-

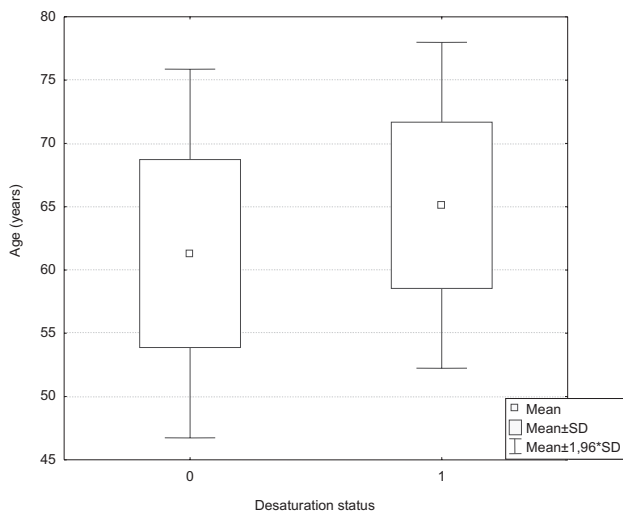


Fig. 1. Desaturation status and age. Desaturation status: 0 – without prolonged desaturation, 1 – with prolonged desaturation. Prolonged desaturation – rSO<sub>2</sub> AUC<20% baseline of more than 150 min% or rSO<sub>2</sub> AUC<50% absolute of more than 50 min.

cal significance, but the lowest values of rSO<sub>2</sub> during operation were significantly deeper in desaturation group (p<0.001). The number of interventions was significantly

higher in desaturation group (p<0.001) as it was the number of patients who got blood transfusion (p<0.001) to maintain adequate rSO<sub>2</sub> (Table 2).

Stroke, coma or stupor was recognized in three patients in rSO<sub>2</sub> desaturation group but no one in another group, which has reached statistical significance (p=0.03). There was no statistically significant difference in the incidence of delirium between groups (Table 3).

The duration of ICU staying was not statistically different between groups. The percentage of patients who needed hospitalization for more than seven days after the surgery was higher in desaturation group (67 vs. 42%) but this wasn't statistically significant (p=0.09).

In multivariate logistic regression model independent preoperative variables were age, sex, diabetes, hypertension, EuroSCORE, ejection fraction, and perioperative variables CPB time, ACC time, baseline rSO<sub>2</sub> and ICU staying, Dichotomous variable – prolonged rSO<sub>2</sub> desaturation was dependent variable. In the multivariate logistic regression model with the use of stepwise procedure the variables – age (p=0.04) with odds ratio (OR)=1.10 (95% confidence interval [95%CI];1.004–1.200) and diabetes mellitus (p=0.02) with OR=5.07 (95%CI;1.37–18.82) were recognized as statistically significant predictors of prolonged rSO<sub>2</sub> desaturation during coronary artery bypass grafting.

TABLE 1  
PATIENTS' CHARACTERISTICS AND PREOPERATIVE DATA

Parameter	Without prolonged desaturation* N=40	With prolonged desaturation* N=18	p-value Odds ratio (95%CI)
Age – years	61.3±7.4	65.1±6.6	p=0.07 OR=1.10 (1.004–1.20)
Female sex	8 (20)	6 (33)	p=0.32
EuroSCORE – %	2.0±1.6	2.6±2.3	p=0.27
EF – %	56±10	56±10	p=0.94
Comorbidity			
Diabetes mellitus	8 (20)	9 (50)	p=0.02** OR=5.07 (1.37–18.82)
Hypertension	33 (83)	12 (67)	p=0.2
IM < 1 month	4 (10)	0	p=0.3
COPB	4 (10)	3 (17)	p=0.67
Atrial fibrillation	2 (5)	1 (5)	p=1.0
Current smoker	10 (25)	5 (28)	p=1.0
History of smoking	14 (35)	3 (17)	p=0.16
Medications			
β-blockers	37 (92)	15 (83)	p=0.36
ACE inhibitors	30 (75)	12 (67)	p=0.2
Calcium channel blockers	13 (32)	5 (28)	p=0.72
Antilipemics	34 (85)	15 (83)	p=1.0

Data are expressed as frequencies numbers (%) or X±SD (mean±standard deviation)

OR – odds ratio, 95%CI – 95% confidence interval

\* prolonged desaturation – rSO<sub>2</sub> AUC<20% baseline of more than 150 min% or rSO<sub>2</sub> AUC<50% absolute of more than 50 min%

\*\* statistically significant value

EF – ejection fraction, IM < 1 month – myocardial infarction within 1 month, COPB – chronic obstructive pulmonary disease

**TABLE 2**  
INTRAOPERATIVE PARAMETERS

Parameter	Without prolonged desaturation* N=40	With prolonged desaturation* N=18	p-value
Number of grafts	2.4±0.6	2.5±0.5	p=0.97
CPB time – min	90±36	97±27	p=0.46
ACC time – min	62±24	68±21	p=0.35
Duration of operation – min	306±69	319±52	p=0.46
CI before CPB – L/min/m <sup>2</sup>	2.4±0.4	2.4±0.3	p=0.13
CI after CPB – L/min/m <sup>2</sup>	2.8±0.6	2.8±0.5	p=0.85
Single clamp – number of patients	33 (83)	17 (94)	p=0.42
Blood during CPB – ml	216±254	493±380	p=0.007**
Blood after CPB – ml	128±211	178±201	p=0.39
Inotropes – number of patients	15 (37)	12 (67)	p=0.04**
Baseline rSO <sub>2</sub> left – %	74±6	70±9	p=0.11
Baseline rSO <sub>2</sub> right – %	72±7	69±9	p=0.12
The lowest rSO <sub>2</sub> – %	51.9±7	42.5±7	p<0.001**
Desaturation AUC – min%			
rSO <sub>2</sub> AUC<20% baseline	42±42	617±997	p<0.001**
rSO <sub>2</sub> AUC<50% absolute	5±11	150±202	p<0.001**
rSO <sub>2</sub> AUC<40% absolute	0	13±29	p<0.001**
Number of interventions	4.4±5.4	8.8±5.6	p<0.001**
Blood transfusion as an intervention – number of patients	8 (20)	13 (72)	p<0.001**

Data are expressed as frequencies numbers (%) or X±SD (mean±standard deviation)

\* prolonged desaturation – rSO<sub>2</sub> AUC<20% baseline of more than 150 min% or rSO<sub>2</sub> AUC<50% absolute of more than 50 min%

\*\* statistically significant values

CPB – cardiopulmonary bypass, ACC time – aortic cross-clamping time, CI – cardiac index, rSO<sub>2</sub> – regional cerebral oxygen saturation, AUC – area under the curve

## Discussion and Conclusion

In this study we observed the consequences of cerebral oxygen desaturation measured by INVOS system during coronary bypass graft surgery. We introduced INVOS 5100 (Somnastics, Troy, USA) monitoring in our cardiac anesthesia department in 2009. All interventions undertaken to maintain cerebral oxygenation above threshold of 20% under the baseline value were in the range of good clinical practice. In some cases, despite very strict approach in desaturation treatment, there was no improvement in rSO<sub>2</sub> values.

Preoperative data revealed age as important predictor of prolonged rSO<sub>2</sub> desaturation. Age is earlier identified as a major risk factor for neurologic impairment after cardiac surgery because of aberrations in cerebral autoregulation associated with reduced cerebral blood flow<sup>20,21</sup>.

According to results of current study diabetes mellitus is also strong predictor of prolonged rSO<sub>2</sub> desaturation during coronary artery bypass grafting and the prolonged rSO<sub>2</sub> desaturation is five times more common among patients with diabetes compared to patients without diabetes. Diabetes mellitus is well-known risk factor for the development of coronary artery occlusive disease,

but also one of the major predisposing factors for development of postoperative neurological impairment after coronary artery bypass graft surgery. Postoperative neurological deficits in patients with diabetes mellitus are considered to be related to the impairment of cerebral perfusion and autoregulation during cardiac surgery under cardiopulmonary bypass<sup>22–24</sup>. It is reported that CPB

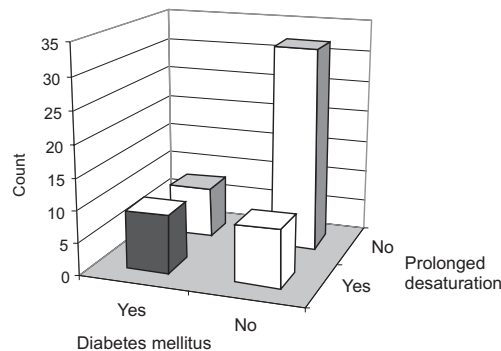


Fig. 2. Desaturation status and diabetes mellitus. Prolonged desaturation – rSO<sub>2</sub> AUC<20% baseline of more than 150 min% or rSO<sub>2</sub> AUC<50% absolute of more than 50 min%.

**TABLE 3**  
POSTOPERATIVE PARAMETERS

Parameter	Without prolonged desaturation* N=40	With prolonged desaturation* N=18	p-value
Blood in ICU – ml	205±269	182±284	p=0.78
CI – arrival in ICU – L/min/m <sup>2</sup>	2.9±0.6	2.9±0.6	p=0.96
CI – after 24 h – L/min/m <sup>2</sup>	3.1±0.5	3.2±0.5	p=0.45
Troponin T – arrival in ICU – ng/ml	0.46±0.3	0.92±0.9	p=0.07
Troponin T POD 1– ng/ml	1.17±1.1	1.08±0.9	p=0.76
Troponin T POD 2– ng/ml	0.63±0.8	0.63±0.4	p=0.46
Ventilatory time – hours	10.9±9.3	15.1±12.7	p=0.13
Postoperative complications – number of patients (%)			
Stroke, coma, stupor	0	3 (16)	p=0.03**
Delirium	4 (10)	5 (27)	p=0.11
Atrial fibrillation	5 (12)	6 (33)	p=0.08
Respiratory insufficiency	1 (2.5)	2 (11)	p=0.22
Dialysis	0	1	p=0.31
Infection	6 (15)	2 (11)	p=1.0
ICU length of stay – days	2±0.6	3.9±6.6	p=0.17
Hospital staying longer than 7 days – number of patients (%)	17 (42)	12 (67)	p=0.09
SAPS II – arrival in ICU	18.0±6.8	20.0±4.4	p=0.53
SAPS II – ICU discharge	10.5±4	12.4±4	p=0.11

Data are expressed as frequencies numbers (%) or X±SD (mean±standard deviation)

\* prolonged desaturation – rSO<sub>2</sub> AUC<20% baseline of more than 150 min% or rSO<sub>2</sub> AUC<50% absolute of more than 50 min%

\*\* statistically significant value

ICU – intensive care unit, CI – cardiac index, POD – postoperative day, SAPS – Simplified Acute Physiology Score

can alter the cerebral endothelial and nitric oxide function more extensively in diabetic patients than in non-diabetic patients. Cerebrovascular CO<sub>2</sub> reactivity, which is very important for cerebral flow autoregulation, can be reduced in diabetic patients with consecutive impairment in cerebral oxygenation<sup>25</sup>. Miyoshi et al. reported that diabetic patients experienced cerebral desaturation during CPB, assessed by jugular bulb oxygen saturation (SjvO<sub>2</sub>), more often than non-diabetic patients<sup>26</sup>. On the contrary, regarding off-pump coronary artery bypass grafting, Oh et al. reported that cerebral oxygenation in diabetic patients was similar to that of non-diabetic patients<sup>27</sup>.

Normal absolute value for rSO<sub>2</sub> has not been established but group mean rSO<sub>2</sub> value of 67±10 has been observed in conscious healthy volunteers and cardiac patients<sup>28</sup>. The degree of cerebral desaturation which can be followed by higher risk for postoperative complications is still not adopted. Yao et al. revealed that nadir rSO<sub>2</sub><35% or rSO<sub>2</sub>AUC<40% of more than 10 min% significantly increased the incidence of neuropsychological decline in patients undergoing cardiac surgery with cardiopulmonary bypass<sup>11</sup>. Slater et al. defined a prolonged rSO<sub>2</sub> desaturation as rSO<sub>2</sub> score greater than 50 min% below 50% saturation threshold<sup>14</sup>. These values of prolonged rSO<sub>2</sub> desaturation were associated with increased risk of neurocognitive decline. Murkin et al. showed that

patients having prolonged desaturation, defined as area under the curve (AUC) below 70% of baseline for more than 150 min%, tended to have more frequently major organ morbidity and mortality compared to patients without such prolonged desaturation<sup>12</sup>. Based on these studies, we defined prolonged desaturation rSO<sub>2</sub> as an AUC of more than 150 min% under 20% of baseline value, or rSO<sub>2</sub> AUC of more than 50 min% under 50% of absolute value. 31% of our patients had prolonged rSO<sub>2</sub> desaturation despite of interventions undertaken to maintain rSO<sub>2</sub> above the threshold of 20% under the baseline value. Slater et al. in their prospective study randomized CABG patients monitored with INVOS to a blinded control group and unblinded intervention group<sup>14</sup>. They observed almost identical desaturation rates in both control (30%) and intervention group (26%) and explained the results as a poor compliance to the treatment protocol. On the contrary, Murkin et al. concluded that intervention protocol undertaken to return rSO<sub>2</sub> to baseline, in most cases resulted in a rapid improvement of rSO<sub>2</sub> without added risk to the patient. The overall success rate was about 80%<sup>12</sup>. Neither of these studies analyzed patients without appropriate response to interventions used to maintain rSO<sub>2</sub> in normal range.

The most frequent interventions (after repositioning the head or perfusion cannulae) to maintain rSO<sub>2</sub> in our

patients were increasing MAP and FiO<sub>2</sub>, increasing arterial CO<sub>2</sub> partial pressure – PaCO<sub>2</sub>, blood transfusion and increasing pump flow. There were significantly more interventions in desaturation group (p<0.001).

The results of our study show significantly higher incidence of blood transfusion as intervention to maintain cerebral saturation in desaturation group compared to another group. The blood transfusion was assumed as intervention only in case when cerebral desaturation was followed by decreasing of hematocrit value to less than 22%, so the indication for transfusion was in accordance with recommendations of good clinical practice. Murkin et al. concluded in their study that patients undergoing cerebral oximetry were not at increased risk of receiving blood transfusion as a consequence of monitoring rSO<sub>2</sub>, because there was no difference in blood transfusion rates between intervention and control INVOS group<sup>12</sup>. Torella et al. proposed that NIRS could be used as a monitor of blood loss and they observed good correlation between blood loss and NIRS parameters<sup>29</sup>.

In our study there were significantly more patients in desaturation group who needed inotropic support (p=0.04), although »inotropes« were relatively seldom used as intervention to maintain rSO<sub>2</sub>. Inotropic support was more related to hemodynamic parameters (cardiac index less than 2 L/min/m<sup>2</sup>) and data obtained with transesophageal echocardiography (contractility, ejection fraction). This finding is in correlation with higher values of troponin T after admission in ICU in desaturation group, although statistical significance is not achieved (p=0.07). The results suggest that cerebral desaturation may be in relation with impaired cardiac function. There are only few studies about relationship between brain oximetry and cardiac function<sup>30,31</sup>.

The incidence of coma, stupor and stroke in our study was significantly higher in desaturation group (p=0.03). This findings confirm the results of previous studies about significant association of cerebral desaturation with adverse neurological outcome. Goldman et al. demonstrated a decrease in the stroke rate in cardiac surgical patients after implementation of cerebral oximetry but

they didn't verify if patients in rSO<sub>2</sub> monitored group who developed stroke, had or had not prolonged desaturation<sup>10</sup>.

Statistical significance between groups for other postoperative complications was not detected in the circumstances of our study.

Interventions carried out during the use of cerebral oximetry in most patients resolved decrease in rSO<sub>2</sub>, but in some patients there was no success and prolonged desaturation occurred. We presume that those patients have some problems with cerebral vascular autoregulation and may deserve more attention during surgery and early postoperative period.

Some of limitations of this study are small sample size and the fact that there was a lack of rSO<sub>2</sub> monitoring during early postoperative period when cerebral desaturation and some of complications can occur. Nevertheless, patients were treated according to same standard protocol during the postoperative period.

In conclusion, although monitoring of cerebral oxygenation gives us possibility to maintain balance in oxygen supply and demand for the purpose of patients' clinical benefit, we observed some patients who didn't respond to our interventions. The consecutive prolonged rSO<sub>2</sub> desaturation in our study was associated with higher incidence of neurological complications. The question is how to manage those patients. There is no data about those patients in literature and about difference in outcome between »responders« and »nonresponders« to interventions undertaken to prevent prolonged desaturation. We hope that our study will prompt other researchers to carefully analyze data based on larger number of patients – nonresponders to interventions for maintenance of rSO<sub>2</sub>.

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## UTJECAJ DUGOTRAJNE CEREBRALNE DESATURACIJE KISIKOM NA POSLIJEOPERACIJSKI ISHOD KOD BOLESNIKA PODVRGNUTIH KIRURŠKOJ REVASKULARIZACIJI MIOKARDA

### SAŽETAK

58 bolesnika podvrgnutih kirurškoj revaskularizaciji miokarda uz upotrebu kardiopulmonalnog bypassa, praćeno je bliskom infracrvenom spektroskopijom (near infrared spectroscopy- NIRS) glede promjena u regionalnoj cerebralnoj saturaciji kisikom ( $rSO_2$ ). U slučaju pada  $rSO_2$  tijekom operacije za više od 20% od bolesnikove bazalne vrijednosti, poduzete su standardizirane intervencije radi održavanja  $rSO_2$ . Usprkos tim intervencijama, kod nekih bolesnika smo primijetili nemogućnost održavanja  $rSO_2$  iznad te granične vrijednosti. Bolesnike smo stoga radi analize podataka podijelili u dvije grupe: 1. bez dugotrajne  $rSO_2$  desaturacije; 2. s dugotrajnom  $rSO_2$  desaturacijom (površina ispod krivulje >150 min% za  $rSO_2 < 20\%$  od bazalne vrijednosti te >50 min% za  $rSO_2 < 50\%$  apsolutne vrijednosti). Podaci su analizirani da bi se utvrdilo da li postoje značajne razlike u konačnom ishodu ovih dviju grupa. 18 od ukupno 58 bolesnika (31%) imalo je dugotrajnu  $rSO_2$  desaturaciju za vrijeme operacije. U grupi bolesnika sa dugotrajnom  $rSO_2$  desaturacijom utvrđen je značajno veći broj onih koji boluju od dijabetesa ( $p=0,02$ ). Ujedno, u grupi bolesnika sa dugotrajnom  $rSO_2$  desaturacijom, podaci vezani uz operaciju pokazuju značajno veću potrošnju krvi tijekom kardiopulmonalnog bypassa ( $p=0,007$ ) i veću potrebu za inotropnom terapijom ( $p=0,04$ ). Tri su bolesnika iz navedene grupe imala moždani udar, komu ili stupor, dok u drugoj grupi niti jedan ( $p=0,03$ ). Analizom podataka metodom logističke regresije utvrđeno je da su dijabetes i godine starosti značajni prediktori za dugotrajnu  $rSO_2$  desaturaciju. Zaključili smo da je dugotrajna  $rSO_2$  desaturacija tijekom operacije povezana sa značajno lošijim neurološkim ishodom kod bolesnika kod kojih primjena standardiziranih postupaka nije dovela do mogućnosti održavanja  $rSO_2$  iznad spomenutih vrijednosti.