ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

Investigation of the effect of anesthesia implementation with bispectral index on postoperative neurocognitive functions and delirium in open heart surgery

Emir Izzet[1], Borulu Ferhat[2], Coskun Ceyhun[3], Muhammed Onur Hanedan[4], Mataracı Ilker[5]

[1]Erzincan Binali Yıldırım University, Faculty of Medicine, Department of Cardiovascular Surgery, Erzincan / Turkey, [2]Ataturk University. Faculty of Medicine, Department of Cardiovascular Surgery, Erzurum / Turkey, [3]Yalvaç State Hospital, Cardiovascular Surgery Clinic, Isparta / Turkey, [4,5]Ahi EvrenThoracic Cardiovascular Surgery Education and Research Hospital, Trabzon, Turkey

Submission: 24-09-2020 Revision: 15-01-2021 Publication: 01-03-2021

ABSTRACT

Background: Neurological complications of coronary artery bypass surgery are still the major causes of mortality and morbidity despite all advances in this field. **Aims and Objectives:** We investigated the effect of bispectral index (BIS) monitoring of the patient consciousness on the postoperative neurocognitive functions in our study. **Materials and Methods:** A total of 40 patients in the age range from 25 to 75 years were included in our study, who were electively operated for isolated coronary artery bypass grafting (CABG) surgery in the period from January 2014 to June 2014. The patients were assigned to two groups based on whether BIS monitoring was performed or not. The patients were consecutively allocated to either group when they were found eligible to be included based on the exclusion criteria. Administration of the anesthesia was monitored with BIS in the respective group (Group 1). All patient follow-up parameters were compared in both groups. Neurocognitive function tests (the clock drawing test and standardized mini mental test) were administered to the patients in the preoperative and postoperative period(1 st day and day before discharge). The results were compared. **Results:** There were no significant findings in the demographic features and the routine follow-up parameters between the two groups. The time of extubation, intensive care unit (ICU) follow-up parameters, and the length of stay in the ICU were not significantly different between the groups; however, the length of stay at the hospital was significantly longer in the group of patients, who were not monitored with BIS ($p<0.05$). The mean arterial blood pressure was statistically significantly higher in group 1 (BIS monitoring) at all phases of the operation and during the postoperative follow-ups. A significant acidosis was present in the arterial blood pressure tests of the patients in group 1 during their stay at the ICU. The Po2 values following cross-clamping and extubation were significantly higher in group 1. In the group monitored with BIS, the results of the neurocognitive tests, which were the clock drawing test and the standardized mini mental test, were both clinically and statistically superior ($p<0.05$). **Conclusıons:** BIS monitoring provides favorable contributions for the follow-up of the patients undergoing CABG surgery and it is helpful in estimating the consciousness state of the patients after the surgery.

Key words: Bispectral index; Neurocognitive functions; Heart surgery

Access this article online

Website:

http://nepjol.info/index.php/AJMS

DOI: 10.3126/ajms.v12i3.31438

E-ISSN: 2091-0576

P-ISSN: 2467-9100

INTRODUCTION

Despite the advances in the methods used in surgery and anesthesia, there is a likelihood of developing postoperative complications following heart surgeries using cardiopulmonary bypass (CPB). Among the most critical complications occurring after open heart surgeries are the central nervous system complications.

Address for Correspondence:
Dr. Ferhat Borulu, Ataturk University. Faculty of Medicine, Department of Cardiovascular Surgery, Erzurum / Turkey. **Tel:** +90-5053511762. **E-mail:** fborulu@gmail.com

Several complications may occur after surgeries with extracorporeal circulation; including neuropsychological disorders, cognitive and intellectual disabilities, delirium, seizures, encephalopathy, and intracerebral hemorrhage. However; among all, ischemic stroke is the one associated with the most severe clinical pictures and the poorest clinical prognosis. The etiology of the neurologic and neuropsychologic complications developing after open heart surgeries is multifactorial. The most significant etiological factors include impaired cerebral flow due to emboli or abnormal cerebral perfusion, inflammatory and neurohumoral mechanisms, co-existing premorbid diseases, and the advanced age. The final consequence is neuronal hypoxia and ischemia regardless of the cause.[1]

The neurological and neuropsychiatric complications developing after heart surgeries usually occur due to embolization and hypoperfusion.[2] In more than half of the cases, neurological or neuropsychological changes may occur in the first week after the cardiac surgery. Some neurological complications, developing due to global ischemia associated with the impaired cerebral flow, can be seen in 30-80% of the patients in the postoperative period and cannot be detected with radiological methods. Neurophysiological tests reveal this clinical picture, in which the patient may show intellectual disabilities or deterioration in the cognitive functions developing memory disorders, postoperative confusion, agitation, delirium, prolonged somnolence, or temporary signs of parkinsonism. Changes in neurocognitive functioning, resulting from an altered cerebral flow, may persist until the 6th month.[3] The rates of neurocognitive (cognitive) dysfunctioning may reach rates of 80% at the time of discharge from the hospital. It is reported that these rates are found regressed to 10-35% and 10-15% in the tests performed after the 6th week and after the first year, respectively.[4-6]

In this study, we investigated the effects of intraoperative BIS monitoring on the postoperative neurocognitive functions in the patients, who underwent a coronary artery bypass surgery with CPB.

MATERIAL AND METHOD

This randomized controlled study was conducted in our clinic after obtaining the approval with 12th March 2014 decision date and 2014/04-04 decision number from the local ethics committee. A total of 40 patients in the age range from 25 to 75 years, who underwent an isolated coronary artery bypass grafting surgery in the period from March 2014 to July 2014, and who provided informed consents were included in the study. The exclusion criteria included the presence of a serious valvular pathology, an ejection fraction below 50%, the presence of a rhythm disorder, a BMI value <20 or >30, history of a cerebrovascular event, history of psychiatric and/or neurological disorder and associated medication use, and the presence of carotid artery stenosis of 50% or over. Patients who died due to other reasons during the operation or in the early period, or who lacked biochemical data were excluded (One patient was not included in the study because of the development of acute renal failure and two patients were missing data). The patients were allocated to two groups based on whether BIS monitoring was performed during the operation. (Group 1 = BIS monitoring was performed; Group 2 = BIS monitoring was not performed). Patients were included in the groups in order. The neurocognitive changes in the postoperative period, the intraoperative and postoperative data, and all follow-up parameters were compared between the two groups. The clock drawing test and the mini mental test were used for evaluating neurocognitive functions.

Surgical procedures

Sedation with midazolam and fentanyl was applied to all patients as a standard procedure of our clinic. Invasive arterial pressure monitoring was performed via the right radial artery (Nova Cath, Medipro, Turkey). Anesthesia induction was performed in all patients with 10-15μg/kg fentanyl and 2-3 mg/kg propofol. Preoxygenation of the patients was performed with the inhalation of 100% O_2 for 2 minutes. Vecuronium at a dose of 0.1 mg/kg was administered to the patients for the ease of endotracheal intubation. In the normothermic phase, anesthesia was maintained by fentanyl infusion (0.3-0.5μg/kg/min), propofol infusion (1-2μg/kg/min), and by 1-2% sevoflurane inhalation. In the hypothermic phase during the cardiopulmonary bypass, fentanyl and propofol infusion rates were reduced by half, maintaining muscle paralysis with intermittent bolus injections of vecuronium.

In group 1, infusions were adjusted in order to maintain BIS in a range from 40 to 60. In patients with BIS values of 60 and over, additional bolus injections of 30-50 mg propofol were performed and 3% sevoflurane was administered until BIS values decreased below 60. Infusions stopped when BIS values decreased below 40. Infusions started again when BIS values became 40 or over. BIS values shown on the monitor were recorded at those following time points including the time before the anesthesia induction, after the induction, in the minute 1 of the induction, at the start of the cardiopulmonary bypass (CPB), at the time of cross-clamping, at the end of the cardiopulmonary bypass, at the time of ICU admission, and after the extubation.

All patients were operated by the same surgical team. After connecting the aorta to the cardiopulmonary bypass (CPB) device by the standard method of atrial cannulation, the surgical procedure was performed. The pump flow was adjusted to maintain the arterial pressure at 60-70 mmHg during the CPB. After completing the operation, the patients were transferred to ICU, where they were followed up with standard follow-up procedures. The patients were extubated when they met the criteria for extubation based on blood gas parameters and neurological examination. The patients having no problems in the postoperative follow-up period were discharged from the hospital on the postoperative 6th to 7th day.

Bispectral index (BIS)

Bispectral Index (BIS) is a complex EEG parameter, which was approved by the FDA in January 2004.[7] The BIS algorithm can be calculated using the four sensors placed on the head. BIS may offer anesthetists better options to adjust and improve the administration dosages of hypnotic medications. BIS provides information on the level of anesthesia administered to the patient and allows for adjusting the dosages of hypnotic medications.[8] BIS does not monitor analgesia, cannot predict the spinal cord reflexes such as hemodynamic responses or movements in response to painful stimuli or cannot determine the exact moment of returning to normal consciousness again.

The three major features of BIS are as follows:

1. Some EEG activities reflect the activity in the deep brain structures and this component is subject to change during the sleep.
2. BIS is an empirical measure calculated by statistical analysis.
3. BIS quantifies the state of the brain for that specific moment. It does not quantify the dosages of specified medications.[9]

BIS algorithm operates on a complex formula. This formula determines a BIS value in the range from 0 to 100 by using a method, which rejects artifacts at extreme values (Table 1).[7]

BIS monitoring helps customize the administration of hypnotic agents based on unique personal needs and eliminate the possibility to administer high or insufficient doses; ensuring a shorter and comfortable recovery period.[10]

The clock drawing test

The patient is asked to draw a clock, place the numbers in appropriate positions, and to mark the time announced to the patient. It tests the constructional praxis, and the ability to comprehend and plan. It is scored on a six-point scale. Scores below 4 indicate cognitive dysfunction. The scoring is performed as follows:

- The position of number twelve is correct: 3 points,
- All twelve numbers were written down: 1 point,
- The hour and minute hands were drawn: 1 point,
- The time announced to the patient was marked correctly: 1 point.

Table 1: BIS Scale

BIS	Clinical condition EEG
90-100	Awake Normal
70-80	Loud verbal, limited touch Synchronized, high frequency
60-70	Loud verbal, strong touch Beta activity
40-60	Deep sedation, no verbal warning Normalized low frequency
<40	Deep hypnotic condition Suppression in activity
<20	Respiratory reserve limited,Increased suppression
Preserved protective reflexes	
0	No response to alert Isoelectric

The advantages of the clock drawing test include the facts that it is a brief test, it requires a shorter time to be administered, and has a high negative predictive value. However, test scoring is subjective and the results have a high level of false negativity as the disadvantages.[11,12]

Standardized mini mental test (SMMT)

The standardized mini mental test is used for quantification of cognitive performance. Although it has limited specificity for differentiating clinical syndromes, it can be used for a global assessment of cognition as a brief, convenient, and standardized method. It comprises eleven items categorized under five major themes, which are the orientation, registration memory, attention and calculation, recall, and language. The highest total score of the test is 30.

Statistical analysis

The statistical analyses of the data were performed using the SPSS 17.0 packet program. The continuous data were expressed as mean and standard deviation, and the categorical data were presented as percentages. The categorical data were compared using the Pearson Chi-Square test and using Fisher's Exact test when necessary. The continuous data were compared with the student t-test. A p-value smaller than 0.05 was accepted to be statistically significant.

RESULTS

No significant differences were detected in the demographic and surgical data of the patients who were monitored with BIS or who were not (Table 2). There were no statistically significant differences in the duration of perfusion ($p = 0.342$) and the duration of aortic clamping ($p = 0.314$) between the groups when the patients were applied CPB.

There were no significant differences between the two groups in the time of extubation and the length of ICU stay, which were considered to be associated with the hemodynamic parameters and neurocognitive functioning in the postoperative period; however, the length of stay was statistically significantly longer in group 2 ($p<0.05$).

Table 2: Demographic and operative data

Variables	Group 1	Group 2	P value
Age	62.5±7.2	58.7±7.8	0.117
Hypertension (n)	12 (60%)	11 (55%)	
Diabetes mellitus (n)	5 (25%)	3 (15%)	
Hyperlipidemia (n)	10 (50%)	14 (70%)	
Cigarette (n)	11 (55%)	11 (55%)	
COPD (n)	3 (15%)	0	
CVE story (n)	0	1 (5%)	
BMI	26.4±1.7	25.5±2.3	0.188
EF (%)	60.8±6.7	61±3.8	0.886
CPB time (min)	97.8±29.6	89.6±20.1	0.342
Cross clamp time (min)	64.5±21.4	58.4±15.6	0.314
Extubation time (hours)	8±4.6	8.6±3.5	0.660
ICU time (hours)	75.9±46.1	81±91.8	0.821
Hospital stay (hours)	200.5±55.3	168.2±32.9	0.032

BMI: Body mass index, EF: Ejection fraction, COPD:C hronic Obstructive Pulmonary Disease, CPB: Cardiopulmonary bypass, CVE: Cerebro Vascular Event, ICU: Intensive Care Unit

The mean arterial pressure (MAP) values were statistically significantly higher in Group 1 in all phases of the surgery and in the postoperative follow-up period. The mean BIS values ranged from 36 to 42 during the surgery (Table 3). Statistically significant acidosis was detected in the pre-operative and postoperative results of blood gas tests of the patients in Group 1 during their stay in ICU (7.33±0.05 vs 7.37±0.05; $p=0.037$). It was noted that the levels of pO_2 were significantly higher following the cross-clamping and after extubation in group 1 ($p=0.02$). The levels of pO2 pressure in group 2 patients after cross-clamping were observed to be lower compared to group 1 patients.

No clinically and statistically significant differences were detected in the remaining parameters. When the preoperative and postoperative follow-up laboratory test results of the patients were compared between the two groups, no significant differences were found. Among the biochemical parameters, statistically significant differences ($p>0.05$) were observed only in the INR (international normalized ratio) values obtained on the postoperative third day (Table 4).

When the results of the clock drawing test (CDT) and the standardized mini mental test (SMMT) were examined to

Table 3: BIS and follow-up values in peroperative period

Timing		Group 1	Group 2	P value		Variables	Group 1	Group 2	P value
Before induction	BIS	84.2±10.73	-	-	After cross-clamping	BIS	41±5.98	-	-
	pH	7.41±0.03	7.45±0.14	0.334		pH	7.38±0.07	7.7±0.09	0.704
	pO2	97.1±22.9	99.5±29.3	0.762		pO2	275.5±53.5	227.6±71.6	0.020
	MAP (mmHg)	91.3±19.3	78.2±15.4	0.024		MAP (mmHg)	65.3±10.1	60.1±4.9	0.049
	SaO2	97.2±2.44	96.4±1.76	0.243		SaO2	98.1±3.3	99.5±0.8	0.077
	Body temperature(˚C)	36.4±0.2	36.3±0.1	0.140		Body temperature(˚C)	32.4±1.2	32.1±1.03	0.486
After Induction	BIS	42±9.9	-	-	CPB Output	BIS	39.7±11	-	-
	pH	6.64±3.3	7.39±0.33	0.325		pH	7.3±0.09	7.33±0.06	0.334
	pO2	162.4±67.2	133.2±56.6	0.145		pO2	183±113.8	175.2±85.6	0.807
	MAP (mmHg)	78.3±15.4	68.9±14.9	0.058		MAP (mmHg)	69.2±8	65.4±7.1	0.121
	SaO2	98.8±1.1	98.5±1	0.297		SaO2	97.3±3.3	99.4±0.6	0.01
	Body temperature(˚C)	35.9±0.5	36.3±0.3	0.150		Body temperature(˚C)	36.8±0.4	36.8±0.4	0.02
Incision 1.minutes	BIS	38.7±8.7	-	-	Intensive care	BIS	61.4±8.4	-	-
	pH	7.38±0.04	7.4±0.14	0.514		pH	7.33±0.05	7.37±0.05	0.037
	pO2	206.1±57	189.4±78	0.445		pO2	134.3±48.8	149.7±46.6	0.315
	MAP (mmHg)	78.1±12.2	65.2±11.5	0.001		MAP (mmHg)	78.1±6.9	72±6.8	0.007
	SaO2	99.3±0.7	99±0.1	0.141		SaO2	96.9±1.9	97.5±1.7	0.345
	Body temperature(˚C)	35.8±0.5	36.2±0.2	0.012		Body temperature(˚C)	36.4±0.2	36.5±0.2	0,390
CPB entry	BIS	36.1±6.34	-	-	Extubation	BIS	85.3±7.8	-	-
	pH	7.39±0.07	7.41±0.07	0.375		pH	7.36±0.05	7.39±0.04	0.177
	pO2	311.1±76.5	329.6±177.5	0.671		pO2	97.8±27.9	136.7±23.9	0.231
	MAP (mmHg)	67.4±11.8	59.9±4.8	0.012		MAP (mmHg)	79±10.9	71.6±8.3	0.021
	SaO2	99±0.9	99±0.9	1		SaO2	96.1±1.3	95.7±2.1	0.430
	Body temperature(˚C)	33.9±1.7	32.5±0.5	0.003		Body temperature(˚C))	36.5±0.22	36.6±0.17	0.123

CPB: Cardiopulmonary bypass, MAP: Mean Arterial Pressure, pO2: Partial oxygen
BIS: Bispektralindeks, SaO2: Oxygen Saturation

evaluate the neurocognitive functions, it was found out that the results of the patients in group 1 were statistically significantly better compared to those of the patients in group 2 (Table 5).

No significant differences were observed in the intraoperative vital sign parameters between the two groups in our study. The doses of the anesthetic medications were adjusted according to BIS values of the patients. The mean intraoperative and postoperative arterial pressure values of the patients in group 1 were in the range from 65 to 70 mmHg, which were approximately 5-10 mmHg higher compared to those in group 2.

DISCUSSION

There is a high number of studies in the literature about the type of surgery directly affecting the development of cognitive dysfunction.[13] It has been demonstrated that cognitive dysfunction is most commonly seen after cardiac surgery at a rate from 40% to 60%.[14] Among the complications of cardiac surgery, neurologic complications predominate, especially in the postoperative period. This occurs mainly due to potential embolization and hypoperfusion, which may develop especially during the catheter placement or during the extracorporeal circulation. Yao et al. investigated the relationship between the cerebral oxygen and neuropsychological dysfunction in patients undergoing cardiopulmonary bypass and they demonstrated that the neuropsychological dysfunction after cardiopulmonary bypass resulted from the decrease in the cerebral oxygen saturation in the intraoperative period.[15] However, Murkin et al suggested that cerebral emboli were not involved in the development of cognitive dysfunction in cardiac surgery patients followed up by transcranial Doppler.[16] In our study; high levels of pO2 were observed in group 1 patients compared to those in group 2, in the blood gas tests performed after induction and in the following time points including the first minute after the incision, at the start and end of CPB, and after cross-clamping. These high levels of pO2 and the low rates of postoperative neurocognitive dysfunctioning suggested that our study results were in alignment with those reported in the literature. Furthermore, these results suggest the unfavorable effects on brain oxygenation.

The main aims of anesthesia, which is a major part of the cardiac surgery, include ensuring hypnosis, analgesia, neuromuscular block, and reduced reflex responses. Subjective clinical findings including pupil size, light reflex, cornea and eyelash reflexes, and changes in the blood pressure and heart rate are commonly used in determining the depth of anesthesia. The use of EEG in determining the depth of anesthesia provides more objective data. BIS (Bispectral Index) is a method based on EEG recordings and it is used for determining the degree of sedation, hypnosis, and unconsciousness, and the depth of anesthesia. We aimed to investigate the effects of intraoperative BIS monitoring on the cerebral circulation and early cognitive functions in the patients undergoing CABG surgery.

Hypnosis is induced by inhalation or intravenous administration of medications during anesthesia. Opioids and/or local anesthetics can be used for analgesia. The important issue in anesthesia is to create unconsciousness in the patient, to provide a safe and fast induction, and ensure appropriate awakening following anesthesia while controlling the hemodynamic parameters. Generally, the dosages of hypnotic and/or analgesic medications were adjusted according to somatic and autonomic clinical findings in the clinical practice of anesthesia. However, these findings do not provide information reliable enough to evaluate the consciousness state of the patient.

Table 4: Laboratory data between groups

Variables	Timing	AVERAGE		P value
		GROUP 1	GROUP 2	
Glucose	Preop	128,1±65	104,1±30,2	0,142
	3.day	165,3±39,8	118,4±40,8	
BUN	Preop	40,4±12,03	32,4±8,4	0,02
	3.day	44,7±11,78	38,2±12,18	0,95
Creatine	Preop	0,84±0,21	0,77±0,21	0,281
	3.day	0,94±0,3	0,86±0,33	0,41
LDL	Preop	132,65±44,4	158,55±47,0	0,081
	3.day	140±42,1	155±32,2	0,192
Triglycerides	Preop	152,5±121,4	131,5±48,1	0,47
	3.day	159,85±112,8	136,3±44,2	0,390
ALT	Preop	42,4±17,7	42,25±42,1	0,988
	3.day	39,65±8,1	38,35±14,4	0,727
AST	Preop	42,8±31,3	40,9±42,0	0,873
	3.day	59,6±25,46	73,65±60,1	0,342
INR	Preop	1,13±0,04	1,11±0,03	0,323
	3.day	1,14±0,05	1,19±0,06	0,016
Platelet	Preop	218,70±49,22	230,30±47,88	0,455
	3.day	160,05±39,90	175,80±40,85	0,225
Hematocrit	Preop	41,18±3,32	42,27±4,99	0,424
	3.day	30,30±4,08	28,21±2,53	0,059

BUN: Blood Urea Nitrogen LDL:Low Density Lipoprotein ALT:Alanine aminotransferase
AST:Aspartate aminotransferase INR:International Normalized Ratio

Table 5: Comparison of inter-group CDT / SMMT data

Variables	Timing	Grup 1	Grup 2	p
Clock Drawing Test	Preoperative	5.3±1.2	5.6±0.5	0.388
	After extubation	4.6±1.1	4.6±0.6	0.864
	Before discharge	5.5±0.7	4.5±0.8	**0,0015***
Standardized Mini Mental Test	Preoperative	25.9±2.6	26±2.2	0,948
	After extubation	23±2.8	21.7±1.9	0,09
	Be fore discharge	25.5±2.9	22.2±1.9	**0,001***

Therefore, several complications including hypnosis, delayed awakening or awareness of superficial anesthesia may occur in relationship with deep hypnosis. Insufficient depth of anesthesia results in intraoperative awareness. The risk of this condition is 0.1% in healthy individuals; however, in high-risk surgeries (cardiac surgery, trauma surgery, cesarean section, airway endoscopy, pediatric surgery) the risk may increase up to 1-1.5%.[17] The hypnotic effect can be quantified with EEG. The EEG findings are correlated with sedation, amnesia, unconsciousness, and reduced cerebral metabolic rate. The real-time quantification of hypnosis with BIS allows for optimal dose administration of medications to patients. Use of BIS aims to quantify the depth of anesthesia and to optimize the administration of appropriate dosages to patients.[18] Although it has been reported that BIS monitoring was associated with the reduction in anesthetic medication use and ease of the recovery, some studies have not been able to demonstrate those effects.[19] In our study, we performed BIS monitoring in the patients in group 1, and we investigated the resulting effects of optimal anesthesia on neurocognitive functions in the early period. Although there are a high number of studies about BIS monitoring in the literature, there are no studies about the resulting effects of BIS monitoring on neurocognitive functions in coronary artery bypass surgery.

We determined to aim BIS values in the range from 40 to 60 during the maintenance period, considering the results of previous studies reporting that BIS values in that range provided a sufficient hypnotic effect during general anesthesia. BIS monitoring reduces the use of propofol, shortens the length of the recovery period, and decreases the use of anesthetic agents, ensuring early awakening of patients.[20,21] Anez et al. conducted a study on 39 patients undergoing vascular or orthopedic surgery and they evaluated propofol use and the time of awakening from anesthesia based on BIS data and clinical findings. They reported that propofol use was lower (8.04±2.52 mg/kg/hour vs 11.94±2.28 mg/kg/hour) and eye opening time (4.63±2.31 min vs 8.7±2.97 min) was sooner in the BIS-monitored group.[22] Considering that the extubation time was correlated with the follow-up of eye-opening time, the shorter extubation time in group 1 in our study suggested a resulting effect of BIS monitoring. Although we did not quantify the amount of propofol used for anesthesia in our study, stopping the use of propofol infusion based on BIS monitoring suggested that a lower amount of anesthetics were used compared to a routine anesthetic administration. The shorter time to extubation in group one compared to that of group 2 in our study demonstrates that our study results are in parallel to those of the abovementioned studies.

Muradlidhar et al. conducted a randomized controlled study on a total of 40 patients undergoing cardiac surgery (off-pump CABG) and they evaluated the use of isoflurane and propofol in a BIS-monitored group and a standard anesthesia group. They determined that the BIS value should be aimed to be 50.[21] They found the propofol use in the BIS and control groups as 3.38±0.99 mg/kg/hour and 5.07±0.7 mg/kg/hour, respectively. We suggest that recording extubation times are important for the value of the study. Although we did not evaluate the medication doses, the time of eye opening or the recovery time in our study; we found out that extubation time was shorter and the postoperative neurocognitive functions were better in the BIS group, considering that these findings have been in alignment with the information in the literature.

We have not quantified the intraoperative awareness risk with a scale in our study because our main aims were the evaluation of the cognitive functions and the characteristics of recovery. However, we questioned it in all of our patients postoperatively. We have not detected any findings in association with intraoperative awareness in any of our patients in either group.

Ganidağlı[23] and Guignard[24] reported in their studies that they did not find any differences in the heart rates and MAP values of the patients, who were monitored with BIS. There were no differences in the heart rates in our study; however, the MAP values were higher in the patients in group 1. There are only a few studies in the literature, conducting BIS monitoring and comparing the intraoperative hemodynamic parameters. In our study, we observed a statistically significant change in the arterial pressure at almost all recorded time points. We consider this as a natural consequence of awakening, which may emerge during consciousness monitoring in anesthesia compared to anesthesia based on monitoring of the hemodynamic parameters.

Cognitive dysfunctioning can be seen at a rate of 40-60% after major cardiac surgery.[25] Temporary delirium and confusion attacks can easily be identified; whereas, less significant defects can be detected by evaluating the preoperative and postoperative functioning with the administration of standard neuropsychiatric tests developed by neuropsychiatrists.[26] We evaluated the neurocognitive functioning of our study patients using the clock drawing test and the mini mental test. We detected significant differences in both tests between the two groups, favoring the patients monitored with BIS.

Of temporary deficits developing after CPB, 80% resolve in a range from 6 months to 5 years after the surgery.[27,28] It is suggested that prolonged neurological deficits commonly result from microemboli. We found statistically significant impairments in the neuropsychiatric test results of the patients who were not monitored with BIS, especially in the tests administered at the time of discharge from the hospital. We suggest that these results will be confirmed more significantly in further more comprehensive larger-scale studies.

Among the complications of cardiac surgery, neurologic complications predominate, especially in the postoperative period. Several risk factors have been suggested to explain postoperative cognitive dysfunctioning. These factors may be not only inherent to the patient but they may also be associated with the postoperative factors or with the operation itself. Among the intraoperative factors; hypotension and medications administered to the patient are listed. The postoperative factors may include infections and insufficient anesthesia administration. Although anesthesia has been demonstrated that it is not a causative factor alone, some anesthetic agents are suggested to be more commonly associated with the development of cognitive dysfunctioning. Our study results confirmed this information.

Limitations of the study

- By determining the depth of anesthesia and customized medication use for the patient needs, as well as quantifying the hypnosis as one of the main aims of anesthesia; favorably constant maintenance of anesthesia is ensured with BIS (Bispectral Index) monitoring, which is based on EEG measurements. As there were no significant differences in the total duration of operation and total duration of CPB, we could not interpret whether BIS monitoring had an impact on the outcomes.
- It should be considered that the results of the cognitive function tests may not always be concordant. Among the significant causes of obtaining different results are the differences in the mood states of the patients and the different the time intervals, in which the tests were performed.
- As the main objectives of the study were the characteristics of recovery and the assessment of the cognitive functioning, we have not assessed the intraoperative awareness risk with a scale. However, we questioned it following the operation in all patients in the ICU. We have not detected any findings in association with intraoperative awareness in any of our patients in either group.

CONCLUSION

BIS (Bispectral Index) monitoring is based on EEC recordings and it allows for ensuring favorably stable maintenance of anesthesia by determining the depth of anesthesia and optimizing the medication use customized for the needs of each patient; as well as quantifying hypnosis, which is among the main aims of anesthesia.

In conclusion, we are of the opinion that maintaining the administration of the anesthetic agent at an optimal level by means of BIS monitoring will have a favorable effect on the clinical course of the patient both intraoperatively and postoperatively; and it will create significantly positive differences in the neurocognitive tests both clinically and statistically.

REFERENCES

1. Bokesch PM. Brain injury and brain protection. In EstafanousFg, Barash PG, Reves JG. Cardiac Anesthesia: Principles and Clinical Practice, 2nd edition, Philadelphia: Lippincott Williams & Wilkins, 2001:p465-475.
2. Cook DJ. Neurologic effects. In: Gravlee GP, Davis RF, Kurusz M, Utley JR, editors. Cardiopulmonary bypass - principles and practice. Philadelphia: Lippincott Williams & Wilkins; 2000: 403-31.
3. Tuman KJ, McCarthy RJ, Najafi H and Ivankovich AD. Differential effects of advanced age on neurologic and cardiac risks of coronary artery operations. J Thorac Cardiovasc Surg.1992; 104: 1510-1517.

   https://doi.org/10.1016/S0022-5223(19)33877-2
4. Murkin J: Protection of the brain during cardiac surgery. In: Hensley FA, Martin DE, Gravlee GP. Cardiac Anesthesia. 4th edition Philadelphia, USA 2008; 626-640.
5. Rasmussen LS, Christiansen M, Eliasen K, Sander-Jensen K and Moller JT. Biochemical markers for brain damage after cardiac surgery-time profıle and correlation with cognitive dysfunction. Acta Anaesthesiol Scand. 2002; 46: 547-551.

   https://doi.org/10.1034/j.1399-6576.2002.460512.x
6. Grocott HP and Stafford-Smith M. Organ protection during cardiopulmonary by pass In: Kaplan JA, Reich DL. Kaplan's Cardiac Anesthesia. 5th edition. Philadelphia, USA. 2006;30: 985-996.
7. Johansen JW. Update on Bispectral Index monitoring Clinical Anaesthesiology. 2006; 20: 81-99.

   https://doi.org/10.1016/j.bpa.2005.08.004
8. Marais ML, Maher MV and Wether B. Reduced demand on recovery room resources with propofol compared to thiopental isoflurane. Anaesthesiology. 1989; 16: 28-40.
9. Edmonds H, Rodriguez RA, Audenaert SM, Austin EH, Pollock SB and Ganzel BL. The role of neuromonitoring in cardiovascular surgery. J Cardiothorac Vasc Anesth 1996; 10: 15-23.

   https://doi.org/10.1016/S1053-0770(96)80174-1
10. Stanski DR. Monitoring depth anesthesia. In: Miller RD (ed). Anesthesia Churchill Livingstone Inc, New York, 2000: 1087–116.
11. Ravaglia G, Forti P, Maioli F, Arnone G, Pantieri G, Cocci C, et al. The clock-drawing test in elderly Italian community dwellers: associations with sociodemographic status and risk factors for vascular cognitive impairment. Dement Geriatr Cogn Disord 2003; 16:287-295.

    https://doi.org/10.1159/000072815
12. Nagahama Y, Okina T,Nabatame H, Matsuda M, Murakami M, et al. Clock drawing in dementia: its reliability and relation to

the neuropsychological measures. Rinsho Shinkeigaku 2001; 41:653-658.

13. McKhann GM, Grega MA, Borowicz LM Jr, Baumgartner WA and Selnes OA. Stroke and encephalopathy after cardiac surgery: an update. Stroke. 2006; 37: 562-571.
https://doi.org/10.1161/01.STR.0000199032.78782.6c
14. Ahonen J and Salmenperä M. Brain injury after adult cardiac surgery. Acta Anaesthesiol Scand 2004; 48: 4-19.
https://doi.org/10.1111/j.1399-6576.2004.00275.x
15. Yao FS, Tseng CC, Ho CY, Levin K and Illner P. Cerebral oxygen desaturation is associated with early postoperative neuropsychological dysfunction in patients undergoing cardiac surgery. J Cardiothorac Vasc Anesth 2004; 18: 552–558.
https://doi.org/10.1053/j.jvca.2004.07.007
16. Murkin JM. Neurocognitive outcomes: the year in review. CurrOpinAnaesthesiol 2005; 18: 57-62.
https://doi.org/10.1097/00001503-200502000-00010
17. Miller's Anesthesia 2010 Seventh Edition, Editor Ronald D. Miller. Churchill Livingstone Elsevier Philadelphia, USA 1229-1232.
18. Morgan GE, Mihail MS and Murrey MJ. Nonvolatile anesthetic agents. In: Morgan GE, Mihail MS, Murrey MJ(editors) Clinical Anesthesiology. Newyork, Lange medical books/Mc Graw-Hill Medical publishing division, 2002; 151-177.
19. Tuman KJ, McCarthy RJ, Najafi H and Ivankovich AD. Differential effects of advanced age on neurologic and cardiac risks of coronary artery operations. J Thorac Cardiovasc Surg. 104;1510-1517.
https://doi.org/10.1016/S0022-5223(19)33877-2
20. Gan TJ, Glass PS, Windsor A, Payne F, Rosow C, Sebel P, et al. Bispectral index monitoring allows faster emergence and improved recovery from propofol, alfentanil, and nitrous oxide anesthesia. BIS Utility Study Group. Anesthesiology. 1997; 87:808-815.
https://doi.org/10.1097/00000542-199710000-00014
21. Muralidhar K, Banakal S, Murthy K, Garg R, Rani GR and Dinesh R. Bispectral index-guided anaesthesia for off-pump coronary artery bypass grafting. Annals of Cardiac Anaesthesia. 2008;11(2):105-110.
https://doi.org/10.4103/0971-9784.41578
22. Anez C, Papaceit J, Sala JM, Fuentes A and Rull M. The effect of encephalogram bispectral index monitoring during total intravenous anesthesia with propofol in outpatient surgery. Revista Espanola de Anestesiologia y Reanimacion 2001;48(6):264-269.
23. Ganidağlı S, Demirbilek S, Baysal Z, Kılıç İH and Becerik C. Anesthesia depth and bispectral index monitoring. Journal of Anesthesia. 2001; 9: 260-264.
https://doi.org/10.5152/TJAR.2013.48
24. Guignard B, Menigaux C, Dupont X, Fletcher D and Chauvin M. The Effect of Remifentanil on the Bispectral Index Changeand Hemodynamic Responses After Orotracheal Intubation. Anesth Analg. 2000; 90:161-167.
https://doi.org/10.1097/00000539-200001000-00034
25. Moller JT, Cluitmans P, Rasmussen LS, Houx P, Rasmussen H, Canet J, et al. Long-term postoperative cognitive dysfunction in the elderly ISPOCD1 study. ISPOCD investigators. International Study of Post-Operative Cognitive Dysfunction. Lancet. 1998; 351: 857-861.
https://doi.org/10.1016/S0140-6736(97)07382-0
26. Doğancı S. Organ damage. Ed. UfukDemirkılıç. Extracorporeal circulation. 1st edition. Ankara; 2008, 133-145.
27. Keçeligil HT. Intensive Care After Adult Heart Surgery. In: Duran E, ed. Cardiovascular Surgery. Çapa Medical Bookstore. İstanbul 2004:1133-1149.
28. Postoperative Care. In: Kirklin/Barratt-Boyes Cardiac Surgery: morphology, diagnostic criteria, natural history, techniques, results and indications 3rd ed. Kouchoukos et al, Philadelphia, Pa: Elselvier Science, 2003:p.195-253.

Author's Contributions
IE - Concept and design of the study; prepared first draft of manuscript; reviewed the literature; ınterpreted the results; **FB -** Concept and design of the study;prepared first draft of manuscript; reviewed the literature; revision of the manuscript; **CC -** Review of literature and manuscript preparation; **MOH -** Statistically analysed and interpreted; revision of the manuscript; **IM-** Concept and coordination of the overall study, reviewed the manuscript preparation.

Work attributed to:
Ahi EvrenThoracic Cardiovascular Surgery Education and Research Hospital, Trabzon, Turkey.

Orcid ID:
Dr.İzzet Emir - https://orcid.org/0000-0002-1098-4889
Dr.Ferhat Borulu - https://orcid.org/0000-0001-9731-9998
Dr.Ceyhun Coşkun - https://orcid.org/0000-0001-9106-1113
Dr.Muhammed Onur Hanedan - https://orcid.org/0000-0002-8363-7861
Dr. Mataracı İlker - https://orcid.org/0000-0002-7853-3144

Source of funding: Nil, **Conflict of Interest:** None declared.