SANATORIUM
Medical Journal

Original Article

Effect of Monitoring with Bispectral Index (BIS) on Depth of Anaesthesia and Recovery in Sevoflurane and Isoflurane Anaesthesia

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Abstract

Aim: We aimed to evaluate the effect of bispectral index (BIS) monitoring on anaesthesia depth and recovery in patients undergoing thoracic surgery under sevoflurane and isoflurane anaesthesia.

Material Method: After the hospital ethics committee approval, sixty ASA class I-II and the ages between 20-60 years elective thoracotomy patients were randomly divided into four groups; Group 1: Sevoflurane-Control, Group 2: Sevoflurane-BIS, Group 3: Isoflurane-Control, and Group 4: Isoflurane-BIS. Invasive arterial pressure and BIS monitorization were performed with standard anaesthesia guidelines. After midazolam premedication, standard anaesthesia induction was performed. However, in the groups where BIS monitorization was performed, sevoflurane and isoflurane were adjusted to provide 45-55 BIS values during the operation and 60-75 in the last 15 minutes of the surgery. The initial parameters, BIS, end-tidal carbon dioxide ($EtCO_2$), fractioned inspired volatile anaesthetic concentration (FiVAC), end-tidal volatile anaesthetic concentration (ETVAC), minimum alveolar concentration (MAC) values, total additional fentanyl and vecuronium bromide doses, time to respond to a verbal stimulus after anaesthetic gas was interrupted, durations of extubation, orientation, and recovery of the patients were recorded. In addition, they were asked whether they remembered anything about the operation 24 hours later postoperatively.

Results: No significant difference was found between intraoperative hemodynamic data, FİVAC, ETVAC, MAC values, and BIS values between the groups ($p > 0.05$). No difference was found from the point of view of time for response to verbal stimulus, extubation, orientation, and recovery between the control and BIS groups, and none of the subjects remembered anything about the operation 24 hours later postoperatively.

Conclusion: Our study showed that adequate depth of anaesthesia was achieved in both the control and BIS groups BIS monitoring was not found to improve quality of awakening and recovery. It was thought that BIS monitoring might be useful for those with less clinical experience rather than for experienced anaesthesiologists.

Keywords
Sevoflurane, Isoflurane, Bispectral Index (BIS), Recovery

Article process:
Submitted: 21-03-2025
Revised: 26-03-2025
Accepted: 28-03-2025
Published: 01-05-2025

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Cite as: Uluçınar E, Tunç M, Alagöz A, İbiş F, Ulus F, Karslıoğlu O, Sazak H. Effect of Monitoring with Bispectral Index (BIS) on Depth of Anaesthesia and Recovery in Sevoflurane and Isoflurane Anaesthesia. Sanatorium Med J 2025;1 (1): 37-44

Access website of SMJ

Introduction

A balanced general anaesthesia consists of hypnosis, analgesia and a still surgical field [1]. Although we can monitor the inspired and expired concentrations of anaesthetics, these measurements do not provide insights into pharmacodynamic parameters, such as the depth of hypnosis. It remains unclear whether patient FIVAC responses, like hypertension or movement, are due to insufficient hypnosis or inadequate analgesia [2,3].

The Bispectral Index (BIS) is a processed electroencephalography (EEG) parameter designed to assess the hypnotic effects of anaesthetic and sedative drugs on the brain. As the depth of anaesthesia increases, the amplitude of the EEG waves increases and the frequency decreases. The BIS value is calculated using the time, frequency and bispectral axis parameters after the artifact-free waves. Intraoperative monitoring facilitates measurement of depth of anaesthesia and titration of anaesthesia. It evaluates the levels of sedation, loss of consciousness, and recall [4,5]. The BIS scale ranges from 0 to 100 (0, no cortical activity or coma; 40-60, general anaesthesia; 70-90, various levels of conscious sedation; 100, fully awake). Research indicates that using BIS can lead to reduced drug dosages, decreased awareness during surgery, improved postoperative alertness, faster awakening times without an increase in undesirable clinical responses, shortened recovery periods, and overall reduced hospital expenses [4,6,7].

The hypothesis is that BIS values are similar in general anaesthesia induced with sevoflurane and isoflurane was changed from included to maintained. The primary outcome of our study was to investigate the effect of BIS monitoring on depth of anaesthesia and recovery in patients undergoing thoracotomy with sevoflurane and isoflurane anaesthesia.

The secondary outcome was to evaluate the minimal alveolar concentration (MAC), the fractionated inspired volatile agent concentrations (FiVAC) and the expired volatile agent concentration (ETVAC) parameters of these two agents at similar BIS values.

Material and Method

Setting and populations

The study was initiated with the approval of the Ethics Committee of Atatürk Chest Diseases and Thoracic Surgery Training and Research Hospital (decision dated 04.06.2004 and numbered 82) and the consent of the patients.

Sixty patients aged 20-60 years, randomly selected from the ASA I-II risk group, were included in the study. Participants scheduled for elective thoracotomy for non-cardiac thoracic surgery were informed about the study during their preoperative visit one day before the procedure. Informed consent was obtained during this evaluation. Patients with renal failure, hepatic dysfunction, cardiac disease, hypertension, history of chronic drug use, electrolyte imbalances, central nervous system disorders, psychiatric disorders, pregnant women and patients with difficult intubation were excluded.

Monitorization and Follow-up

During the surgery, we monitored and recorded several parameters, including ECG, mean blood pressure (MBP), peripheral oxygen saturation (SpO_2), and Bispectral Index (BIS) values (using the BISTM Quatro Monitor, Aspect Medical Systems, 2003, USA, EU). We also measured the end-tidal CO_2 concentration ($ETCO_2$) and MAC values (Dräger, Primus). For BIS monitoring, the skin on the forehead and temples was cleaned with an alcohol swab and allowed to dry. The four electrodes of the disposable BIS sensor were then placed at the appropriate points.

The BIS values the timing as follows: T1: before premedication, T2: before induction, T3: one minute after induction, T4: three minutes after intubation, T5: after the skin incision, T6: during retractor placement, T7-18: every five minutes for one hour after the retractor is placed, T19: fifteen minutes before the end of surgery, T20: ten minutes before the end of surgery, T21: five minutes before the end of surgery, T22: at the end of surgery, T23: response to verbal stimulation, T24: at extubation, T25 when orientation is achieved, and T26: when recovery is achieved.

For premedication, all patients received 1 mg of midazolam intravenously 10 minutes before induction. Following preoxygenation, each patient was administered 2 μg/kg of fentanyl, 2 mg/kg of propofol, and 1 mg/kg of 2% lidocaine intravenously for anaesthesia induction. Invasive arterial blood pressure monitoring was conducted via the radial artery. Intubation occurred 3 minutes after administering 0.1 mg/kg of vecuronium bromide intravenously as a muscle relaxant. After the third minute of intubation, patients were randomly divided into four groups for maintenance of anaesthesia as follows: Group 1: Sevoflurane-Control, Group 2: Sevoflurane-BIS, Group 3: Isoflurane-Control, and Group 4: Isoflurane-BIS.

In the control groups, FiVAC of sevoflurane and isoflurane were adjusted based on hemodynamic and superficial anaesthesia observations, such as the presence of tears, sweating, eye-opening, swallowing, and movement. Anaesthetic adjustments were made in response to a 30% increase or decrease in heart rate (HR) and a 20% increase in mean blood pressure (MBP) from the initial values. In the groups monitored with BIS, FiVAC values were adjusted to maintain a BIS score within the range of 45-55. To minimize bias from the investigator, the entire control group was studied first, followed by the BIS group, without randomizing the cases.

The FiVAC, ETVAC, and MAC values are numbered as follows: T1: 3 minutes after intubation, T2: immediately after skin incision, T3: when the retractor is placed, T4-15: every 5 minutes for 1 hour after the retractor is placed, T16: 15 minutes before the end of surgery, T17: 10 minutes before the end of surgery, T18: 5 minutes before the end of surgery, T19: at the end of surgery, T20: response to verbal warning, T21: at extubation, T22: when orientation is achieved, and T23: when recovery is achieved.

The patients received 50-100% oxygen along with sevoflurane at a concentration of 1-2% and isoflurane at 0.5-2%, with a fresh gas flow rate of 4 L/min. In the control groups, the FiVAC was maximized, with sevoflurane and isoflurane both at 2%. In the groups monitored by BIS, the score ranged from 45 to 55. When hemodynamic changes occurred specifically if the heart rate exceeded 30% of the baseline value or mean blood pressure (MBP) exceeded 20% of the baseline value-50 µg of fentanyl was administered. Muscle relaxation was maintained with 0.03 mg/kg of vecuronium bromide. The total doses of additional fentanyl and vecuronium bromide were recorded.

All patients were ventilated using controlled mechanical ventilation to maintain an end-tidal CO2 concentration (EtCO2) between 35% and 40%. Atropine at a dose of 0.5 mg was administered to patients experiencing bradycardia (heart rate below 45 beats per minute), while fluid replacement and intravenous ephedrine at 10 mg were provided for patients with hypotension (mean arterial pressure below 60 mm Hg). In groups 2 and 4, sevoflurane and isoflurane concentrations were reduced to a BIS of 60-75 fifteen minutes before the end of the operation, and these agents were discontinued when the last skin suture was placed. In the control groups (groups 1 and 3), sevoflurane and isoflurane were gradually reduced according to standard anaesthesia practice as skin sutures began and were turned off when the last skin suture was placed. After the patients resumed spontaneous breathing, they received 1.5 mg of neostigmine and 0.5 mg of atropine intravenously to reverse the effects of muscle relaxants. Patients were extubated as soon as their breathing was adequate, and their laryngeal reflexes returned to normal.

The time taken from the cessation of anaesthetic gas until the patient responded to verbal commands was recorded as the response time to verbal stimuli. The duration until extubation was noted as the extubation time. The time taken for the patient to state their name, surname, age, and location was recorded as the orientation time. Additionally, the time when the Modified Aldrete score [8] reached 9-10 was documented as the recovery time. The patients were also asked whether they remembered anything about the operation 24 hours post-surgery.

Statistical Analysis

Data were recorded on a computer using SPSS for Windows version 11.5 and subsequently analysed. The Kruskal-Wallis Test was employed to evaluate demographic data, as well as operation and anaesthesia times. The Mann-Whitney U Test was used to assess response times to verbal stimuli, extubation, orientation, and recovery times. In all study groups, differences between groups, changes within groups over time, and group-time interactions were examined using Repeated Measures ANOVA. The sphericity assumption was tested with Mauchly's Test; when sphericity was not achieved, corrections were made using the Greenhouse-Geisser method. A p-value of less than 0.05 was considered statistically significant.

Results

A total of 60 patients were evaluated. The groups included 15 patients each in the following categories: control sevoflurane, BIS sevoflurane, control isoflurane, and BIS isoflurane **(Figure 1).**

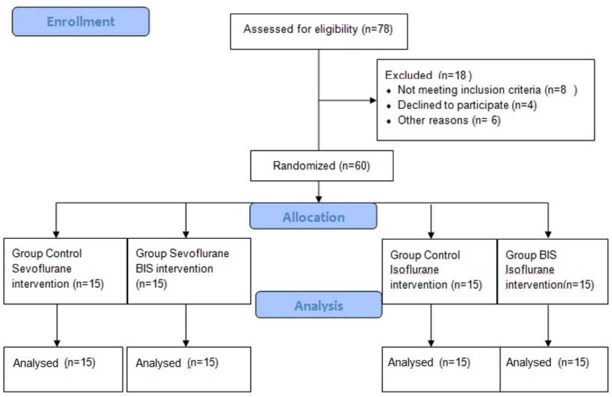

Figure 1: CONSORT diagram

There were no statistically significant differences among the groups regarding age, weight, height, or gender (p>0.05). Additionally, no significant differences were observed in anaesthesia duration or operation duration among the groups (p>0.05) **(Table 1).**

When comparing the groups, no statistically significant difference was found in total vecuronium bromide and additional fentanyl doses (p>0.05) **(Table 2).**

No statistically significant differences were identified when the mean blood pressure (MBP), cardiac output (CO) and oxygen saturation (SpO2) values were compared between the groups (p>0.05). The interaction between the groups over time was also similar (p > 0.05). Of particular note, SpO2 levels did not fall below 90% in either group.

When BIS values were analysed, no significant difference was found between the groups (p > 0.05), and the interaction over time remained similar (p > 0.05).

Table 1: Comparison of demographics, operation times, and anaesthesia duration.

	Control Sevoflurane n:15 Mean ± SD	**BIS Sevoflurane n:15** Mean ± SD	**Control Isoflurane n:15** Mean ± SD	**BIS Isoflurane n:15** Mean ± SD
Age (year)	35.67±3.983	41.07±12.538	34.53±14.909	39.93±12.859
Weight (kg)	66.13±13.596	69.47±15.720	67.53±14.332	74.20±12.718
Height (cm)	168.47±8.927	165.47±9.433	168.67±8.499	171.53±6.266
Sex (M/F)	10/5	9/6	10/5	12/3
Duration of Surgery (min)	189.33±43.46	146.67±36.87	172.67±42.21	157.33±49.92
Duration of anaesthesia (min)	214.67±49.15	173.67±37.05	200.67±46.59	184.00±47.59

Data presented as Mean ± SD. **BIS:** Bispectral index

Table 2: Comparison of groups in terms of total vecuronium bromide and additional fentanyl doses used.

	Control Sevoflurane Mean ± SD	**BIS Sevoflurane** Mean ± SD	**Control Isoflurane** Mean ± SD	**BIS Isoflurane** Mean ± SD	**p value**
Fentanyl (μgr)	116.67±44.98	125.33±92.88	76.67±49.52	113.33±63.99	0.183
Vecuronium bromide (mg)	13.73 ± 4.511	12.60 ± 3.376	12.53 ± 4.07	15.53 ± 3.482	0.116

Data presented as Mean ± SD. **BIS:** Bispectral index

However, significant changes were observed within each group. The BIS value decreased before induction and at one minute of induction in comparison to the measurement taken prior to premedication. A further increase was observed at 3 minutes following intubation, and this continued to rise at 15, 10 and 5 minutes prior to the conclusion of surgery, at the end of surgery when verbal stimulation was given, during extubation and throughout the orientation and recovery phases. These findings were statistically significant ($p < 0.05$) **(Figure-2)**.

When comparing the FiVAC values between the groups, it was observed that the FiVAC value in the BIS sevoflurane group was lower than that in the control sevoflurane group during retractor placement, which was statistically significant ($p < 0.05$). Additionally, the FiVAC value remained lower in the BIS sevoflurane group compared to the control sevoflurane group 15 minutes before the end of the surgery, also with statistical significance ($p < 0.05$). This indicates that the BIS monitoring reduced the consumption of volatile agents in the sevoflurane group.

However, no statistically significant difference was found between the FiVAC values of the isoflurane control group and the isoflurane BIS group ($p > 0.05$). Furthermore, the interaction between the groups over time was similar ($p > 0.05$) as shown in **Figure 3a.**

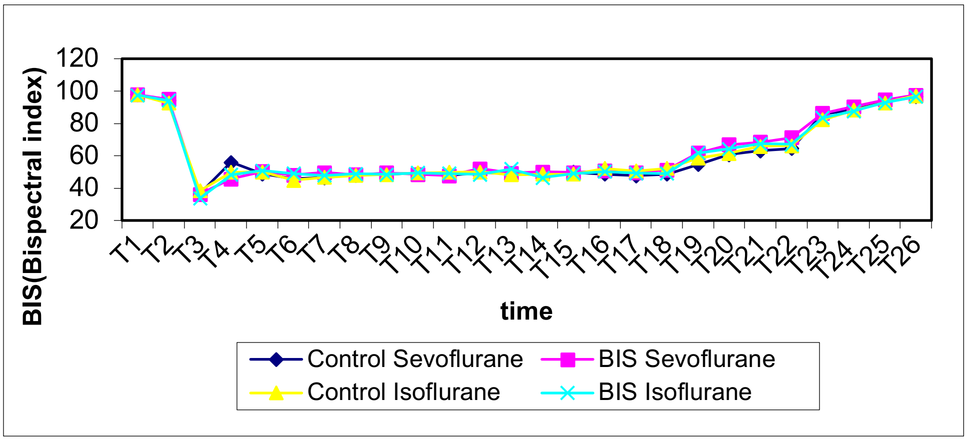

Figure 2: Mean BIS Values of the Groups.

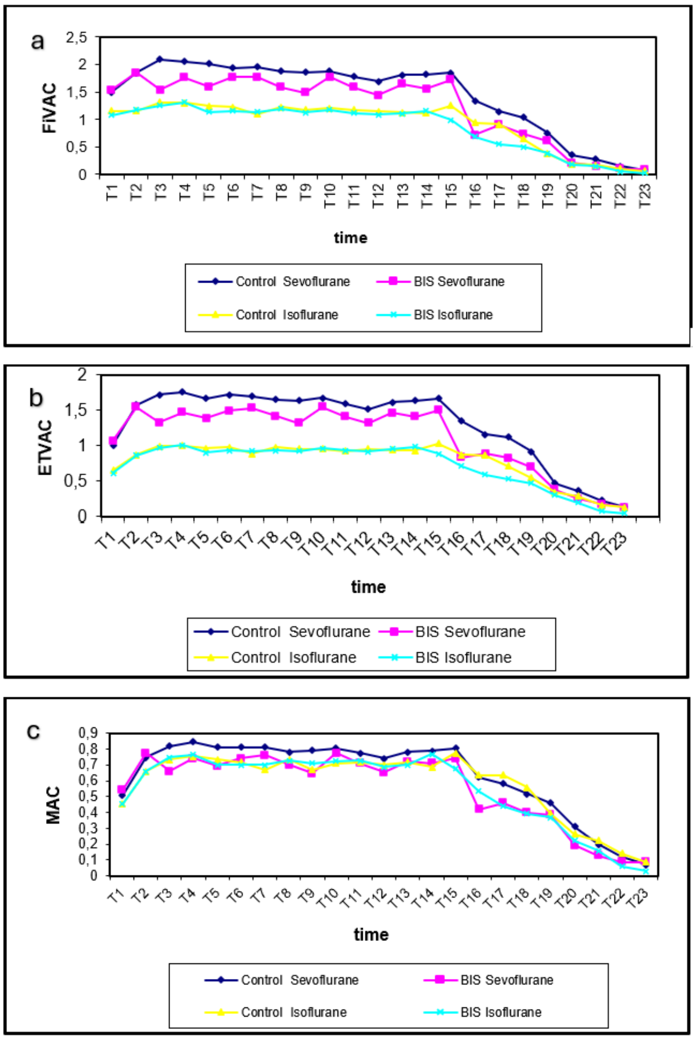

Figure 3: Average FiVAC (a), ETVAC (b), and MAC (c) values of the groups.

When comparing ETVAC values between the groups, the BIS sevoflurane group exhibited significantly lower ETVAC values than the control sevoflurane group during retractor placement ($p<0.05$). Similarly, 15 minutes before the end of surgery, the ETVAC values were also lower in the BIS sevoflurane group compared to the control sevoflurane group, which was statistically significant ($p<0.05$). In contrast, there was no statistically significant difference in ETVAC values between the isoflurane control group and the isoflurane BIS group ($p>0.05$). Additionally, the interaction of the groups over time showed no significant differences ($p>0.05$) **(Figure 3b)**.

When MAC values were compared between the groups, no significant difference was found ($p>0.05$) **(Figure 3c)**.

When comparing the groups in terms of response time to verbal stimulation and extubation time, no statistically significant difference was found ($p > 0.05$) **(Table 3).**

In terms of orientation time, the control isoflurane group had a longer duration compared to both the control sevoflurane group and the BIS sevoflurane group, which was statistically significant ($p < 0.05$). Additionally, when examining recovery time, the control isoflurane group also exhibited a longer recovery time than the control sevoflurane group and the BIS sevoflurane group, both of which were statistically significant ($p < 0.05$). Furthermore, the recovery time in the BIS isoflurane group was longer than that in the BIS sevoflurane group, reaching statistical significance ($p < 0.05$). The early recovery associated with sevoflurane will be discussed further.

Twenty-four hours after the operation, the patients were asked if they remembered anything about it, and all of them stated they did not recall anything.

Table 3: Comparison of groups concerning response to verbal warnings, extubation, orientation, and recovery times

	Control Sevoflurane n:15 Mean ± SD	**BIS Sevoflurane n:15** Mean ± SD	**Control Isoflurane n:15** Mean ± SD	**BIS Isoflurane n:15** Mean ± SD	**p value**
Time to response verbal stimulation (min)	4.87±1.88	4.13±1.80	5.60±2.58	4.47±2.29	0.346
Duration of extubation (min)	6.67±1.87	6.20±2.14	7.93±2.57	6.47±2.80	0.201
Orientation time (min)	9.87±2.35	9.33±2.22	13.40±3.96	10.80±2.70	0.008*
Duration of recovery (min)	12.93±3.30	11.67±2.66	16.13±4.30	14.20±2.85	0.005*

Data presented as Mean ± SD. **BIS:** Bispectral index

Discussion

Our study evaluated the effectiveness of BIS monitoring in two different applications of volatile anaesthetics, along with their respective control groups. The results indicated that a sufficient depth of anaesthesia was achieved in both the control and BIS groups. Ultimately, BIS monitoring did not enhance the quality of awakening and recovery. Therefore, it is suggested that BIS monitoring may not be necessary for experienced anaesthesia practitioners.

While hemodynamic responses are typically used to evaluate the depth of anaesthesia, it is important to note that these changes can sometimes be misleading [9]. Those factors such as blood volume, cardiac contractility, sympathetic tone, age, and acid-base balance also contribute to hemodynamic variations [10]. Therefore, the primary goal of titrating anaesthesia is not solely to determine the right depth of anaesthesia, but rather to minimize cardiovascular toxicity [11, 12]. Research shows that BIS monitoring effectively assesses anaesthesia depth, but it may not adequately detect autonomic responses and associated hemodynamic changes [13,14].

Gökahmetoğlu et al. [15] conducted a study on patients undergoing gynaecological surgery with inhalation anaesthesia. They stated that BIS monitoring may be useful for assessing the hypnotic effect of anaesthesia but might not effectively evaluate autonomic responses. Moreover, they concluded that there was no correlation between changes in BIS and hemodynamic responses. In the present study, the lack of change in BIS despite observable hemodynamic responses during retractor placement was consistent with these findings. Ganidağlı et al. [16] found no significant difference in the total fentanyl dose or anesthesia duration between the two groups where sevoflurane was adjusted based on FIVAC and BIS values (50&60). Similarly, our study revealed comparable results regarding the total additional fentanyl dose and anaesthesia duration across both groups, supporting the findings of researchers. In another study involving orthopaedic surgery, patients were divided into two groups: the control group, where isoflurane was titrated according to standard clinical practices, and the BIS group, where BIS was maintained between 50-60. If the heart rate exceeded 90 beats per minute during the operation or mean blood pressure (MBP) rose above 25% of the preoperative value, the researchers administered a supplemental dose of 25-50 µg of fentanyl. The results indicated that isoflurane consumption was 30% lower in the BIS group, with no differences observed between the two groups regarding muscle relaxant and fentanyl doses. Additionally, the duration for achieving an Aldrete score above 9 was shorter in the BIS group, while BIS monitoring did not appear to affect postoperative cognitive functions. In our study, we also found no statistical difference between the groups in terms of total doses of vecuronium bromide and additional fentanyl, which aligns with the findings of Wong et al. [17]. Furthermore, recovery times were similar in the control and BIS groups receiving isoflurane.

In the study conducted by Pavlin et al [18] on 236 male and 229 female patients undergoing day surgery, propofol was used for the induction of anaesthesia and sevoflurane for maintenance. Three different teams were involved in the anaesthesia administration: an anaesthesia nurse, a junior anaesthetist, and an anaesthetist with 2-3 years of experience. The patients were divided into two groups: one that utilized BIS monitoring and another that did not. Significant differences were observed between the groups, particularly with the junior anaesthetist. The difference was less pronounced with the anaesthesia nurse and was not significant with the senior anaesthetist. When BIS monitoring was not employed, junior anaesthetists tended to maintain a higher end-tidal concentration of sevoflurane compared to their more experienced colleagues. Conversely, when BIS monitoring was used, junior anaesthetists maintained a lower end-tidal concentration of sevoflurane than the senior anaesthetists. These findings suggest that BIS monitoring can assist those who are new to anaesthesia practice in reducing errors related to adjusting the depth of anaesthesia. As a result, the study reported a 13% reduction in anaesthetic consumption for both women and men, along with an 11% faster recovery in men. In our study, which was conducted by senior anaesthesiologists, we found that in the control group using sevoflurane, the ETVAC values were higher than in the BIS group. However, this difference was not significant. We believe that experience plays a crucial role in the titration of inhalational agents during the maintenance of anaesthesia. The observed variations in FiVAC, ETVAC, and MAC values at only a few time points, along with no differences in BIS levels, support this conclusion.

During surgery, events can be recalled due to insufficient anaesthesia when the hypnotic level is not continuously monitored. While complete amnesia is associated with adequate anaesthesia, patients may remember dreams under lighter anaesthesia, and awareness can occur even at a more superficial level. [19,20]. Many patients often hesitate to share their experiences unless prompted. It's important to recognize that they may not remember certain events immediately following surgery, but their recollections can emerge in the weeks that follow [21].

In our study, when patients were asked 24 hours post-operation if they heard conversations, voices, or experienced dreams during the procedure, they reported no memories of anything that occurred. All patients indicated that they remembered the conversations we had when they woke up or while in intensive care. Our study found no differences between the groups regarding awareness.
Our study has several limitations that should be acknowledged. Firstly, it was conducted at a single centre with a relatively small number of patients. The study included patient groups who underwent thoracotomy. Studies evaluating the effects of BIS monitoring in different types of surgery should be conducted. To obtain more reliable results, larger multicentre studies are needed. Although we collected data on awareness, we were unable to assess long-term cognitive functions and delirium. Additionally, the study was carried out solely by anaesthesiologists with a specific level of experience, which may limit the generalizability of our findings to all anaesthesiologists.

Conclusion

In conclusion, our control groups, where the concentration of volatile agents was adjusted according to standard clinical practices, showed no significant differences in intraoperative hemodynamic data, FiVAC, ETVAC, MAC values, or BIS values. There were also no differences between the control and BIS groups regarding response times to verbal stimulation, extubation, orientation, and recovery times. Furthermore, none of the cases recalled the operation 24 hours post-surgery, indicating that adequate anaesthesia depth was achieved in both the control and BIS groups. These results suggest that BIS monitoring does not enhance the quality of awakening and recovery. We believe that experienced anaesthesiologists may not require BIS monitoring, while those with less clinical experience might find it helpful for adjusting the depth of anaesthesia.

Author contribution statement

All authors (EU, MT, AA, Fİ, FU, OK, HS) participated in the planning, writing, editing, and review of this manuscript.

Conflicts of interest

All the authors declare that they have no financial or personal relationships with other people or organizations that could potentially and inappropriately influence (bias) their work and conclusions.

Ethical approval

The study was initiated with the approval of the Ethics Committee of Atatürk Chest Diseases and Thoracic Surgery Training and Research Hospital (decision dated 04.06.2004 and numbered 82) and the consent of the patients.

Acknowledgement

None

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