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Effects of Cerebral Oxygen Desaturation during One Lung Ventilation on Postoperative Cognitive Function as assessed by Cerebral Oximetry: a Prospective, Observational Study

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Abstract

Purpose: In thoracic surgery, there are many physiologic disturbances that affect tissue oxygenation and cause cerebral desaturation. The causes of cerebral desaturation are more related to perioperative hypoxemia than hemodynamic deterioration. The aim of our study is to evaluate the effects of cerebral oxygen desaturation during one-lung ventilation, on the postoperative early and late period cognitive functions.

Methods: Regional cerebral tissue oxygen saturation ($SctO_2$) was continuously monitored intraoperatively using near-infrared spectroscopy (NIRS) starting before anesthesia induction until extubation on 83 consecutive patients undergoing thoracic surgery with one-lung ventilation (OLV) in this prospective, observational study.

The mini–mental state examination (MMSE) was performed before surgery to exclude the preoperative sub clinical dementia or cognitive dysfunction. Cognitive function was assessed post operatively, in prior to discharge and at one month using a battery of standardized neurocognitive tests. We used the test battery which included Trail Making Test A and B, Digit Span Test, Stroop Test to evaluate cognitive decline.

Cerebral desaturation events (CDE) was accepted as 20% or greater decrease from baseline saturation that was measured while the patient was in room air. The association between intraoperative CDE and postoperative cognitive decline was estimated.

Results: Our study showed significant impairments in postoperative early and late period Trail Making Tests' and Stroop Tests' performances in desaturation group patients, whereas desaturation and non-desaturation groups' test performance trends showed improvement at 1 month.

Conclusion : Cerebral desaturation events have an adverse impact on postoperative cognitive function. This adverse effect has declined over time but has continued till the end of the first postoperative month. Prolonged desaturation periods results in a more deterioration of cognitive function. Thus, cerebral desaturations should be prevented and treated. Cerebral oximetry guided therapy may reduce postoperative cognitive dysfunction while increasing the quality of life.

Keywords: Thoracic surgery; One lung ventilation; Cerebral desaturation; Neurocognitive decline

Introduction

Monitoring of cerebral oxygen saturation has become increasingly important in cardiac and non-cardiac surgery. Studies in cardiac surgery have shown that treating cerebral oxygen desaturations can improve postoperative cognitive function and reduce complications [1]. Besides the studies in cardiac surgery, there are studies showing a significant incidence of cerebral oxygen desaturations in non-cardiac surgery, such as neurosurgery, carotid surgery, general surgery and thoracic surgery [2].

In thoracic surgery, there are many physiologic disturbances that affect tissue oxygenation and cause cerebral desaturation. The causes of cerebral desaturation are more related to perioperative hypoxemia than hemodynamic deterioration. Proposed physiologic disturbances for cerebral desaturation focus on perioperative hypoxemia due to the effects of one-lung ventilation (OLV) [3]. There is only one study published which investigated early cognitive function after thoracic surgery [4]. But in this study [4] determination of cognitive function after thoracic surgery is evaluated by only one cognitive function test (Mini-Mental Status Exam) and reliability of the study is subdued. Cerebral oxygen desaturations increase the risk of the poor postoperative outcome in patients undergoing thoracic surgery with OLV [5,6]. Hence, more studies indicating the impacts of the cerebral desaturation on the cognitive dysfunctions during the late period after thoracic surgery are lacking [7].

The Mini-Mental Status Exam (MMSE) can be used to identify preoperative subclinical dementia that would be a risk factor for developing postoperative cognitive dysfunction (POCD). Trail making test A and B, Digit Span test, and Stroop test are psychometric tests verifying diagnosis of POCD in a consensus recommendation on POCD issued in 1995 to assess cognitive performance in patients [8]. Trail Making Tests measure sequencing ability, psychomotor speed, complex attention, visual scanning and mental flexibility [9]. Stroop test measures the selective attention and response inhibition [10]. Digit span test is a widely used neuropsychological measure, known as a test of attention and working memory [11].

The aim of our study is to evaluate the effects of cerebral oxygen desaturations detected by using cerebral oximetry during one-lung ventilation, on the postoperative early and late period cognitive functions.

Materials and Methods

Study population

The study was confirmed and approved (Ethical Committee N° 09.2013.0279) by the Ethical Committee of Marmara University School of Medicine, Istanbul, Turkey (Chairperson Prof H. Direskeneli) on 01 November 2013. The study protocol complies with the Declaration of Helsinki.

Study subjects were recruited from consecutive 83 patients who gave a written informed consent, aged 18 years or greater, undergoing elective thoracic surgery with OLV of an expected duration of more than 45 min. Patients who had previous cerebral disease, dementia, severe problems in hearing and understanding, or who were unable to provide informed consent, were excluded.

Cerebral oximetry

Adverse cerebral outcomes remain a continued problem in patients undergoing surgical procedures. Cerebral oximetry using near-infrared spectroscopy (NIRS) is a continuous, noninvasive monitor in perioperative settings [12]. Using similar principles as pulse oximetry, a light source generates the near-infrared beams which pass through the tissues and are detected by optodes placed a short distance away from the source. The differential absorption of these beams by oxygenated and deoxygenated hemoglobin determines the brain tissue saturation [13].

Slater et al. noted that an absolute value of 50% regional cerebral oxygen saturation was required before any adverse effect was observed in a cardiac surgery patient by using cerebral oximetry [14].

In a similar study, Samra et al. [15] showed that a 20% relative decrease from baseline regional cerebral oxygen saturation have a sensitivity of 80% and a specificity of 82% to determine a threshold rSO_2 value for neurological dysfunction in patients undergoing awake carotid endarterectomy.

Clinical management

After venous line placement and before general anesthesia, an epidural catheter was inserted at T4-5 or T5-6 level for postoperative analgesia. Anesthesia was induced with propofol 2-2.5 mg kg^{-1}, fentanyl 1-2 µg kg^{-1} and rocuronium 0.5 mg kg^{-1}. For further muscle relaxation rocuronium 0.25 mg kg^{-1} was applied as clinically required. A radial arterial cannula was placed for continuous arterial pressure. A left or right sided double-lumen tube was inserted with bronchoscopic guidance. Anesthesia was provided using sevoflurane (0.8–1.5 MAC) and FiO_2 0.40. The ventilator parameters consisted of volume control mode, PEEP 5 cm H_2O, Peak pressure less than 30 cm H_2O, tidal volume 6-8 ml kg^{-1}, at a rate of breath min^{-1} that maintaining $EtCO_2$ 30–35 mm Hg. The FiO_2 was set 1.0 during one-lung ventilation. When the peripheral oxygen saturation decreased below 90%, insufflation of 2-4 lt dk^{-1} oxygen was applied to the dependent lung. If the peripheral saturation didn't improve, one lung ventilation was terminated and switched two lung ventilation, and these patients were excluded from the analysis. Also, patients who had perioperative unstable hemodynamics, who were administered inotropic therapy and who were postoperatively discharged to the intensive care unit were excluded. Standard monitoring variables such as peripheral oxygen saturation, mean arterial pressure (MAP), and heart rate were recorded every 5 min. For surgery, the patient was placed on the left or the right lateral decubitus position.

Cerebral oximetry monitoring

The cerebral oximeter sensors were applied to the forehead, and cerebral oxygen saturation ($SctO_2$) was monitored continuously using the INVOS 5100C (Covidien, CO, USA) cerebral oximeter starting before anesthesia induction until extubation. Baseline $SctO_2$ values were taken in room air when the patient was awake and also after 2 mins of breathing 100% oxygen through a face mask. Cerebral oxygen desaturation was accepted as 20% decrease from baseline saturation that was measured while the patient was in room air. In addition, from the intraoperative cerebral oximetry data, patients dropping below the value of 50% saturation threshold were reevaluated. At the end of surgery, duration of one lung ventilation was recorded.

Cognitive assessment

The mini–mental state examination (MMSE) was performed before surgery to exclude the preoperative subclinical dementia or cognitive dysfunction. Patient, who had MMSE score ≤ 25, were excluded. After surgery, a battery of standardized neurocognitive tests was performed prior to patient's discharge and at one month follow up to assess postoperative cognitive function by a resident who was not aware of intraoperative oximetry values. The test battery included Trail Making Test A and B, Digit Span Test, Stroop Test. We intend to measure sequencing ability, psychomotor speed, complex attention, visual scanning and mental flexibility with Trail Making Tests; the selective attention, response inhibition with Stroop test and attention, working memory with Digit span test. Different preoperative and postoperative tests were used in this study to prevent learning effect.

Statistical analysis

Datasets were analyzed using the SPSS ver. 21.0 statistical software (SPSS Inc., USA). Data were analyzed using descriptive statistical methods (frequency, percentage, mean, standard deviation) as well as to examine the normal distribution of Kolmogorov - Smirnov test was used for distribution. Demographic and clinical factors are expressed in percentages and median. In the comparison of qualitative data, Pearson's chi-square test or the Fisher exact test was used. Between the groups comparison of quantitative data, Mann-Whitney U test, was used. Pearson correlation analysis, to determine the relationships between measurements, was used within the Group. Results at 95% confidence interval, $p<0.05$ level of significance $p<0.01$ and $p<0.001$ significance level in advanced was assessed.

Results

Eighty-three patients were enrolled in the study between November 2013 and May 2014 in Marmara University Hospital, İstanbul, Turkey but 12 of those patients had to be excluded, and data of 71 patients were analyzed. Three patients were excluded due to the need for an ICU stay that may increase the risk of developing POCD. Two patients were excluded due to desaturations while induction before starting OLV; also, four patients due to failing test follow-up, two patients due to massive bleeding resulting hemodynamic instability and one patient due to the need for inotropic support were excluded from the analysis.

During our study of 71 patients undergoing thoracic surgery, 35%(n:25) patients had a reduction in cerebral oxygen saturation more than 20% from their preoperative baseline values and 38% (n:27) patients' cerebral oxygen saturations dropped below the value of 50%.

The desaturation and non-desaturation groups were found to be similar in gender, age, education of patients, and duration of OLV, (p>0,05). Average cerebral oxygen saturation was lower (p<0,001) in desaturation group than in non-desaturation group (Table 1).

Desaturation group patients had significant impairments in early and late period Trail Making Tests' and Stroop Tests' performances, whereas desaturation and non-desaturation groups' test performance trends showed improvement at 1 month (Table 2).

	Non-desaturation Group (n=46)		Desaturation Group (n=25)			
	n	%	n	%	X^2	P value
Gender						
Male	29	66%	15	34%	0,064	0,804
Female	17	63%	10	37%		
Operated lung side						
Right	26	58%	13	52%	0,217	0,641
Left	19	42%	12	48%		
Education						
Primary School	20	44%	16	64%	5,561	0,135
Secondary School	6	13%	4	16%		
High School	5	11%	3	12%		
University	15	33%	2	8%		
	Mean	**SD**	**Mean**	**SD**	**MW**	**P value**
Age	52,3	11,7	55,1	10,7	478,5	0,245
Average $SctO_2$	68,7	6,7	59,3	9	227	**0,000*** **
Duration of OLV (min)	184,9	89,7	195,6	87,6	533	0,613

Table 1: Comparison between the Desaturation and Non-desaturation Group Based on Demographic and Clinical Factors
*p<0,05
**p<0,01
***p<0,001
n: number; SD: Standard deviation; MW: Mann Whitney U Test; X^2: Chi-Square Test; $SctO_2$: Cerebral oxygen saturation; OLV: One lung ventilation

Time Point	Cognitive Tests	Baseline $SctO_2$ decrease ≤ 20% (n=46)		Baseline $SctO_2$ decrease ≥ 20% (n=25)		P value
		Mean	SD	Mean	SD	
Prior to discharge	TMT Score (second)	62,590	36,416	98,120	78,315	**0,046***
	Forward DST Score	5,54	1,048	5,16	0,898	0,160
	Backward DST Score	3,39	0,954	3,24	0,831	0,663
	ST Score (second)	66,82	28,162	70,76	36,995	0,763
	ST Wrong Word count	1,52	2,248	3,36	3,796	**0,010***
At one month	TMT Score (second)	38,870	25,867	72,960	64,908	**0,025***
	Forward DST Score	5,96	0,893	5,56	1,044	0,195
	Backward DST Score	3,89	0,795	3,64	1,075	0,177
	ST Score (second)	43,50	18,885	65,92	58,001	0,250
	ST Wrong Word count	0,67	1,230	1,64	2,841	0,194

Table 2: Postoperative Test Results prior to discharge and at one month in groups dividing by 20% decreases from the Baseline Cerebral Oxygen Saturation
*p<0,05
**p<0,01
***p<0,001
n: number; SD: Standard deviation; $SctO_2$: Cerebral oxygen saturation; TMT: Trail making test; DST: Digit span test; ST: Stroop test

In desaturation Group, prolonged OLV and duration of desaturation below the 50% threshold had a correlation (p<0,05) with deterioration of cognitive test performance (Table 3).

After reevaluation of data, patients whose cerebral oxygen saturations were dropping below the value of 50%, had significant impairments in postoperative early and late period Trail Making Tests' and Stroop Tests' performances as patients who experienced cerebral desaturation that was accepted as 20% decrease from baseline cerebral oxygen saturation (Table 4).

The relationship of two different desaturation criteria with postoperative cognitive functions were similar.

In non-desaturation group, the relationship between age and Trail Making test performance is that patients who were older had poorer test

		Desaturation Group (n=25)	
		Duration of $SctO_2 \leq 50$	Duration of OLV
TMT score (second)	r	0,338	0,408
	p	0,098	**0,043***
Forward DST score	r	-0,25	-0,143
	p	0,229	0,497
Backward DST score	r	-0,404	-0,492
	p	**0,045***	**0,013***
ST score (second)	r	0,339	0,472
	p	0,098	**0,017***
ST Wrong Word Counts	r	0,481	0,421
	p	**0,015***	**0,036***

Table 3: Correlation Analyses of prolonged OLV and duration of desaturation below the 50% threshold between cognitive test performances in desaturation group.
*p<0,05
**p<0,01
***p<0,001
n: number; $SctO_2$: Cerebral oxygen saturation; OLV: One lung ventilation; TMT: Trail making test; DST: Digit span test; ST: Stroop test; r: Correlation coefficient; p: p-value

Time Point	Cognitive Tests	$SctO_2 \geq 50\%$ (n=44)		$SctO_2 \leq 50\%$ (n=27)		P value
		Mean	SD	Mean	SD	
Prior to discharge	TMT Score (second)	58	32,186	102,96	75,69	**0,004****
	Forward DST Score	5,57	1,087	5,15	0,818	0,156
	Backward DST Score	3,43	0,925	3,19	0,879	0,405
	ST Score (second)	66,36	29,097	70,3	35,189	0,781
	ST Wrong Word count	1,57	2,286	3,15	3,728	**0,026***
At one month	TMT Score (second)	36,32	23,418	74,59	62,62	**0,004****
	Forward DST Score	5,98	0,927	5,56	0,974	0,177
	Backward DST Score	3,98	0,792	3,52	1,014	**0,013***
	ST Score (second)	43,77	20,029	63,81	55,802	0,311
	ST Wrong Word count	0,61	1,205	1,67	2,746	0,063

Table 4: Postoperative Test Results prior to discharge and at one month in groups dividing by the value of 50% Cerebral Oxygen Saturation
*p<0,05
**p<0,01
***p<0,001
n: number; SD: standard deviation; $SctO_2$: Cerebral oxygen saturation;TMT: Trail making test; DST: Digit span test; ST: Stroop test

		Non-Desaturation Group (n=46)	
		Age	Education
TMT score (second)	r	0,366	-0,098
	p	**0,012***	0,517
Forward DST score	r	0,116	0,447
	p	0,442	**0,002****
Backward DST score	r	0,239	0,491
	p	0,110	**0,001****
ST score (second)	r	-0,140	-0,143
	p	0,353	0,343
ST Wrong Word Counts	r	-0,022	-0,322
	p	0,884	**0,029***

Table 5: Correlation Analyses of age and educational levels between cognitive test performances in non-desaturation group. *p<0,05
**p<0,01
***p<0,001
n: number; TMT: Trail making test; DST: Digit span test; ST: Stroop test; r: Correlation coefficient; p: p-value

performance. Differences in educational levels of the patients influenced Digit Span Test, Stroop Test performances (Table 5). We couldn't see similar relations in desaturation group because effect of desaturation on each patient is different.

Discussion

Our study showed significant impairments in postoperative early and late period Trail Making Tests' and Stroop Tests' performances in desaturation group patients, whereas desaturation and non-desaturation groups' test performance trends showed improvement at 1 month.

Patients, who underwent thoracic surgery with OLV, showed a reduction in cerebral oxygen saturation. All cerebral desaturation events happened when peripheral oxygen saturation was above 90%, and patients whom peripheral oxygen saturation was below the hypoxic limit of 90% were excluded from our study. The main result of our study was cerebral desaturations during OLV correlated with deterioration in cognitive test performances.

Significant physiological disturbances accompany OLV as a result of hypoxemia, such as decreasing arterial oxygen saturation, changing cardiac output and activation of inflammatory processes [16]. Prolonged OLV leads to severe oxidative stress and free radical generation [17]. During OLV, hypoxemia episodes trigger proinflammatory cytokines that (are associated with) effect neurotransmitter system, indicating a relation between the inflammatory process and neurocognitive performances [18,19]. Likewise our study showed that prolonged OLV resulting in increased duration of hypoxic episodes had a correlation with deterioration of cognitive test performance in desaturation group.

Studies in cardiac and non-cardiac surgery have shown a relation between cerebral oxygen desaturation and cognitive dysfunction [20].

The incidence of POCD after noncardiac surgery at one week is defined 19-41% in patients older than 18-year-old [21]. The incidence of postoperative cognitive dysfunction for thoracic surgery is still unknown and often underestimated [18]. Patients may experience POCD that reduce the quality of life after surgery. There is no currently adequate treatment for POCD, but risk factors should be identified and eliminated. Intraoperative monitoring of cerebral oxygen saturation can be useful to detect and prevent cerebral desaturations and possibly POCD [18].

In thoracic surgery during OLV the incidences of cerebral oxygen desaturation that is 20% decreases from baseline saturation were resulted 57% [5], 56% [4], 70% [6], 27% [22] and showed diversity in the studies. The variety of incidence depends on different evaluation of baseline cerebral oxygen saturation that leads to the need for a change in the definition of cerebral desaturation. In our study, baseline cerebral oxygen saturation was evaluated before anesthesia induction in room air, and thirty-five percent of the patients had cerebral oxygen desaturation.

Tang et al. [5], and Kazan et al. [4] were estimated baseline cerebral oxygen saturation after 2 mins of breathing 100% oxygen through a face mask in the patients who were awake in their studies. In another study, Hemmerling et al. [6] evaluated baseline cerebral saturation as highest cerebral oxygen saturation value before OLV. Brinkman et al. [22] estimated baseline cerebral saturation as highest cerebral oxygen saturation value during two lung ventilation.

Brinkman et al. [22] were recorded cerebral oxygen saturation of patients in room air before induction, after induction , during two lung ventilation, and one lung ventilation. Prior to induction value of cerebral oxygen saturation, showed 13% increase after induction during two lung ventilation and the decreases starting after one lung ventilation. After induction or 2 min s of breathing 100% oxygen through a face mask increased the value of baseline cerebral oxygen saturation and 20% decreases from the increased value of baseline saturation didn't reflect correct desaturation events. Thus, incidence of desaturation was high. In these studies, the incidences of desaturation were not considered clinically significant, adding an important limitation to the studies. So, we need more studies demonstrating real desaturation events and the frequency of desaturation events to determine the clinical outcomes' correlation with desaturation periods [7].

In our study, baseline cerebral oxygen saturation was taken when the patient was in room air, because patients' cognitive functions were considered normal at baseline cerebral oxygen saturation. We tried to demonstrate the real desaturation incidences and the relation with deterioration of cognitive functions. Here baseline cerebral oxygenation values were recorded when patients were awake in room air, and also after 2 minutes of breathing 100% oxygen through a face mask to see if there is a difference in intraoperative cerebral desaturation. When the baseline cerebral oxygenation taken after 2 minutes of breathing 100% oxygen was taken into account , we observed that extra six patients showed cerebral desaturations. But, analysis of patients whose baseline cerebral oxygenation were recorded after 2 minutes of breathing 100% oxygen, were not taken into account in our study.

A 20% relative decrease from baseline cerebral oxygen saturation occurred in patients who had a neurologic change and regional ischemia. This decrease was accepted as cut-off value with a resultant sensitivity and specificity of 80% [23,24]. But, there is no consensus about defining critical cerebral desaturation yet. In previous studies, cerebral desaturation has been defined by either decrease from a baseline or absolute threshold (i.e., dropping below 50% value of cerebral saturation) [7]. In our study cerebral oxygen desaturation was recorded as both 20% decreases from baseline saturation and dropping below the 50% saturation threshold that was measured from patient in room air to define which cerebral oxygen desaturation criteria was significant. According to our study results, thirty-five percent of the patients had a decrease of 20% from baseline values and thirty-eight percent of patients cerebral saturation were dropping below the value of 50%. Deteriorations of cognitive test performance (in Trail Making Test and Stroop Test) was found similar by using both cerebral desaturation criteria.

To date, most thoracic surgery studies [4-6,22] have emphasized cerebral desaturation, used the FORESIGHT cerebral oximeter that shows absolute value without trends. In our study, we used INVOS cerebral oximetry (Covidien, CO, USA) that can demonstrate decreases from baseline saturation value and evaluate the area under the curve, and also show absolute value.

Tang et al. [5] showed a relationship between the desaturation and cognitive dysfunction that was assessed only by MMSE. MMSE is the most widely used measure to screen for cognitive status in medical and neuropsychological research. But , using MMSE for retesting may lead to some of the questions being remembered by the participants and rehearsing the answers given previously. Also, prior to the retesting the person knows that a cognitive test will occur and be more alert [25]. The MMSE has been considered for determination of gross cognitive changes as in Alzheimer dementia and has been designed to be administered in a single session to give an estimation of absolute function. The test is inappropriate for assessing POCD as it was not designed to measure the changes in cognitive functions [26].

In our study, we preoperatively used MMSE to determine patients who had cognitive dysfunction or dementia and then to exclude them from the study. Postoperative four different tests, that was recommended by a consensus in 1995 [8], was used to evaluate cognitive function such as sequencing ability, psychomotor speed, complex attention, visual scanning, mental flexibility, the selective attention, response inhibition, working memory. We combined a test battery to provide a high level of sensitivity and increase the probability of detecting deterioration in cognitive function. Different preoperative and postoperative tests were used in this study to prevent learning effect.

In fact, using different tests pre- and postoperatively may be named as a limitation of our study. Although POCD is diagnosed by comparing pre- and postoperative findings on psychometric tests in the literature, there is no consensus how to define POCD [27]. According to our results, we couldn't confirm that the patients who had intraoperative cerebral desaturations had POCD, but we can say that cognitive functions deteriorated in desaturation group with respect to the non-desaturation group.

In desaturation group, patients had significant impairment on Trail Making Test and Stroop Test performances that measure frontal lobe psychomotor speed, complex and selective attention, visual scanning and mental flexibility, information processing speed, response inhibition and executive function.

Although both groups' test performance trends showed improvement at one month, desaturation group's test performances were still lower in respect to non-desaturation group. This improvement at one month can be explained by learning after retesting or recovery of cognitive function, but the difference between the groups in cognitive test performance has been kept at 1 month.

Some studies showed that the right sided surgery is a risk factor for hypoxemia during OLV [28], whereas cerebral desaturation and operated side of the patients demonstrated no statistically significant relationship in our study.

In conclusion, patients undergoing OLV develop cerebral oxygen desaturations. Cerebral oxygen desaturations have an adverse impact on postoperative cognitive function. This adverse effect has declined over time but has continued till the end of the first postoperative month. Prolonged desaturation periods result in a more deterioration of cognitive function. Thus, cerebral desaturations should be prevented and treated. Cerebral oximetry guided therapy may reduce postoperative cognitive dysfunction while increasing the quality of life.

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Conflict of Interest: None.

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