Journal of The Cardiovascular Thoracic Anaesthesia and Intensive Care Society

GKDA Derg 2022;28(2):122-128
DOI: 10.14744/GKDAD.2022.05668

Research Article / Araştırma

Can Intraoperative Near-Infrared Spectroscopy Monitoring a Reliable Monitoring Method in Preventing Neurocognitive Dysfunction in Cardiac Surgery? Neurocognitive Monitoring Method in Cardiac Surgery

Kalp Cerrahisinde İntraoperatif Yakın Kızıl Ötesi Spektroskopi Takibi Nörokognitif Disfonksiyonu Önlemede Güvenilir Bir Takip Yöntemi midir?

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ABSTRACT

Objectives: Our study aims to investigate whether changes in cerebral oximetry as assessed by the use of near infrared spectroscopy are a reliable monitoring method in preventing post-operative neurocognitive dysfunction in patients undergoing cardiac valvular surgery.

Methods: The study included 43 patients who were to undertake valvular cardiac surgery between March 2014 and March 2015 and agreed to take part in the study. All patients received cerebral oximetry monitoring by near-infrared spectroscopy before induction and during the operation. The group of patients who demonstrated a ≥20% decrease in cerebral oximetry and received intervention were called Group A (n=18), and the group of patients with a <20% reduction in cerebral oximetry was called Group B (n=25). Neurocognitive assessments were performed 2 days before and 1 week after surgery. The mini-mental test, visual-spatial functions test, and clock-drawing test were utilized for this purpose.

Results: Patients in groups A and B were compared in terms of age, gender, educational status, and additional disease status, and the groups were found to be similar. There was no difference between the two groups in terms of peroperative cardiopulmonary bypass times and cross-clamp times. There was no significant difference between the groups in the minimental test, visual-spatial functions test and clock drawing test values performed one week after the surgery. No significant difference was

ÖZ

Amaç: Calışmamızda, kalp kapak cerrahisi sırasında hastalarda, yakın infrared spektroskopisi kullanımıyla değerlendirilen serebral oksimetrideki değişikliklerin postoperatif norokognitif disfonksiyonu onlemede guvenilir bir takip yontemi olup olmadığının araştırılması amaclandı.

Yöntem: Mart 2014-Mart 2015 tarihleri arasında kalp kapak cerrahisi gecirecek, calışmayı kabul eden en az ilkokul mezunu 43 hasta (20 erkek, 23 kadın; yaş dağılımı 18-75 yaş) calışmaya dahil edildi. Tum hastalara induksiyon oncesinde ve operasyon suresince yakın infrared spektroskopisi ile serebral oksimetri takibi yapıldı. En duşuk ve ortalama rSO_2 (rejyonel hemoglobin oksijen saturasyonu) değerleri kaydedildi. Yakın infrared spektroskopisi takibinde rSO_2 değerinde %20 ve uzerinde duşme olup mudahalede bulunan gruba A grubu (n=18), %20'den daha az duşme olan gruba B grubu (n=25) şeklinde isim verildi. Kardiyopulmoner baypas yonetimi ve cerrahi protokolu tum hastalarda aynı şekilde uygulandı. Norokognitif değerlendirme operasyondan en az iki gun once, operasyondan bir hafta sonra yapıldı. Bu amacla minimental test, gorsel mekansal işlevler testi ve saat cizim testi uygulandı. Sonuclar istatistiksel olarak değerlendirildi.

Bulgular: A ve B grubundaki hastalar karşılaştırılmış benzer bulunmuştur. Gruplar arasında ameliyattan bir hafta sonra yapılan minimental test, gorsel mekansal işlevler testi ve saat cizim test değerleri arasında anlamı

Please cite this article as: "Ürküt Baz N, Karaca Baysal P, Yıldırım Özkan P, Savluk ÖF. Can Intraoperative Near-Infrared Spectroscopy Monitoring a Reliable Monitoring Method in Preventing Neurocognitive Dysfunction in Cardiac Surgery? Neurocognitive Monitoring Method in Cardiac Surgery. GKDA Derg. 2022;28(2):122-128".

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Submitted Date: December 28, 2021 **Accepted Date:** May 09, 2022 **Available Online Date:** June 14, 2022

found in terms of intensive care and hospital stay for these two groups.

Conclusion: We believe that near-infrared spectroscopy monitoring against such a decrease and immediate intraoperative intervention as necessary based on near-infrared spectroscopy monitoring may be important in preventing post-operative neurocognitive dysfunctions.

Keywords: Neurocognitive dysfunction, Near İnfrared spectroscopy, open heart surgery

bir farklılık bulunmamıştır. Bu iki grup icin yoğun bakımda ve hastanede kalış acısından da anlamlı bir fark bulunamamıştır.

Sonuç: Kalp kapak cerrahisinde serebral perfuzyon bircok nedenle bozulabilir. Bu durumun yakın infrared spektroskopisi ile takibi ve gereğinde intraoperatif mudahale postoperatif norokognitif fonksiyonları onlemede onemli olabilir duşuncesindeyiz.

Anahtar sözcükler: Açık kalp cerrahisi, nörokognitif disfonksiyon, yakın infrared spektroskopisi

Introduction

Post-operative cerebral damage is still common despite the recent advances in surgical and anesthetic techniques. Such damage may range from serious but rare conditions including stroke to the more common cognitive dysfunction, which is not life threatening but may impair quality of life and also may prolong hospital stay.[1,2] These post-operative cerebral complications are multifactorial but result from hypoperfusion, hypoxia, inflammatory response, and embolism, leading to a disturbance in oxygen and supply balance.[3]

Post-operative cognitive dysfunction (POCD) is described as impaired focus, comprehension, and memory which develop following surgery. Post-operative cognitive impairments, on the other hand, cover a wide range from post-operative cognitive dysfunction to dementia and post-operative delirium. The majority of patients recover to pre-operative state during the 1st post-operative week. However, patients undergoing certain types of surgeries, those with some certain medical conditions, preexisting cognitive dysfunction, and elderly patients are at an increased risk of developing post-operative cognitive disorder. Such patients may suffer from long-term cognitive impairment.[1,4] POCD is a more important problem in cardiac compared to non-cardiac surgeries. Frequencies ranging from 25% to 80% are being mentioned, depending on the type of surgery, method of evaluation, and definitions.[5]

Transcranial near-infrared spectroscopy offers a means to obtain continuous non-invasive data on the regional oxygen saturation of the brain (rSO_2). It is easy to use and reliable in different temperature, perfusion, saturation, and pH ranges.[6] Low regional cerebral oxygen saturation measured by near-infrared spectroscopy (NIRS) has been shown to be associated with neurological complications and cognitive disorder in the previous studies.[5] An association between evaluating the brain as a reference organ in coronary bypass surgery and major organ failure in the presence of cerebral desaturation and length of hospital stay was also demonstrated. Reported NIRS baseline rSO_2 data range from 65% to 70% in healthy individuals compared with 60–65% in patients with cardiac disease. In cardiac surgery, patient monitoring by NIRS demonstrating a >20% reduction from baseline measurement suggests a problem in oxygen supply.[6]

The present study aims to investigate the effects of cerebral oximetry changes as detected by NIRS and the interventions to correct any decrease in this value on post-operative neurocognitive impairments in cardiac surgery patients, in whom post-operative neurocognitive impairment is common.

Methods

After obtaining the approval of the Institutional Review Board and the written informed consents of the patients, the study enrolled 43 patients, aged 18-75 years, who were candidates for cardiac surgery (27 mitral valve replacement, nine aortic valve replacement, and seven aortic and mitral valve replacement) and were at least primary school graduates. The enrollment took place in Kartal Koşuyolu Training and Research Hospital between March 2014 and March 2015. One patient who had a cerebrovascular accident and four patients whose post-operative tests could not be completed were excluded from the final sample. The study was thus completed with 43 patients. The group of patients who demonstrated a ≥20% decrease with cerebral oximetry measurement and received intervention were called Group A, and the group of patients with a <20% reduction were called Group B.

Patients with drug and/or alcohol dependency, major psychiatric conditions, central nervous system disorders, patients receiving treatment with major tranquilizers or antidepressants, patients with advanced heart failure, patients with a preexisting pre-operative infection, significant organ failure (end-stage hepatic impairment and dialysis-dependent renal impairment), serious pulmonary hypertension, and patients undergoing combined operation and emergency surgery were excluded from the sample. Patients' conditions that may hinder communication, including advanced impairment of sight and hearing, insufficient level of Turkish language or reading-writing ability, were also excluded from the study.

The patients were given intravenous midazolam 0.02-0.09 mg/kg as premedication. Electrocardiography (ECG) and

rSO_2 monitoring and invasive blood pressure measurement from the radial artery were performed in the operating room before induction. Midazolam at 0.05-0.1 mg/kg, propofol at 0.5-1.5 mg/kg, rocuronium at 0.5-1.0 mg/kg, and fentanyl at 5-10 to µg/kg were administered to each patient for anesthesia induction. Following induction, all patients were catheterized with central venous catheters from the vena jugularis interna using the Seldinger technique. Artificial respiration following intubation was administered using a 30-70% v/v mixture of air and oxygen in volume-controlled mode to provide 6-8 ml/kg tidal volume, and applying a frequency to maintain end-tidal CO_2 ($etCO_2$) between 35 and 40 as positive end expiratory pressure (PEEP) at 5 cm H_2O. The lungs were allowed for passive deflation at the cardiopulmonary bypass (CPB) phase. Non-pulsatile perfusion technique was used. Anesthesia was maintained by intermittent bolus doses of rocuronium, midazolam, and fentanyl.

All patients were operated by the same surgical team. Surgeries were performed under moderate hypothermia at 28-32°C. Moderate hemodilution (hematocrit: 26-28%) based on temperature was applied and blood pressure was maintained between 50 and 70 mmHg throughout CPB. To achieve this, pump flow rates were set to 3.5-4 L/min/m^2 during the normothermic phase and to 2-2.8 L/min/m^2 during the hypothermic phase. "Isothermic blood cardioplegia" induced by K, Mg, and $NAHCO_3$ added to the perfusate for myocardial protection was administered anterograde (10 ml/kg) and as maintenance bolus (5 ml/kg) every 20 min. Cardiovascular stability at pump outlet was achieved using appropriate fill pressures and inotropic support as necessary. All surgeries were performed under intraoperative transesophageal echocardiography (TEE), and air evacuation at CPB end was realized by TEE.

Oximeter probes were placed at the right and left frontal area before anesthesia for all patients included in the study. Regional cerebral oximetry determination was performed before anesthesia and throughout surgery, which involved measuring and recording of the lowest, highest, and mean cerebral saturation rate before, during, and after CPB. The measurements were performed using the NIRS Invos (Covidien, Ireland) cerebral oximetry device which is currently being used in our clinic and is an easy-to-use and reliable tool in different temperature, perfusion, arterial saturation, and pH ranges.

With NIRS monitoring, the group of patients with a ≥20% decrease in rSO_2 for >1 min were called Group A, and the group of patients with a <20% reduction in rSO_2 were called Group B. In Group A, decreased rSO_2 was increased to 100% inspired O_2, the surgical team was cautioned and cannula sites were confirmed. Partial pressure of carbon dioxide ($PaCO_2$) <40 mmHg measured in arterial blood gas was increased to >40 mmHg, and mean arterial pressure (MAP) values <50 mmHg were increased to >60 mmHg, pump flow was increased, blood transfusions were given to patients with hematocrit levels dropping below 24%, and anesthesia depth was increased by administering thiopental sodium.

A battery of neuropsychological tests including the mini-mental test, clock-drawing test, and visual-spatial functions was used. The mini-mental test involves eight subgroups including orientation (space and time), registration, attention and calculation, recall, language (naming, repetition, reading, three-stage command, and writing), and praxis. It is a quantitative and practical test to evaluate patients' cognitive status. The maximum score is 30 and the minimum is 0. Scores below 23 (inclusive) indicate cognitive impairment. The clock-drawing test is acknowledged as one of the first tests that show impaired results at the early stages of dementia. It is a test that evaluates the planning and appropriately ordering of objective-oriented complex behaviors. Patients are asked to place the numbers of a clock in a circle and to mark the time they are told. It is a 6-point test, with scores below 4 indicating impaired cognitive function. The visual-spatial functions test allows for the evaluation of complex perceptive functions and psychomotor functioning. Patients are asked to mimic the hand gestures presented by the experimenter. Each accurately mimicked gesture equals to 2 points, for a total of 10 points. Scores below 6 indicate impaired cognitive function. The tests were performed at two time points, that is, preoperatively (t_0) and at week 1 (t_1) and the results were documented. A ≥ an deterioration compared to pre-operative time point in neuropsychological tests is considered as cognitive dysfunction. Comparison of the two groups (the group of patients who experienced a ≥per reduction in rSO_2 values and received intervention vs. the group of patients who experienced a <20% reduction in rSO_2 values) with respect to the performance demonstrated in neuropsychological tests was selected as the primary endpoint of the study.

Statistical Analysis

Number and percentage for discontinuous variables and mean±standard deviation (SS) for continuous variables were

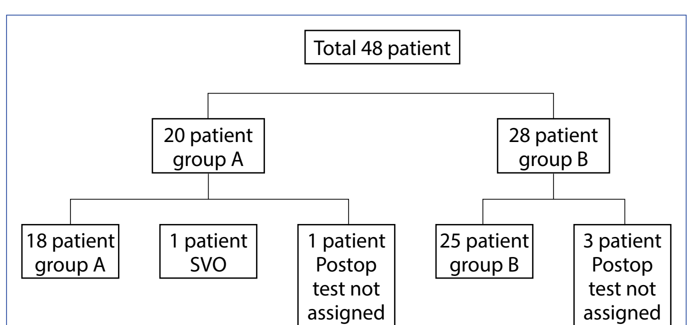

Figure 1. Distribution of patients.

SVO: Cerebrovascular disease.

used for descriptive statistics. Fit to normal distribution was evaluated by means of the Kolmogorov-Smirnov test. Chi-square test was used to compare discontinuous variables between Groups A and B. For comparison of continuous variables, Mann-Whitney U-test was used for non-parametric variables. The data were evaluated using the SPSS 15.0 software. Level of statistical significance was set at $p<0.05$.

Results

Forty-eight patients who met the inclusion criteria were included in this study. One patient who had a cerebrovascular accident and four patients whose post-operative tests could not be completed were excluded from the study. Thus, the study was completed with 43 patients in total (Fig. 1).

The group of patients who experienced a ≥20% decrease in NIRS and received intervention, that is, Group A, included 18 patients, and the group of patients with a <20% reduction in NIRS, that is, Group B, included 25 patients. The two groups did not differ significantly with respect to age, sex, level of education, comorbidities, ejection fraction, and rhythm (Table 1). Perioperative cross-clamp and CPB durations were also evaluated and were not different significantly between the two groups (Table 2). Patients' mean duration of intensive care unit stay was 2.5 days and their mean duration of hospital stay was 8 days, with no statistically significant difference between the two groups (Table 2).

Scores from the mini-mental test (pre- and postoperatively), visual-spatial functions test (pre- and postoperatively), and clock-drawing test (pre- and postoperatively) that indicate cognitive functions were compared between the two groups and no statistically significant difference was determined (Table 3).

Cognitive dysfunction was detected in 11 of 43 patients. However, no significant difference was found between the two groups in terms of post-operative cognitive dysfunction. In our study, we determined the presence of POCIB as a decrease of two units or more from any test value. This method is one of the definitions suggested in other studies.

Table 1. Intergroup comparison of sociodemographic and pre-operative data

Parameters	Group A (n=18)		Group B (n=25)		p
	n	%	n	%	
Age					
≤64 years	12	66.7	16	64.0	0.856
≥65 years	6	33.3	9	36.0	
Sex					
Female	10	55.6	13	52.0	0.818
Male	8	44.4	12	48.0	
Educational status					
Primary school	12	66.7	16	64.0	0.417
Secondary school	3	16.7	1	4.0	
High school	2	11.1	6	24.0	
University	1	5.6	2	8.0	
Comorbidities					
Yes (DM, KOAH, HT)	7	38.9	7	28.0	0.452
No	11	61.1	18	72.0	
Rhythm					
NSR	12	66.7	16	64.0	0.856
AF	6	33.3	9	36.0	
EF					
<60%	6	33.3	7	28.0	0.816
>60%	12	66.7	18	72.0	

DM: Diabetes mellitus; KOAH: Cronic obstructive lung disease; HT: Hypertansion; NSR: Normal sinus ritm; AF: Atrial fibrillation; EF: Ejeksiyon fraksiyonu.

Discussion

Our study investigated the effects of reductions in cerebral oximetry readings as monitored by NIRS and the interventions performed subsequently on post-operative cognitive functions in patients undergoing cardiac surgery accompanied by CPB. The groups of patients who experienced >20% decrease in cerebral oximetry reading from baseline and received intervention were compared with patients with <20% decrease with respect to post-operative cognitive dysfunction and intensive care and hospital stay. No differences were observed between these two groups.

Table 2. Intergroup comparison of clinical data

Parameters and results	Group A (n=18)		Group B (n=25)		p
	Mean±SD	Min-max	Mean±SD	Min-max	
Cross duration (min)	98.7±37.7	56-192	88.2±33.6	15-180	0.530
Perfusion duration (min)	131.7±38.0	78-210	133.2±57.0	40-300	0.786
Duration of ICU stay (days)	2.5±1.6	1-8	2.7±1.6	1-7	0.601
Duration of hospital stay (days)	8.0±1.9	5-14	8.8±2.7	6-20	0.217

ICU: Intensive care unit; SD: Standard deviation.

Table 3. Intergroup comparison of cognitive tests

Results	Group A (n=18)		Group B (n=25)		p
	Mean±SD	Min-max	Mean±SD	Min-max	
Mini-mental test score (pre-operative)	23.7±5.0	12.0-30.0	24.2±4.0	16.0-30.0	0.951
Mini-mental test score (post-operative)	23.3±5.3	11.0-30.0	23.5±4.7	13.0-30.0	0.961
Visual-spatial functions test (pre-operative)	9.5±1.0	6.0-10.0	9.4±1.1	6.0-10.0	0.687
Visual-spatial functions test (post-operative)	9.5±0.9	7.0-10.0	9.2±1.2	6.0-10.0	0.514
Clock-drawing test (pre-operative)	5±1	4.0-6.0	4±2	3-6	0.76
Clock-drawing test (post-operative)	4±1	3-6.0	4±1	3-6.0	0.78

SD: Standard deviation.

Neurologic complications are currently more frequent despite the marked decline in the mortality of cardiac surgery. Embolism, cerebral blood flow changes, local or systemic inflammatory response, and reperfusion damage mechanism play an important role in the occurrence of neurologic complications following adult cardiac surgery. Central nervous system complications have a very wide overall incidence with the incidence of neurologic injury ranging between 1 and 5% and the incidence of subclinical neurological damage including cognitive dysfunction ranging between 50 and 70%.[7] Ahonen et al.[8] evaluated clinical outcomes of cerebral complications following cardiac surgery individually and found the following ratios: 1-9% for stroke, 13-30% for delirium, and 60% at the early and 25-30% for the late phase for regression of cognitive disorders including motor slowing and memory and attention deficits.

In our study, cognitive dysfunction was observed in 25% of the patients in the early post-operative period. Newman et al.[9] observed POCD in 245 of the patients in their study group which was comparable with our study population with respect to mean age. These percentages are lower compared with other studies. Tourney-Jette et al.[10] found that 80.7% of the 61 patients with a mean age of 70 years who underwent cardiac surgery experienced cognitive dysfunction over the post-operative 1 week. Neurocognitive tests were repeated during the post-operative month 1 in this study and the percentage was reported to have dropped to 38%. Elderly patients are not only at a higher risk of POCD but also duration of cognitive dysfunction is longer in these patients.

Altered brain blood flow is the most frequent cause of cerebral complications in cardiac surgery. This alternation may manifest as hypoperfusion or hyperperfusion. Pathologies that interfere with autoregulation, impaired collateral circulation, non-homogenous periods of warming and cooling, perioperative cardiac arrest, and occurrence of critical events such as hemorrhage are influential in blood flow disturbances. Cerebral monitoring offers significant benefits in detecting such events. In our study, we performed interventions to elevate rSO_2 by predicting cerebral hypoperfusion and desaturation with the help of cerebral monitoring. For Group A, rSO_2 decreases were managed, respectively, by warning the surgical team and confirming cannula locations, increasing the inspired O_2 to 100%, and increasing $PaCO_2$ <40 mmHg measured in arterial blood gas to >40 mmHg, and increasing MAP to >60 mmHg if it was <50 mm Hg, increasing pump flow, giving blood transfusions to patients whose hematocrit levels dropped below 24%, and increasing anesthesia depth by administering thiopental sodium. We intended to demonstrate that it is possible to prevent occurrence of neurocognitive impairments this way. Slater et al.,[11] Murkin et al.[12] and Kati Bocmann et al.[13] followed similar interventions to elevate rSO_2. Neurocognitive impairments following cardiac surgery both delays post-operative recovery and prolongs hospital stay.

There is no universal definition of the extent to which a decrease in $Sc0_2$ during cardiac surgery constitutes an abnormal finding. Both relative reductions from baseline (e.g., 20% reduction) in rSO_2 and studies that looked at the absolute threshold rSO_2 (e.g., <50%) were used.[14] Thresholds of rSO_2 values indicative of cerebral ischemia have been derived mostly from data obtained from patients undergoing carotid endarterectomy. In those studies, a reduction from baseline in $rScO_2$ ipsilateral to carotid artery clamped from 5% to 15% was found to be associated with reductions in transcranial Doppler measured cerebral blood flow velocity, slowing of the electroencephalogram (EEG), or changes in somatosensory evoked potentials (SSEP) with a sensitivity that ranges between 44% and 100% and specificity between 44% and 82%.[14-19] It is unclear whether these data can be predicted for patients undergoing cardiac surgery where the mode of anesthesia and body temperature differ from those in carotid surgery.[14]

Novitzky et al.[20] reported that maintaining baseline rSO_2 values above 80% and above 50% as measured by NIRS reduced neurologic complications. As a matter of fact, cerebral oxygen saturation falling 50% below the reference value was shown to increase the risk of developing a post-operative cognitive disorder by 7-fold. Similarly, the authors suggested that a 30% decrease would lead to up to 3-fold increase in POCD frequency. The results of this study seem to be consistent with those reported by Tournay-Jette et al.[10] There is, however, no trend as to which of these two thresholds (absolute value with degree of reduction from baseline) would provide a better prediction.[11] In our study, we considered a 20% decrease in rSO_2 from baseline as significant. We took this evaluation into account while grouping the patients and performed our interventions based on these values. We observed more than 20% decrease from baseline values of over 3 min in rSO_2 values as a result of the interventions performed. Correcting rSO_2 was demonstrated to result in improved outcome parameters, and cognitive dysfunctions, which could have resulted from an association between the intervention and corrected rSO_2 values, were thus prevented.

Murkin et al.[12] associated cerebral saturation with several systemic events. The authors randomized 200 patients 1:1 who are to undergo coronary bypass surgery into two groups. One group was to receive intervention if rSO_2 decreased (e.g., increasing pump flow and increasing mean arterial pressure) and the other group was intended to act as the control group and was not to receive any intervention if rSO_2 decreased. Intensive care and hospital stay were longer in the control group. Mortality, mechanical ventilation >48 h, risk of stroke, and multiorgan failure were also higher in the control group. However, Murkin et al.[12] did not perform a specific test to evaluate patients' cognitive functions. The study, therefore, fell short in evaluating neurological functions.

Another important topic is evaluation of cognitive functions. A test to evaluate post-operative cognitive dysfunction that can be regarded as the golden standard is yet to be developed. For the currently available tests, there is no consensus as to which test or group of tests should be used or the most accurate time to implement the test or tests[21] Negarger et al.[22] intended to investigate the effects of intraoperative decrease in rSO_2 on post-operative cognitive functions in 72 patients who were to undergo cardiac surgery. The authors determined no correlation between altered cerebral oxygen saturation and post-operative neurological complications which they measured with the mini-mental test only. They attributed this result rather to 52% sensitivity and 87% specificity of the mini-mental test used in determining POCD following cardiac surgery. On the other hand, Nollert et al.[23] and Yao et al.[24] and R. Srinivas,[25] found an association between low rSO_2 and decreased mini-mental test score. The mini-mental test, clock-drawing test, and visual and spatial functions test were used in our study. The tests were overall designed to evaluate attention, memory, and motor fine function. In our study, we determined POCD presence as evidenced by a reduction from 1 standard deviation in two or more tests. The primary cause of using a limited number of tests in our study is because we were unable to implement tests that require advanced cognitive skills given the low educational levels of our patients. Although using multiple tests make the evaluation process harder and prolong the process, we believe that such approach is more valuable in interpreting different cognitive domains.

This study had several limitations. First of all, our patients had other causes of POCD occurrences other than cardiac surgery and anesthesia. A number of reasons may be responsible for this. Education level is a critical variable in the neurocognitive tests we use.[26] Some researchers have suggested that there is an association between lower education levels and decreased cerebral reserve and increased POCD. Hong et al.[27] observed lower levels of education in patients who developed POCD. The patients included in the sample in our study were at least primary school graduates, and 66% of the patients did not complete 8 years of basic education. In other studies, education levels were relatively higher (mean years of education 10.4±4 years).[18] Second, the number of patients was low. Third, a more elaborate set of psychometric tests could be used to measure patients' post-operative cognitive status.

Conclusion

We did not observe a significant difference for the development of POCD although there was a 20% rSO_2 decrease compared to baseline as determined by NIRS in our study. NIRS monitoring enabled us to timely and rapidly act in the event of rSO_2 decreases. This allowed us to establish optimal cerebral blood flow by increasing patients' both medical and cerebral perfusion flow. We are in the opinion that using NIRS monitoring is the optimal method in preventing POCD development, especially in cardiac surgery.

Disclosures

Ethics Committee Approval: The study was approved by The Istanbul Kartal Kosuyolu High Specialization Training and Research Hospital Ethics Committee (Date: 20/10/2016, No: 2017/4/21).

Informed Consent: Written informed consent was obtained from all patients.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Financial Disclosure: The authors declared that this study has received no financial support.

Authorship Contributions: Concept – N.Ü.B., Ö.F.S., P.K.B., P.Y.Ö.; Design – N.Ü.B., Ö.F.S., P.K.B., P.Y.Ö.; Supervision – N.Ü.B., Ö.F.S., P.K.B., P.Y.Ö.; Fundings – Ö.F.S.; Materials – N.Ü.B., P.Y.Ö.; Data collection &/ or processing – N.Ü.B.; Analysis and/or interpretation – N.Ü.B.; Literature search – Ö.F.S., P.K.B.; Writing – N.Ü.B.; Critical review – N.Ü.B.

Etik Kurul Onayı: Çalışma İstanbul Kartal Koşuyolu Yüksek İhtisas Eğitim ve Araştırma Hastanesi Etik Kurulu tarafından onaylandı (Tarih: 20/10/2016, Numara: 2017/4/21).

Hasta Onamı: Hastalardan yazılı onam alınmıştır.

Hakem değerlendirmesi: Dışarıdan hakemli.

Çıkar Çatışması: Çıkar çatışması bulunmamaktadır.

Finansal Destek: Yazarlar bu çalışmanın herhangi bir finansal destek almadığını beyan etmişlerdir.

Yazarlık Katkıları: Fikir – N.Ü.B., Ö.F.S., P.K.B., P.Y.Ö.; Tasarım – N.Ü.B., Ö.F.S., P.K.B., P.Y.Ö.; Denetmeler – N.Ü.B., Ö.F.S., P.K.B., P.Y.Ö.; Kaynaklar – Ö.F.S.; Malzemeler – N.Ü.B., P.Y.Ö.; Veri Toplanması ve/veya İşlemesi – N.Ü.B.; Analiz ve/veya Yorum – N.Ü.B.; Literatür Taraması – Ö.F.S., P.K.B.; Yazıyı Yazan – N.Ü.B.; Eleştirel İnceleme – N.Ü.B.

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