

# Comparative Efficacy of Bispectral Index Monitoring and Clinical Assessment in The Recovery of Patients Undergoing Open Renal Surgery: A Randomized, Double-Blind Study

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## Abstract

**Background and Aims:** Maintaining the sufficient depth of anesthesia with an adequate anesthetic drug dosage in patients undergoing surgery is one of the most significant issues. Inadequate depth of anesthesia can cause significant disturbances in hemodynamic parameters. In this study, clinical assessment and bispectral (BIS) index monitoring compare the depth of general anesthesia and recovery time in patients undergoing open renal surgery.

**Method:** In this double-blind, randomized, controlled trial, all patients undergoing open renal surgery were enrolled and randomly divided into a BIS group and clinical assessment group (control). In the BIS group, the electrodes of BIS monitoring system were placed on frontal and temporal lobes of the patient. The time of eye opening, verbal response to verbal stimulation, extubation time, the duration of stay in the recovery unit, the first-time of narcotic usage, and total dosage of intravenous narcotics were assessed in 2 groups.

**Results:** A total of 96 patients were enrolled. Sex, age, BMI, duration of surgery, length of stay in the recovery room and first-time narcotic drug usage were not significantly different in the two groups. However, the length of time from the anesthetic drug discontinuation to eye opening, verbal responses to verbal stimulation and extubation was significantly lower in the BIS group than the control group, respectively ( $P = 0.002$ ,  $P = 0.007$ ,  $P = 0.019$ ).

**Conclusions:** The evaluation of the anaesthesia status of patients based on the BIS index would be more efficient in decreasing the emergence anaesthesia including eye opening, verbal response, extubation after anesthesia.

**Keywords:** BIS, Clinical Assessment, Monitoring, Open Renal Surgery

## 1. Introduction

The aim of anesthesia during renal surgery is administering special intravenous or inhalation anesthetic drugs with little impact on their pharmacodynamics and pharmacokinetics (1).

Maintaining an adequate depth of anesthesia in the intraoperative period is considered as one of the main points of anesthesia that is dependent to adequate doses of anesthetic (2). As a low dose of drugs leads to awareness, generous doses lead to significant disturbance in the hemodynamic parameters (such as heart rate and blood pressure), delayed recovery, and an increase in other complications; therefore increasing the depth of anesthesia at aged patients and certain patients is considered important (2-7). Selecting an appropriate supervision can help optimize the quality of drug delivery, possibly reduce costs, and improve the outcomes of surgery (8).

A common method to assess the depth of anesthesia in the operating room is based on changes in heart rate, blood pressure, pupil size, tearing, sometimes limb and head movements, and respiratory rate, which are not a reliable method (9). However, monitoring methods directly assess analgesic and hypnotics effects of an anesthetic during surgery, which enables the anesthesiologist to maximize satisfactory effects of anesthesia drugs and to minimize the adverse cardiopulmonary effects. Bispectral (BIS) index is one of the scales (10). BIS is a mathematically derived electroencephalographic (EEG) derivative. The BIS value between 90 and 100 indicates an active central nervous system and shows that the patient is fully awake. The BIS of 0 indicates an isoelectric EEG. The BIS at a range of 70-90 indicates the loss of consciousness and sedation. BIS values of 60 indicate a light anesthesia state. BIS value lower than 40 specifies that the patient is in a deep anesthesia state. A BIS value between 40 and 60 indicates an appro-

appropriate level for general anesthesia and surgery. BIS monitoring indicates that cortex electrical status is similar to EEG monitoring (11). BIS application could be beneficial in reducing the use of anesthetic drugs, recovery time from anesthesia and the incidence of intraoperative awareness (12).

The aim of this study was to compare the depth of intraoperative anesthesia and recovery time in patients undergoing open renal surgery by clinical assessment and BIS monitoring.

## 2. Methods

The present study, after approval by the ethics committee of the Guilan University of Medical Sciences, was registered in Iranian registry of clinical trials (IRCT2015042111766N2). All patients within the ages of 15 - 65 years, undergoing open renal surgery from October 2014 to October 2015, at Razi hospital, were enrolled in the study. A blocked randomization scheme was applied for allocating subjects in two groups (BIS group and control group). Written informed consent was obtained from each patient. The exclusion criteria included: personality disorder, neurological disorders, and prior history of head trauma, drug abuse, drugs that affect the central nervous system, craniofacial anomalies, abnormal forehead, uncontrolled blood pressure (systolic more than 160 mmHg and diastolic more than 105 mmHg) insulin - dependent diabetes, BMI greater than 33, emergency operations, and ASA class  $\geq$  II (2) (Reviewer 1).

Induction of anesthesia and following intubation was performed with propofol 2 mg/kg, fentanyl 2  $\mu$ g/kg, and then with atracurium 0.5 mg/kg. For anesthesia maintenance, infusion combinations of propofol 50  $\mu$ g/kg/min, and remifentanyl, 0.1  $\mu$ g/kg/min (Reviewer 1) was applied via an infusion pump. A mix of nitrous oxide and oxygen (50 - 50) were used for inhalation anesthesia and atracurium, 0.1 mg/kg every 30 minutes was administered intravenously (Reviewer 1). For monitoring patients during anesthesia, standard medical monitors, including ECG, heart rate (HR), non-invasive blood pressure (NIBP), pulse oximeters (Massimo SAADAT Company, Iran) every 5 minutes were applied. Depth of anesthesia in the control group was measured based on heart rate, blood pressure, respiratory rate, sweating, tearing, and pupil dilatation. In case of a 20% increase from the baseline in hemodynamics parameters or occurrence of any other factors, opioids would be injected (remifentanyl 20% more than the initial dose). In the BIS group, the electrodes of BIS monitoring system (Aspect A2000, USA) were placed on the frontal and temporal lobes. A BIS value between 40 and 60 indicates an appropriate level and throughout the surgery, BIS value

was maintained. If the BIS value increased above 60 and the initial administered dose of propofol would not be effective, then 20% more than the initial dose of remifentanyl was administered.

After the surgery in both groups, the length of time from anesthetic drug discontinuation to eye opening, verbal response to verbal stimulation, extubation time, the duration of stay in the recovery unit, the first-time of narcotic usage, and total dosage of intravenous narcotics was assessed. Based on the Aldret score  $\geq$  9, recovery discharge of patients was done by a blind anesthesiologist resident. Intra- and postoperative opioid consumption (if visual analog score (VAS) > 3, pethidine 1mg/kg was administered in the recovery unit) and the first narcotic injection were recorded. After data collection, the data were then entered into SPSS version 17. For analyzing quantitative variables the t test was used, for qualitative variables Chi square, and for calculating survival function of the 2 groups (calculated using the Kaplan-Meier method) log-rank test were used (Figure 1).

## 3. Results

Between March 2015 and October 2015, a total of 96 patients within the age range of 15 - 65 years who were undergoing elective open renal surgery were included in the study. Of these, 63 patients were male (65.6%) and 33 female (34.4%). In the clinical assessment (control) group, 32 (66.7%) patients were male and 16 (33.3%) patients were female. In the BIS group, the number of male and females were 31 (64.6%) and 17 (35.4%), respectively.

The mean age in the control group was  $43.64 \pm 16.46$  and the BIS group  $41.18 \pm 12.65$ . The mean BMI in the 2 groups were  $26.24 \pm 3.8$  and  $24.9 \pm 3.54$ , respectively. As shown in Table 1, there is no significant difference between both groups regarding age, sex, and BMI.

No differences in the main intraoperative such as operative time and anesthesia time were found between groups ( $P = 0.33$ ;  $0.71$ , respectively) (Table 2).

Elapsed time since the discontinuation of anesthetic drugs to open the eyes in the control group was  $11.25 \pm 3.63$  minutes and in the BIS group  $8.85 \pm 3.77$  minutes ( $P = 0.002$ ).

The time for verbal response to verbal stimulation in the control group was  $12.89 \pm 3.67$  minutes and the BIS group  $10.81 \pm 3.65$  minutes ( $P = 0.007$ ). Extubation times were  $8.89 \pm 2.94$  and  $7.34 \pm 2.81$  minutes in 2 groups, respectively ( $P = 0.019$ ). Figure 2 shows that all this time has been significantly lower in the BIS group. Although admission to the recovery in the BIS group was lower ( $30.97 \pm 6.01$  minutes against  $33.85 \pm 10.11$  minutes), the difference was not statistically significant ( $P = 0.11$ ).

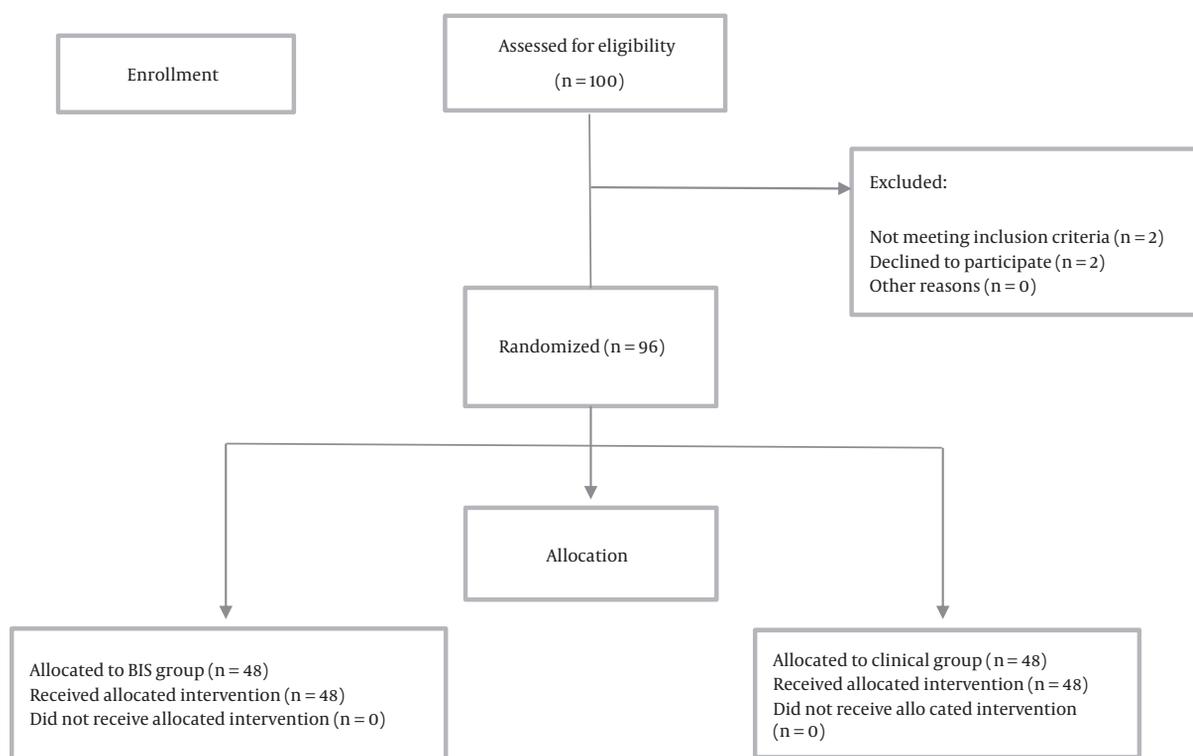


Figure 1. Consort Diagram (Reviewer 1)

Table 1. Distribution of Demographic Characteristics of Patients Undergoing Open Surgery in Both Clinical and Bispectral Index Monitoring groups

Variable	Clinical Group	BIS Group	Total	P Value
<b>Sex</b>				0.83
Male	32 (66.7)	31 (64.6)	63 (65.6)	
Female	16 (33.3)	17 (35.4)	33 (34.4)	
<b>Age, y</b>				0.97
< 30	13 (27.1)	14 (29.2)	27 (28.1)	
31 - 50	21 (43.8)	20 (41.7)	41 (42.7)	
> 50	14 (29.2)	14 (29.2)	28 (29.2)	
<b>Total age</b>	43.64 ± 16.46	41.18 ± 12.64		0.41
<b>BMI</b>				0.159
19 - 25	18 (37.5)	27 (56.2)	45 (46.9)	
25 - 30	26 (54.2)	17 (35.4)	43 (44.8)	
> 30	4 (8.3)	4 (8.3)	8 (8.3)	
<b>Total BMI</b>	26.24 ± 3.8	24.9 ± 3.54		0.078

Even though, it was the first time for a pethidine injection, the total amount of analgesic consumption and pain score on the VAS in recovery unit in the BIS group were lower than clinical assessment group, however, these dif-

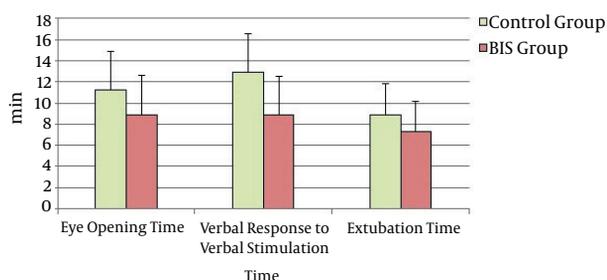
ferences were not statistically significant ( $P = 0.66$ ; 0.256 and 0.56 respectively) (Table 3).

The amount of remifentanyl used in the control group was  $937.5 \pm 322.2 \mu\text{g}$  and in the BIS group  $781.2 \pm 245.3 \mu\text{g}$ ,

**Table 2.** Comparison of Mean Operative and Anesthesia Time in 2 Groups

Variable	Mean ± SD	P Value <sup>a</sup>
<b>Operative time, min</b>		0.33
Clinical group	139.58 ± 67.4	
BIS group	132.7 ± 33.34	
<b>Anesthesia time, min</b>		0.71
Clinical group	169.2 ± 68.05	
BIS group	154.37 ± 33.96	

<sup>a</sup>Mann-Whitney U test.



**Figure 2.** Comparison of the Mean Time of the Eyes Opening, Verbal Response to Verbal Stimulation and Extubation Time in Patients Undergoing Open Renal Surgery in Two Groups

which is significantly different ( $P = 0.014$ ).

#### 4. Discussion

Today, all attempts to reduce the risks and complications of anesthesia are running to avoid an unstable situation for patients (13). A routine assessment in an effective and efficient anesthesia is the evaluation of the depth of anesthesia, which is normally done on the basis of clinical signs, following the autonomic nervous system response (tachycardia, increased blood pressure, sweating, tearing, dilated pupils) (14). This information is used to evaluate the anesthetic depth in hemodynamic responses during laryngoscopy, intubation, and skin incision. Signs of increased activity of the autonomic nervous system may not appear to follow the use of opioids, cholinergic, beta blockers, vasodilators, and antihistamines (15, 16). Therefore, the selection of precise criteria, which can be changed less, is considered important.

Focus on direct assessment methods of brain system to evaluate the depth of anesthesia is a new method that is in progress. As previously mentioned, spectral index (BIS) is one of these criterias. Furthermore, other methods in this area are advancing and providing, however, the BIS index is well accepted (17).

In this study, operative time in both clinical and BIS monitored was  $139.58 \pm 67.04$  and  $132.70 \pm 33.34$  minutes, respectively. The anesthesia time was  $169.20 \pm 68.05$  and  $154.37 \pm 33.96$  minutes in the 2 groups, respectively. Although, the duration of anesthesia in the clinical assessment group was about 15 minutes more than the BIS group, this difference was not statistically significant. In addition, we have demonstrated that the use of remifentanyl in the BIS group was significantly lower than the clinical assessment group ( $P = 0.014$ ). It can be assumed that the patient under the clinical assessment blindly received a higher dosage of anesthesia drugs than in the standard BIS monitoring to have adequate anesthetic depth and to prevent awakening during surgery (2). Gan et al. in the same study, showed that the dose of propofol in the group monitored with BIS is shorter than the other group (18).

Patients in the BIS group need less time to open their eyes and respond verbally to verbal stimulation and also, the extubation and recovery times were shorter after discontinuing the anesthetic drugs.

Except for the time of discharging from recovery unit in all other cases, the BIS group took statistically significantly less time than the clinical groups. Gan et al. finding were similar to what we saw in our study, thus, the recovery and extubation time in their study was also lower in the group monitored with BIS compared to the control group (18).

In our study no difference was observed between the 2 groups in terms of the use of opioids after surgery and VAS score however, generally, the drug necessity and VAS score was lower in the BIS group.

Although Vakkuri et al. in 2005, had used the EEG spectral entropy monitoring during surgery, they reported similar results and showed that this tool caused lower consumption of propofol and reduced recovery time (19). Of course, the type of administered anesthetic drug is important. As Mueller et al. showed, even with BIS monitoring in groups treated with propofol and etomidate, there is significant difference in hemodynamic changes after intubation (20).

It seems that the spectral index (BIS) enables the anesthesiologist to directly monitor the activity and function of the central nervous system during the use of anesthetic and sedative drugs and also has an accurate assessment of the effects of hypnotic anesthesia. This allows the anesthesiologist with knowledge of anesthesia depth administers a minimum drug dosage to provide effective anesthesia, without consciousness and pain. A clinical assessment may not be able to properly tell us the condition of the patient's consciousness and pain intensity due to the fact that the patient's hemodynamic variables that act related to autonomic nervous system are influenced by other

**Table 3.** Comparison of the Mean First-Time Injection of Analgesic - the Amount of Analgesic Consumption (mg)-Severity of Pain According to VAS Scale in Recovery of Patients Undergoing Open Surgery in Both Groups

Variable	Number	Mean $\pm$ SD	Z	P Value
<b>The first-time injection of pethidine in recovery, min</b>				
Clinical group	24	12.7 $\pm$ 11.65		
BIS group	20	11.6 $\pm$ 8.77	0.43	0.66
<b>Amount of analgesic consumption in recovery, mg</b>				
Clinical group	24	35 $\pm$ 21.36		
BIS group	20	28.5 $\pm$ 13.38	1.13	0.256
<b>The severity of pain according to VAS scale</b>				
Clinical group	48	3.37 $\pm$ 1.28		
BIS group	48	3.18 $\pm$ 1.04	0.57	0.56

factors. Nevertheless, Smajic et al. suggests that BIS monitoring should be used alongside clinical factors and not recommended to be used alone (2).

In conclusion, our study showed that anesthesia monitoring in patients under standard BIS can be effective in reducing the recovery time such as eye opening, verbal response to verbal stimulation, and extubation after anesthesia. It also significantly reduces the intraoperative remifentanyl use.

#### 4.1. Limitations

It is important to emphasize that reliance on BIS monitoring alone for intraoperative anesthetic management is not recommended. Clinical assessment and judgment during interpreting of BIS data is crucial. Unfortunately we did not evaluate and compare BIS data with hemodynamic and other monitoring data as well as observation of clinical signs. To evaluate the hemodynamic effects in each group, titrated to the appropriate anesthesia depth in two groups of patients, further studies are needed (Reviewer 1).

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#### Footnote

**Conflict of Interest:** There is no conflict of interest for this manuscript and there was no financial relationship with any organization.

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