

## Bispectral Index Monitoring and Combinations in Anesthesia Safety

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**Abstract:** Anesthesia should ideally provide adequate hypnosis, analgesia and a suitable environment for surgery. Monitoring the depth of anesthesia is recommended to reduce awareness during anesthesia and improve the administration of anesthetic drugs. Bispectral index (BIS) is a numerical scale based on the analysis of electroencephalogram (EEG) parameters and can reduce the adverse effects associated with over- or under-dosing of anesthetic drugs. BIS monitoring may also provide cost-related advantages, with values between 40 and 60 for BIS indicating adequate depth of anesthesia during the surgical procedure. BIS is the most widely studied and best documented cerebral monitoring method. It can be used in monitoring the depth of sedation in intensive care patients, monitoring EEG suppression in patients with increased intracranial pressure, diagnosis of brain death, and neurologic evaluation after resuscitation. This summary is based on selected literature on BIS monitoring and its combination with other monitoring methods over the last 20 years. ©2024 NTMS.

**Keywords:** Anesthesia General; Bispectral Index; Monitoring; Intraoperative.

## 1. Introduction

The first official endorsement date for brain function monitoring in anaesthesia safety is October 2005. On this date, the House of Delegates of the American Society of Anesthesiologists approved the "Practice Advisory for Intraoperative Awareness and Brain Function Monitoring" <sup>1</sup>. This document recommends risk assessment for patients and the resulting use of cerebral function monitors on a case-by-case basis. Although cerebral function monitors are not included in standard anaesthetic monitoring, it is recommended that they be used in conjunction with other monitoring methods to improve patient safety. Although there are multiple methods for cerebral function monitoring, Bispectral Index (BIS) monitoring is the most widely researched and used method (Fig. 1).

BIS was developed by Aspect Medical Systems in 1985 to quantitatively evaluate the sedative and hypnotic effects of anaesthetic drugs and includes electroencephalogram (EEG) parameters. It was approved by the Food and Drug Administration in 1996 <sup>2</sup>.

The BIS monitor is based on four electrodes placed on the forehead to measure the electromyographic activity of the frontalis muscle (Fig. 2). The BIS monitor collects EEG data and uses an algorithm to analyse it. BIS values range from 0 to 100. A value of 0 indicates an isoelectric EEG with complete suppression of brain activity, while a value of 100 indicates that the patient is awake. Values between 40-60 define the level of immobility and hypnosis required for general

anaesthesia. Below 40 indicates a deep hypnotic state<sup>3</sup>. BIS monitoring can be used for anaesthesia safety in the operating room, sedation assessment in intensive care, neurological status assessment in non-sedated patients and follow-up of patients with possible brain death.



**Figure 1:** BIS monitör

The reasons why new intraoperative haemodynamic monitoring methods have not been included in anaesthesia standardisation in parallel with technological progress are undoubtedly cost and lack of sufficient evidence level. We aimed to answer the question "where is BIS monitoring in anaesthesia safety from past to present? We conducted this literature review to seek an answer to the question.

## 2. Discussion

### 2.1. BIS monitoring and Awareness

Mindfulness can be thought of as the postoperative recall of events that occurred during general anaesthesia. However, there is no clear definition. Awareness is reported in different dimensions, while the difference in the form of questioning (structured questions versus direct questions such as "Did you feel any discomfort during the operation?") changes the data results. Therefore, studies on this topic are still controversial. It is not clear whether cerebral monitoring should be included in standard anaesthetic monitoring.

Awareness under anaesthesia is a highly traumatic experience for patients. Studies have shown that patients can have a state of recall even without changes in haemodynamic parameters<sup>4</sup>. Therefore, we may not be able to prevent awareness with standard anaesthesia monitoring. In BIS monitoring, values below 60 are indicative of the level of hypnosis as well as the immobility required for surgery. Monitoring the BIS value throughout the operation may be a reliable method to prevent awareness.

Studies on the effects of BIS monitoring on awareness date back about 30 years. In a meta-analysis published in 2004, the frequency of anaesthesia awareness was found between 0.1% and 0.2% of all patients

undergoing general anaesthesia in many studies<sup>5</sup>. In 2002, Bergman et al. examined 8372 patients receiving general anaesthesia and reported 81 cases in which perioperative recall was compatible with awareness. After examination of the cases, they found that 36 patients experienced awareness due to inadequate hypnosis due to inadequate volatile anaesthetic concentration, 32 patients experienced awareness due to medication error (pre-induction neuromuscular paralysis), and 13 patients had no apparent reason for awareness<sup>6</sup>. These results suggest that the majority of awareness cases (44%) were due to inadequate depth of anaesthesia and thus could be prevented by monitoring of BIS. The limitations of this analysis are the biases introduced during the use of The Anaesthetic Incident Monitoring Study (AIMS). Data interpretations may be subjective due to the non-standardized narrative in the definition of awareness.

Ekman et al. followed 4945 patients receiving general anaesthesia with BIS monitoring with a BIS value between 40-60 and used 7826 patients without BIS monitoring as a control group. Compared to the control group, the incidence of recall decreased by 77% in the group using BIS<sup>7</sup>.



**Figure 2:** BIS sensor.

Myles et al. examined 2463 patients in a multicenter study. 1225 adult patients were randomized to general anaesthesia with BIS guidance and 1238 patients were randomized to general anaesthesia with routine practice. Patients were evaluated 2 to 6 hours, 24 to 36 hours and 30 days after surgery using a blinded observer. There were 2 reports of awareness in the BIS-guided group and 11 in the routine group. The risk of anaesthesia awareness was reduced by 82% with BIS guidance<sup>8</sup>. In both studies, haemodynamic parameters were used to guide the use of anaesthetic drugs in the non-BIS group. Avidan et al. randomly divided 2000 patients into two groups to reduce anaesthesia awareness in high-risk patients. Patients receiving BIS and anaesthetic agent concentration (ETAC) guided anaesthesia were compared. Postoperative patients were evaluated at intervals (0 to 24 hours, 24 to 72 hours and 30 days after extubation) for anaesthesia awareness. In the BIS and

ETAC groups, 967 and 974 patients were evaluated, respectively. Two definite cases of anaesthetic awareness occurred in each group<sup>9</sup>. This study does not support routine BIS monitoring as part of standard practice, unlike other studies which have shown that anaesthetic awareness is reduced with BIS monitoring. In 2011, Avidan et al. increased the number of patients and centres to overcome the limitations of their previous study and again included patients at high risk for awareness. They performed a randomised controlled trial on 6041 patients without using awareness minor risk factors. By configuring the ETAC protocol, they compared the two methods by monitoring 2852 patients with standard monitoring of ETAC (ETAC < 0.7 or) and 2861 patients with BIS monitoring (BIS kept between 40-60), and reported 7 cases of definite intraoperative awareness in the BIS group and 2 cases in the ETAC group<sup>10</sup>. In this study, the superiority of the BIS protocol could not be demonstrated. Contrary to expectations, fewer realisation cases occurred in the ETAC group. In both studies, the ETAC protocol was not associated with an increase in postoperative mortality or the amount of anaesthetic agent administered.

Sudhakaran et al. divided 70 patients undergoing thoracolumbar spine surgery into 2 groups and studied the depth of anaesthesia and recovery characteristics. In this study, in which they compared BIS and ETAC monitoring, there were significant reductions in awake time, extubation time and name recall time in both groups.

BIS-guided anaesthesia was also associated with reduced time to discharge from the PACU. After 24 hours, none of the patients assessed for awareness complained of awareness, but the study did not specify criteria for assessment of awareness<sup>11</sup>. Considering how low the incidence of awareness is, we do not think it is meaningful to evaluate it in such a small group.

In conclusion, the lack of a clear definition of awareness in the studies on awareness and the use of different methods in its determination, the use of general patient population in some studies and selected high-risk patients in others, the use of hemodynamic parameters as a control group in some studies and ETAC in others may have led to different results. Intraoperative awareness is rare and difficult to detect. Although there is evidence that the use of BIS has positive effects on awareness and early recovery, the level of certainty is low.

## 2.2. Effect of BIS Monitoring on Anesthetic Consumption

The use and control of the appropriate dose of anesthetic agents during the operation is under the control of the anesthesiologist. Improving the use of anesthetic agents is important both in terms of anesthesia safety and cost. Its effect on anesthetic agent consumption makes BIS monitoring valuable in terms of the potential harm of the agents used.

Wong et al, randomly divided 68 patients over 60 years of age who would undergo orthopedic surgery under general anesthesia into 2 groups and examined the effects of BIS monitoring on the recovery profile. In the group not monitored with BIS, they titrated the isoflurane concentration according to clinical practice, and in the BIS group, they titrated it to keep the BIS value between 50-60. Although there was no difference in postoperative cognitive dysfunction between the two groups, total isoflurane use was 30% lower and recovery was significantly faster in the BIS group<sup>12</sup>.

In a large meta-analysis of randomized, controlled trials, examined 1380 outpatients from 11 different studies who were monitored with BIS versus standard practice. BIS monitoring significantly reduced anesthetic use by 19%<sup>13</sup>.

In the B-Aware, B-Unaware and BAG-RECALL studies, there was no significant difference between volatile anesthetic concentrations in patients followed with BIS monitoring and control group patients<sup>8, 10, 14</sup>. In studies with propofol, there are studies showing that BIS monitoring can significantly reduce propofol administration<sup>8, 15</sup>.

In a randomised controlled trial by Chan et al. in 921 non-cardiac surgery patients, BIS-guided anaesthesia reduced propofol use by 21% and volatile anaesthetic use by 30%<sup>16</sup>.

In a meta-analysis, BIS-guided anaesthesia reduced both the need for propofol and the need for volatile anaesthetics (desflurane, sevoflurane, isoflurane)<sup>17</sup>.

There is evidence that the use of BIS monitoring in addition to standard anaesthetic monitoring may prevent both overly deep anaesthesia and inadequate anaesthesia by keeping the depth of anaesthesia constant throughout the operation, but studies are conflicting as to whether it would be beneficial in terms of anaesthetic consumption.

## 2.3. Effects on Postoperative Outcomes

The quality of recovery and incidence of nausea and vomiting in the period after awakening from general anaesthesia show a strong dose-dependent relationship with the degree of exposure to inhalation anaesthesia<sup>18</sup>. In a metanalysis, BIS-guided anaesthesia reduced postoperative nausea and vomiting compared with routine protocols. Regardless of the anaesthetics used, it decreased eye opening time, response to verbal command, extubation time and orientation time, and length of stay in the postanesthesia care unit (PACU)<sup>17</sup>.

However, Pavlin et al. showed in a large, randomized clinical trial that although BIS monitoring was associated with a slight reduction in sevoflurane administration, it had no effect on faster recovery and PACU length of stay<sup>19</sup>.

Similarly, analyses from the BAG-RECALL and B-Unaware study populations and the Michigan Awareness Control Study showed no difference in anaesthesia administration, time to discharge from the postoperative recovery area, or incidence of

postoperative nausea and vomiting when BIS guidance was used compared with controls<sup>10, 14, 20</sup>. In a study of 402 patients, it was reported that when BIS monitoring and ETAC monitoring were compared, there was no difference between extubation and recovery times in the two groups of patients<sup>21</sup>.

Since it is not clear that BIS-guided anesthesia provides dose titration, its effect on early recovery findings is also controversial.

#### 2.4. Combinations of BIS Monitoring

BIS monitoring can be applied in combination with many monitoring methods used for patient safety. In studies conducted with different combinations, it is thought that the monitoring method selected according to the operation may increase safety when used in combination with BIS.

Vakil et al. conducted a study evaluating the safety and efficacy of monitored anaesthetic care in pleuroscopy to assess whether end-tidal capnography and bispectral index (BIS) monitoring during propofol sedation reduces the risk of complications<sup>22</sup>. The primary outcome of this study was the incidence of anaesthetic complications in patients undergoing pleuroscopy. Hypoxia was defined as oxygen saturation below 90% for 2 minutes and hypotension was defined as requiring vasopressors. In terms of anaesthesia-related complications, there was no significant difference between those with and without BIS monitoring. This study demonstrated the safety and efficacy of capnographic monitoring with or without BIS monitoring.

Total intravenous anesthesia (TIVA) is currently used as an alternative to inhalation anesthesia. The fact that many diagnostic and interventional procedures in children are performed outside the operating room requires sedation and/or analgesia in these settings. Although TIVA is a good choice, it is very difficult to administer an effective dose that does not cause respiratory depression. More reliable titration can be achieved by performing respiratory monitoring with oximetry and capnograph and by showing the level of sedation with BIS control<sup>23</sup>. In obese patients, it has been shown that the performance of the Target Controlled Infusion (TCI) system can be improved by administering propofol (Cp 6 µg ml<sup>-1</sup>) and remifentanyl (Ce 2 ng ml<sup>-1</sup>) under BIS guidance<sup>24</sup>.

Today, advanced infusion pumps such as TCI have facilitated TIVA applications. Absolom and Kenny took TCI applications further and developed a closed-loop anesthesia system that automatically delivers the target blood propofol concentration by BIS control. The automated closed-loop control system plays a similar role to anesthesiologist control. It can speed up the drug infusion when the need increases and slow it down when the need decreases. In standard BIS-guided studies, however, it lacks the ability to anticipate changing stimulus intensity and rapidly deliver the required dose. Closed loop systems provide better quality drug delivery. The patient's BIS value controls

the system. The target value is initially selected by the user, then the drug effect is controlled by the device and maintained close to the target value. It has been reported that the quality of recovery in the group receiving closed-loop BIS-controlled propofol infusion was more excellent than in the manually controlled group<sup>25</sup>. In a recent meta-analysis including many studies comparing closed-loop open-loop infusion systems, it has been reported that closed-loop systems reduce propofol requirements during induction, maintain the target depth of anesthesia better and shorten the recovery time<sup>26</sup>.

In a 2016 review, the combined use of cerebral oximetry and BIS monitoring during awake craniotomy was recommended due to significant pharmacokinetic/pharmacodynamic differences between individuals<sup>27</sup>.

In a study involving adult patients undergoing cardiopulmonary bypass surgery, Thudium et al. performed monitoring consisting of assessment of middle cerebral artery flow velocity using Near Infrared Spectroscopy, BIS and transcranial Doppler sonography<sup>28</sup>. Due to the inherent technical limitations of each monitoring component, a multimodal neuromonitoring combining several qualities has been proposed.

### 3. Conclusion

In conclusion, the use of advanced technologies is emerging as methods that reduce the burden of the anesthesiologist and provide standardization in the operating room environment. BIS monitoring can be combined with standard anesthesia monitoring as well as other advanced monitoring techniques. Each monitoring technique used increases the safety but also increases the cost. Therefore, more comprehensive studies are needed.

#### Limitations of the Study

Differences in the way of questioning when awareness is investigated may affect the results in the studies. Therefore, our comments on this subject may be insufficient

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#### Conflict of Interests

The authors have no conflicts of interest to declare.

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#### Author Contributions

Conception and Design of the study, Collection and/or Processing and Literature review, Writing Original Manuscript, Analysis and/or interpretation and final version and is responsible for final approval of the submitted manuscript; ETY.

#### Ethical Approval

None.

#### Data sharing statement

None.

#### Consent to participate

None.

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None.

## References

- American Society of Anesthesiologists Task Force on Intraoperative Awareness. Practice advisory for intraoperative awareness and brain function monitoring: a report by the american society of anesthesiologists task force on intraoperative awareness. *Anesthesiology*. 2006; 104(4):847-64.
- Federal Drug Administration Consumer Guide 1998 July–August. Available at: [http://www.fda.gov/fdac/departs/1998/498\\_upd.html](http://www.fda.gov/fdac/departs/1998/498_upd.html)
- Johansen JW. Update on bispectral index monitoring. *Best Pract Res Clin Anaesthesiol*. 2006; 20(1):81-99.
- Ghoneim MM, Block RI. Learning and consciousness during general anesthesia. *Anesthesiology*. 1992; 76(2):279-305.
- Sebel PS, Bowdle TA, Ghoneim MM, et al. The incidence of awareness during anesthesia: a multicenter United States study. *Anesth Analg*. 2004; 99:833-39.
- Bergman IJ, Kluger MT, Short TG. Awareness during general anaesthesia: a review of 81 cases from the Anaesthetic Incident Monitoring Study. *Anaesthesia*. 2002; 57(6):549-56.
- Ekman A, Lindholm ML, Lennmarken C, Sandin R. Reduction in the incidence of awareness using BIS monitoring. *Acta Anaesthesiol Scand*. 2004; 48(1):20-26.
- Myles PS, Leslie K, McNeil J, Forbes A, Chan MT. Bispectral index monitoring to prevent awareness during anaesthesia: the B-aware randomized controlled trial. *Lancet*. 2004; 363:1757-63.
- Avidan MS, Zhang L, Burnside BA, et al. Anesthesia awareness and the bispectral index. *N Engl J Med*. 2008; 358(11):1097-108.
- Avidan MS, Jacobsohn E, Glick D, et al; BAG-RECALL Research Group. Prevention of intraoperative awareness in a high-risk surgical population. *N Engl J Med*. 2011; 365(7):591-600.
- Sudhakaran R, Makkar JK, Jain D, Wig J, Chabra R. Comparison of bispectral index and end-tidal anaesthetic concentration monitoring on recovery profile of desflurane in patients undergoing lumbar spine surgery. *Indian J Anaesth*. 2018; 62(7):516-23.
- Wong J, Song D, Blanshard H, Grady D, Chung F. Titration of isoflurane using BIS index improves early recovery of elderly patients undergoing orthopedic surgery. *Can J Anesth*. 2002; 49:13-18.
- Liu SS. Effects of bispectral index monitoring on ambulatory anesthesia: a meta-analysis of randomized controlled trials and a cost analysis. *Anesthesiology*. 2004; 101:311-15.
- Mashour GA, Shanks A, Tremper KK, et al. Prevention of intraoperative awareness in an unselected surgical population: a randomized comparative effectiveness trial. *Anesthesiology*. 2012; 117(4):717-25.
- Zhang C, Xu L, Ma YQ, et al. Bispectral index monitoring prevent awareness during total intravenous anesthesia: a prospective, randomized, double-blinded, multi-center controlled trial. *Chinese Medical Journal*. 2011; 124:3664-69.
- Chan MT, Cheng BC, Lee TM, Gin T; CODA Trial Group. BIS-guided anesthesia decreases postoperative delirium and cognitive decline. *J Neurosurg Anesthesiol*. 2013; 25(1):33-42.
- Punjasawadwong Y, Phongchiewboon A, Bunchungmongkol N. Bispectral index for improving anaesthetic delivery and postoperative recovery. *Cochrane Database Syst Rev*. 2014;2014(6):CD003843.
- Verheecke G. Early postoperative vomiting and volatile anaesthetics or nitrous oxide. *Br J Anaesth*. 2003; 90(1):109-10
- Pavlin JD, Souter KJ, Hong JY, Freund PR, Bowdie TA, Bower JO. Effects of bispectral index monitoring on recovery from surgical anesthesia in 1,580 inpatients from an academic medical center. *Anesthesiology*. 2005; 102:566-73.
- Fritz BA, Rao P, Mashour GA, et al. Postoperative recovery with bispectral index versus anesthetic concentration-guided protocols. *Anesthesiology*. 2013; 118:1113-22.
- Chaudhuri S, Banerjee S, Chattopadhyay U, Hussain SS. Comparison of recovery times by using bispectral index monitoring versus end-tidal agent concentration monitoring in patients undergoing inhalational general anaesthesia. *Indian J Anaesth*. 2022; 66(3):161-68.
- Vakil E, Sarkiss M, Ost D, et al. Safety of Monitored Anesthesia Care Using Propofol-Based Sedation for Pleuroscopy. *Respiration*. 2018; 95(1):1-7.
- Anderson BJ, Hodkinson B. Are there still limitations for the use of target-controlled infusion in children? *Curr Opin Anaesthesiol*. 2010; 23(3):356-62.
- Albertin A, Poli D, La Colla L, et al. Predictive performance of 'Servin's formula' during BIS-guided propofol-remifentanil target -controlled infusion in morbidly obese patients. *Br J Anaesth*. 2007; 98:66-75.
- Struys M, De Smet T, Versichelen LF, Van De Velde S, Van den Broecke R, Mortier EP. Comparison of closed-loop controlled administration of propofol using Bispectral Index as the controlled variable versus "Standart Practice" controlled administration. *Anesthesiology*. 2001; 95:6-17.
- Pasin L, Nardelli P, Pintaudi M, et al. Closed-Loop Delivery Systems Versus Manually Controlled Administration of Total IV Anesthesia: A Meta-

- analysis of Randomized Clinical Trials. *Anesth Analg.* 2017 Feb;124(2):456-64.
27. Badenes R, García-Pérez ML, Bilotta F. Intraoperative monitoring of cerebral oximetry and depth of anaesthesia during neuroanaesthesia procedures. *Curr Opin Anaesthesiol.* 2016; 29(5): 576-81.
28. Thudium M, Heinze I, Ellerkmann RK, Hilbert T. Cerebral Function and Perfusion during Cardiopulmonary Bypass: A Plea for a Multimodal Monitoring Approach. *Heart Surg Forum.* 2018; 21(1):E028-E035.



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