

JIMMA UNIVERSITY
INSTITUTE OF HEALTH
FACULTY OF MEDICAL SCIENCES
SCHOOL OF ANESTHESIA



Depth of Anesthesia and Their Associated Factors; Prospective Cross sectional Study at Jimma University Medical Center Jimma, Ethiopia.

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A research report to be submitted to school of anesthesia, faculty of medical sciences, institute of health, and Jimma University for partial fulfillment for the requirement of specialty in anesthesiology, critical care and pain medicine.

September-December, 2021

Jimma, Ethiopia

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Jimma, Ethiopia

ABSTRACT

Background: Nowadays assessing of depth of anesthesia is an important issue across the world, because if it is not assessed or monitored correctly, the consequence can affect both physical and psychosocial health, prolong the recovery time, increase morbidity, and impairs quality of life and increase medical costs. Adequate depth of anesthesia helps to avoid overdose of anesthesia drugs, prevent awareness under general anesthesia, decrease post-operative pain intensity and decrease the analgesic requirements, and also improves patient outcome. The mortality associated with depth of anesthesia monitored with BIS is lower compared to those not monitored. So to overcome such problem it's recommended to use Bispectral index (BIS) monitor during general anesthesia to assess depth of anesthesia which is not available in low income countries including Ethiopia.

Objective: The present study aimed to assess depth of anesthesia, and their associated factors among patients underwent surgery with general anesthesia at JMC.

Methods: Prospective cross sectional study design was applied for four months (September 2021 to December 2021) among patients who underwent surgery with general anesthesia. All patients available during data collection who met inclusion criteria were enrolled in the study as they randomly scheduled for surgery. Data were collected by structured questionnaire. Depth of anesthesia was assessed by BIS intraoperatively. Accidental intraoperative awareness was assessed by Brice questionnaire by hiring the trained data collectors. Data were cleaned, entered in to epidata (version 4.6.1) and finally exported to SPSS (version 26) for analysis. The factors associated with the outcome variables were determined by cross tabulation and logistic regression analysis. The correlation of the variables was analyzed by Pearson correlation. P-value of <0.05 was considered as statistically significant. The finding of the study was expressed by applying statistical analysis (mean, standard deviation, percentage) and presented using tables, graphs, figures and narration.

Results: A total of 100 patients who underwent elective major surgery were enrolled in the study with the mean age of 43 ± 14.9 years that ranged from 18-80 years. Less than half of the patients (43%) had adequate anesthesia depth while the remaining 57% (CI 47.13-66.87%) of surgeries were performed with either light or deep anesthesia. Inadequate depth of anesthesia was affected by mean MAC of isoflurane (<1.117), sex (female), number of premedication (<2), type of current surgery (cholecystectomy) and IV induction agents (thiopentone) having AOR, CI and p-value of 8.1(1.8-36.2), $p=0.006$; 4.1(1.1-14.6), $p=0.032$; 3.4(1.1-10.9), $p=0.04$; 0.1(0.02-0.6), $p=0.016$; 0.03(0.002-0.5), $p=0.014$ respectively.

Conclusion and recommendation: The prevalence of inadequate depth of anesthesia was high (57%).

Key words: Depth of anesthesia; BIS; JUMC; associated factors.

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List of abbreviations

ASA: _____ American Society of Anesthesiology

BIS: _____ Bispectral index score

BP: _____ Blood pressure

BSR: _____ Burst suppression

JUMC: _____ Jimma University Medical Center

MAC: _____ Minimum alveolar concentration

MAP: _____ Mean arterial pressure

PACU: _____ Postanesthesia care unit

PR: _____ Pulse rate

TOF: _____ Train of four

Spo2: _____ Arterial oxygen saturation

CHAPTER ONE

1.1 Introduction

Depth of anesthesia is an ongoing process which involves loss of consciousness to verbal and surgical stimulation caused by anesthetic drugs acting on nervous system. It is the day to day activity of anesthesia provider to assess the adequacy of depth anesthesia to have patients who are satisfied with the procedure perioperatively.^{1 2 3 4 5}. Because the depth of anesthesia is variable for different patients due to different reasons such as age, presence of comorbid diseases, duration of procedure and anesthesia, and the medications we are using, its assessment is challenging for anesthesiologists ^{6 7 8}.

Despite the performance of millions of surgical procedures under general anesthesia, there is still the report of poor assessment of depth anesthesia of because of underdeveloped means for measurement of depth of anesthesia ^{7 9 10}.

Although there are different methods of assessing depth of anesthesia like clinical parameters, recent studies show that using bispectral index score (BIS) is a better indicator of depth of anesthesia^{2 6 11 12}. BIS is monitoring method of the depth of anesthesia with hypnotic anesthetic drugs by means of recording electrical activity of brain using electroencephalogram. It has values which range from 0- 100. Values less than 40 shows that the anesthesia is too deep, values between (40-60) are said to be ideal depth for surgical procedure and score greater than 60 is light anesthesia. ^{1 11 13}.

It is thought that, controlling the depth of anesthesia within acceptable range by using BIS will help the patient in many aspects including reduction of inappropriate dosage and postoperative complications. Over-dosage of anesthetic drugs including both intravenous and inhalational drugs causing too low BIS(less than 30-40) is associated with brainstem depression such as cardiopulmonary system while under-dosage causing high BIS score (greater than 70-80) is associated with light anesthesia which will result in intraoperative awareness. ^{1 3 14}.

It is obvious that poorly monitored intraoperative depth of anesthesia will put patients at risk for many adverse outcomes including mild preoperative stress to the extent of intraoperative arrest, and increased postoperative morbidities; so that all anesthesia providers should have an awareness, knowledge and resources to assess depth of anesthesia using BIS in addition to clinical means of assessment^{12 13}.

Nowadays, the assessment of depth of anesthesia in developing countries including Ethiopia is by using clinical means and this study will help to put a base for assessment of depth of anesthesia by using BIS specifically in JUMC.

1.2 Statement of the problem.

Nowadays assessing of depth of anesthesia is an important issue across the world, because if it is not assessed or monitored correctly, the consequence can affect both physical and psychosocial health, prolong the recovery time, increase morbidity, and impairs quality of life and increase medical costs^{15 16 17}.

Assessing and monitoring depth of anesthesia remained challenge for anesthesia providers⁶. The mortality associated with depth of anesthesia monitored with BIS is lower compared to those not monitored^{18 19}. Combined approach to assessment of depth of anesthesia is better than isolated ones^{13 20}. About 20% post-operative mortality can be associated with deep anesthesia; Especially, if low value of BIS combined with low MAP, low MAC or both it can increase the risk of mortality²¹.

Depending on the surgical procedure and associated risk factors the incidence of intraoperative awareness ranges from 0.08% to 1.5%, and BIS value of less than 60 is associated with least risk of awareness^{2 3 22}.

BIS monitoring is reliable, easily readable and comprehensive method to assess anesthetic depth and it is also beneficial to the patient as it allows titration and avoids over dosage of anesthetic drugs, which enable patients to recover and communicate early^{10 22}.

Recent studies in Ethiopia reported lack of premedication associated with recalling awareness which shows inadequate depth of anesthesia²³. There is no data reporting correlation of depth of anesthesia with other factors, so this study will assess the effect of other factors on depth of anesthesia by using BIS in addition to a clinical means of assessing depth of anesthesia in Jimma University Medical Center.

1.3 Significance of the study

The use of appropriate methods for assessing and monitoring depth of anesthesia, and associated factors in patients undergoing surgery under general anesthesia can be effective in reducing health costs, morbidity and mortality of patients.

Assessment of depth of anesthesia and associated factors is not well addressed in developing countries including Ethiopia. There are insufficient studies which assess the depth of anesthesia in Ethiopia. Therefore, this study will give an insight to how to assess the depth of anesthesia in Jimma University Medical center. Hence, the study results will be used as a milestone to give some picture in assessing the depth of anesthesia and associated factors using BIS in JUMC.

This research may help as foot step for further studies, and provide information regarding monitoring depth of anesthesia using BIS for institutions, researchers and policy makers.

The goal of assessing and monitoring the depth of anesthesia and associated factors in adults based on BIS is to enable anesthesia providers to determine the amount of required anesthetic drug and identify associated factors. Using this index can reduce the likelihood of awakening within surgery and will minimize the risk of intraoperative arrest. Since there are some conflicting reports on means of assessing depth of anesthesia, this study is intended to evaluate the practice of assessment of depth of anesthesia and associated factors.

For Jimma University medical center, it will bring the application and practice of monitoring and assessing depth of anesthesia by BIS.

For patients, if standard depth of anesthesia is applied it decreases the morbidity and mortality, it increases patient satisfaction, and decreases hospital costs.

For researcher it will open the gate for further study. Assessing depth of anesthesia and associated factors is important for policy makers and healthcare providers to increase the quality of care during perioperative period.

CHAPTER TWO

2.1 Literature review

Depth of anesthesia is an ongoing process which involves the loss of consciousness to verbal and surgical stimulation caused by anesthetic drugs²⁰. The depth of anesthesia varies from patient to patient, which makes it more complicated to assess easily¹.

Even though depth of anesthesia is difficult to assess objectively, it is considered if monitored appropriately it will improve patient satisfaction and outcome²⁴. If not assessed adequately, it will negatively affect both intraoperative and postoperative condition of patients^{24 25}. As a consequence of these derangements it may increase morbidity and mortality rate²⁶.

The patient may go to sleep during anesthesia, but there should be balance between dosage of anesthetic drugs and level of consciousness of patient²⁷. To achieve this balance some literatures suggest to assess and monitor depth of anesthesia during surgery by using BIS waveforms throughout intraoperative period, so that subsequent complications can be reduced and the recovery period of the patient after the surgery and immediately after discharge from the hospital can be shortened^{3 28}.

In developing countries assessment of depth of anesthesia has special consideration but there are many obstacles to address and treat adequately; which will result in the probability of over-dosage and under-dosage of anesthetic drugs with their associated complications. The possible incriminated reason for poor assessment and monitoring of depth of anesthesia is lack of instruments like BIS and depending on traditional means of depth assessment especially in developing countries^{9 27}.

Bispectral index score (BIS) is a newly developed tool which is currently used to assess the depth of anesthesia by numerically displaying electrical activity of brain⁷. The value ranges from 0-100²⁹. To assess the degree of depth of anesthesia different literatures categorize as too deep (<40), adequate (40-60) and light anesthesia (>60)^{14 30}.

The depth of anesthesia is affected by different factors that are responsible for either to decrease or increase the BIS values showing depth of anesthesia. Nowadays the anesthesia machine and other electronic materials being used in the operation theatre for anesthetic drug administration are sophisticated enabling anesthesia provider to know the concentration of anesthetic agents delivered to patients including both the inhalational as minimum alveolar concentration (MAC) and intravenous drugs which affect the depth of anesthesia as shown on BIS values resulting from over-dosage or under-dosage. Many evidence suggests that 95% of individuals are considered unconscious when BIS values are ≈ 50 when intravenous anesthetic drugs like propofol or a volatile anesthetic drug is administered alone.^{31 32}

There are even studies comparing the effect of inhalational and intravenous anesthetics on the depth of anesthesia. These studies suggest that inhalational anesthetics are associated with increased risk of cardiorespiratory depression while intravenous anesthetic drugs cause less respiratory and circulatory arrest in addition to fast recovery from anesthesia than inhalational agents³³.

Although it is possible to attain adequate surgical anesthesia with either inhalational or intravenous anesthetic drugs alone, some studies report that using combination of anesthetic drugs including opioids and other anti-pain modalities will synergistically increase the effect of inhalational and intravenous hypnotics anesthetic drugs, and it also decrease the dose other drugs required to obtain adequate depth of anesthesia, indirectly preventing too deep anesthesia. .^{34 35 36} Study done in Egypt by Doha, N. M *et al* reported that using preoperative anti-pain (gabapentin) with other anesthetic drugs for maintenance gave adequate depth of anesthesia.³⁷

Kil, H. K. *et al.*³⁸ demonstrated that psychological factors like preoperative anxiety and pain intensity are important predictors of intraoperative consumption of both inhalational and intravenous anesthetic agents. It also suggests that anesthetic and analgesic dose adjustment could be modified by preoperative anxiety and pain intensity, which necessitates the importance of premedication with antipain and anxiolytics to attain ideal depth of anesthesia.

Other study done in China by Yue, H. *et al*, showed that using muscle relaxants, the most commonly used adjuvant drug for general anesthesia minimizes the adverse effect of deep anesthesia on cardiovascular system; but there is study which reports an increased risk of intra-operative awareness compared to those without muscle relaxants. This study done on two groups of patients and it showed BIS value of between 40 to 60 in the first group without muscle relaxants and the BIS value decreased to less than 20 in the second group with muscle relaxant at different dose of rocuronium.³⁹; Anesthesia and surgery time also affects depth of anesthesia explaining depression of brain activity as it is exposed to anesthetic drugs for prolonged time⁴⁰.

P. L. Purdon *et al.*⁴¹ reported that age of patient affects BIS values which shows depth of anesthesia; it is thought that elderly patients are susceptible to over-dosage of anesthetic agents because of changes both in anatomic and physiologic activity of brain. Study done by Katherine Ni, *et al* reported that minimum alveolar concentration required by elders decrease per decade (the regression analysis showed end-tidal MAC declined by 3.41% per decade after 30 years of age).⁴¹ Additionally; old age patients have decreased activity of all systems putting them at risk of poor tolerance to anesthetic drugs. It is mentioned that the concurrent presence of comorbid conditions such as pulmonary, cardiac, renal, liver and other diseases (like hypoglycemia, cerebral ischemia, hypothermia) apart from the reason for surgery influence the depth of anesthesia by affecting the dose of anesthetic drugs required.^{42 43}

For the brain to function properly its perfusion should be maintained in the normal range usually between 50 to 150mmhg. It is believed that there is linear correlation between mean arterial pressure and bispectral index values showing too deep anesthesia when BIS values are low usually less than 40 and vice versa.^{44 32} The other study done in Egypt by Kaki *et al* reported the effect of position applied for different surgical procedures is also associated with different BIS reading, head-up which decreases bispectral index values and head-down which increase bispectral index value reading⁴⁵.

The intention of assessing depth of anesthesia is to minimize the probability of both intra-operative awareness which is associated with postoperative psychological trauma especially post-traumatic stress disorder syndrome and too deep anesthesia causing cardiorespiratory depression or arrest; study done by Miklos D, *et al* reported that 30-day mortality rate of 0.8% in patients with intraoperative BIS value less than 45 for long duration.⁴⁶

Nowadays, the reported incidence of intra-operative awareness is decreased to 0.1% to 0.2%.⁴⁷ This improvement is attributable to currently developed machines used for monitoring electrical activity of brain such as BIS which is used to assess depth of anesthesia.³².

One institutional cross-sectional study done in Ethiopia reported intraoperative awareness with complaint of pain and anxiety (27.3% and 26.5%) due to inadequate depth of anesthesia based on clinical means of assessing depth of anesthesia²³.

Generally, in developing countries the assessment of depth of anesthesia and associated factors is poor, and it is associated with many complications including postoperative psychological problems and cardiorespiratory depression^{16 14}, but if assessed appropriately it will increase patient satisfaction and improve postoperative outcome such as fast recovery from anesthesia during emergence, early discharge from hospital, early ambulation, decreased analgesic consumption, postoperative nausea and vomiting ⁴⁷.

Conceptual framework

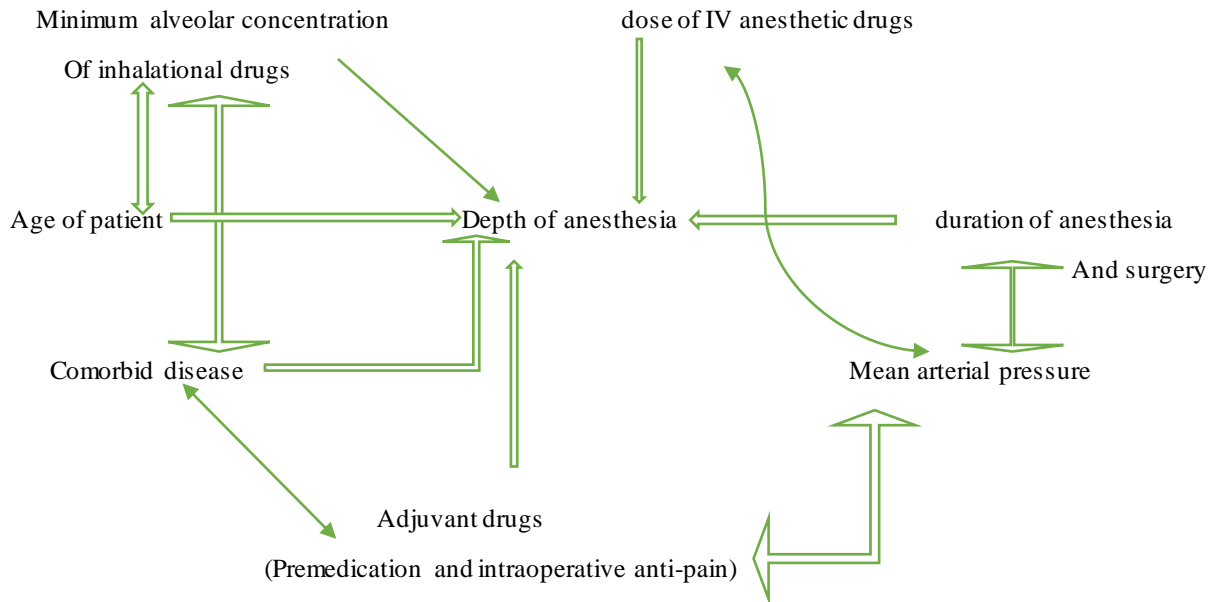


Figure 1 CONCEPTUAL FRAMEWORK TO SHOW FACTORS ASSOCIATED WITH DEPTH OF ANESTHESIA.

CHAPTER THREE: OBJECTIVE

3.1 General Objective

- To assess depth of anesthesia, and their associated among patients underwent surgery with general anesthesia at Jimma University Medical center, Ethiopia

3.2 Specific Objective

- To assess depth of anesthesia among patients underwent surgery with general anesthesia at Jimma University Medical center, Ethiopia
- To identify factors associated with depth of anesthesia status among patients underwent surgery with general anesthesia at Jimma University Medical center, Ethiopia

CHAPTER FOUR: METHODOLOGY

Study area and period

The study was conducted at Jimma University Medical center (JUMC) which is located in Oromia region, 350 km south west of Addis Ababa, Ethiopia. It is one of the largest teaching and referral hospitals with 634 beds and it provides services for a catchment population of about 20 million people. Data were collected from September, 2021 to December, 2021.

4.1.2 Study design:

Prospective cross-sectional study design was used.

4.1.3 Population

4.1.3.1 Source population:

The source population constituted of all patients who had undergone surgery at the major operation theatre of JUMC during the study period.

4.1.3.2 Study population:

The study population included all adult patients who had undergone surgical procedure under general anesthesia and BIS is used during the study period.

4.1.4. Exclusion and inclusion criteria

4.1.5. Inclusion criteria:

All adult (>18 years old) surgical patients with ASA classification I through III who underwent elective surgery with general anesthesia at JUMC, south-western Ethiopia from September 2021 to December 2021.

4.1.6. Exclusion criteria:

- All emergency surgery including caesarian section.
- Who transferred to ICU and put on mechanical ventilation
- Patient unable to communicate

Sample size

According to the following formula, considering the alpha (first error of the study) as 0.05, d (accuracy of the study) as 0.05 and P (adequacy of anesthesia in study) as 0.5, 172 people will be enrolled in the study.

- $N = p(1-p) \times (z_{1-\alpha/2})^2 / d^2 \approx 384.16 \approx 384$
- Since our study population was, <10,000 correction formula was used, where:-
 - $n =$ calculated sample size = 384
 - $N =$ Average number of Source population from morbidity and mortality records over four months period = 313
 - $N =$ final calculated sample size
 - $N = n / (1 + n/N) \approx 172$

Sampling technique

Due to lack of adequate BIS machine for data collection and we couldn't apply one sensor for more than one patient due to Covid-19, we were obliged to collect only 100 patients for analysis. All patients fulfilling the inclusion criteria and for whom BIS machine was used, were included during the study period till the mentioned sample saturated as patients were randomly scheduled for surgery.

Independent variables:

- Age
- Sex
- Induction agents
- Analgesic drugs
- Duration of surgery
- Duration of anesthesia
- Type of surgery
- ASA classification
- Comorbidities
- Substance use

Dependent variable:

Depth of anesthesia

Data collection process and tools

Depth of anesthesia was assessed by BIS intra-operatively. A pilot study was carried out on 10% of patients to test the applicability of the study and to test clarity of the designed questionnaire, as well as to estimate the time needed for each tool. Patients who were eligible and gave consent for the study were monitored with BIS, noninvasive BP, SpO₂, and temperature every five minutes. Nerve stimulator also attached to test the full reversal of muscle relaxants and ToF watch was registered.

Before attaching electrodes, the patient's forehead cleaned with 70% of alcohol and dried with swab and the electrodes were attached as per the standard (E1 was attached at center forehead, 5cm above bridge of nose, E4 was attached directly above eye brow, E3 was attached between corner of eye and hairline, E2 was placed between E1 and E4).

Induction drugs, inhalational, analgesics, muscle relaxants and additional medication were registered on questionnaire too.

Data analysis technique

First the data were checked for completeness and consistency. Then it was coded and the data were exported from Epi data V.4.6.1 to SPSS version 26 for analysis; descriptive summary using frequencies, proportions, graphs and cross tabs was used to present study results. Categorical data were analyzed by Fisher exact test or Chi square test. Numerical data were tested for normal distribution. If distribution is normal, a paired student t-test was performed, if not normal distribution = Wilcoxon signed rank tests was performed.

Ethical consideration

Before data collection, the study was approved by the Jimma University Institutional Review board. After obtaining informed consent, 100 patients were enrolled in the study. A day before surgery, patients were told about the importance of the study and data collector was instructed how to use BIS score. Depth of anesthesia during general anesthesia explained to the patients (where 0-40 represented deep anesthesia, 40-60 adequate and >60 light anesthesia). Data of patients were kept confidentially. For illiterate patients ICF was signed by legally acceptable representative in the presence of GCP (good clinical practical) guidelines.

Operational definition

Induction agents:

- Drugs given for general anesthesia before intubation.

Maintenance drugs:

- Drugs which is used for keeping patient unawake/unconscious throughout the surgery.

Reversal:

- Drug that reverse the action of non-depolarizing muscle relaxants

Analgesic drugs:

- Drugs for pain relief.

BIS (bispectral index score):

- A validated, objective measure for brain electrical activity. It ranges from (0) no electrical activity to Awake (100).
- The bispectral index score is a good, valid and excellent reliable measure to Categorize Brain electrical activity as: too deep anesthesia (<30-40), adequate or ideal (40-60), inadequate or light anesthesia (>60).

Depth of anesthesia:

- The degree to which the central nervous system is depressed by a general anesthetic agent.

Duration of anesthesia:

- Time from intubation up to extubation.

Duration of surgery:

- Time from beginning of skin incision up to closure of skin.

CHAPTER FIVE: RESULTS

5.1 Socio-demographic characteristics of respondents

A total of 100 patients who underwent elective major surgery enrolled in the study with the mean age of 43 ± 14.9 years that ranged from 18-80 years. Majority of the respondents were belonged to age ≥ 40 years (53%), females (52%), Rural dwellers (52%), married (83%) and Muslims (49%) as detailed in Table 1.

Table 1: Socio-demographic characteristics of respondents who underwent elective major surgery under general anesthesia at JMC Jimma, Ethiopia from September to December, 2021 (n=100).

Variables	Statistics
Age in years, Mean \pm SD; Ranges	43 \pm 14.9; 18-80
Sex (Male; Female), Number	48 (48%); 52 (52%)
Religious (Muslim; Orthodox; Protestant), Number	49 (49%); 40 (40%); 11(11%)
Residency (Rural; Urban), Number	52 (52%); 48 (48%)
Educational status (No formal education; Primary school; Secondary school and Diploma and above), Number	45(45%); 33(33%); 11(11%); 11(11%)
Marital status (Married; Single; Widowed), Number	83(83%); 16(16%); 1(1%)

5.2 Clinical profiles and surgery related profiles of respondents

Majority of the patients who underwent elective major surgery belonged to ASA classification II (46%), general surgery (75%), taken premedication (95%) like lidocaine (60%), dexamethasone (60%), morphine (56%), atropine (43%) and pethidine (28%). Patients also underwent surgery with general anesthesia (100%) being induced by propofol (46%), ketofol (30%), thiopentone (17%) and ketamine (7%). Majority of the patients received muscle relaxants (succinylcholine-86% and vecuronium-96%), isoflurane inhalation agent (96%), reversal (95%) and intraoperative antipain (64%) like morphine (24%) and pethidine (23%). The mean duration of surgery and anesthesia was 120 ± 111 and 222 ± 118 respectively.

Less number of patients experienced behavioral substance use habits (smoking (4%, alcohol (11%) and khat (13%)). The prevalence of subject report of history of appetite loss was 56%, emotional problems (38%) and sleep problems (38%) as detailed in Table 2.

Table 2: Clinical profiles and surgery related profiles of respondents who underwent elective major surgery under general anesthesia at JMC Jimma, Ethiopia from September to December, 2021 (n=100):

Variables	Statistics
ASA status (I; II; III), Number	39; 46; 15
History of previous surgery (Yes), Number	26
Type of current surgery (General; Gynecology; Orthopedics; Others), Number	75; 12; 2; 11
Specific type of current surgery (Cholecystectomy; Laparotomy; Mastectomy, Thyroidectomy, Others), Number	17; 54; 8; 4; 17
Presence of co-morbidity (Yes), Number	26
Taken premedication (Yes), Number	95
Induction agents (Propofol; Ketofol; Thiopentone; Ketamine), Number	46; 30; 17; 7
Intubated by succinylcholine (Yes), Number	86
Taken intraoperative antipain (Yes), Number	64
Duration of surgery in minutes, Mean \pm SD; Ranges	120 \pm 111; 60-660
Duration of anesthesia in minutes, Mean \pm SD; Ranges	222 \pm 118; 75-720
Cigarette smoking (Yes), Number	4
Alcohol drinking (Yes), Number	11
Khat chewing (Yes), Number	13
Sleep problems (Yes), Number	38
Appetite loss (Yes), Number	56
Emotional problems (Yes), Number	38

Vital signs of patients were also recorded during the procedures. According, mean and standard deviation of SBP, DBP, and PR were 118.77 \pm 14.2, 69.8 \pm 8.79, and 92.4 \pm 16.9 respectively.

5.3 Depth of Anesthesia status

Depth of anesthesia was measured intrao-peratively by BIS after applying electrodes as the standards. The BIS outputs that displayed on the anesthesia monitoring were recorded from the incision time to surgery end time. BIS of patients can be falsely raised by ketamine utilization as induction agent. Mean BIS of patients induced by ketamine was 65.5984 but it was 57.5733 for patients induced by other IV induction agents is shown in Table 3.

Table 3: Mean BIS of respondents who underwent elective major surgery under general anesthesia at JMC Jimma, Ethiopia from September to December, 2021 (n=100).

	Mean±SD
Patients induced with ketamine (n=37)	65.5984±8.67525
Patients induced with other IV induction agents (n=63)	57.5733 ±9.27781
All patients (n=100)	60.5426 ±9.82032

Jimma, Ethiopia from September to December, 2021 (n=100).

For convenience, mean of BIS score was used to express depth of anesthesia. The BIS score from 40-60 considered as adequate anesthesia depth. Accordingly, less than half of the patients (43%) had adequate anesthesia depth while the remaining 57% (CI 47.13-66.87%) of surgeries were performed with either light or deep anesthesia (Fig 1).

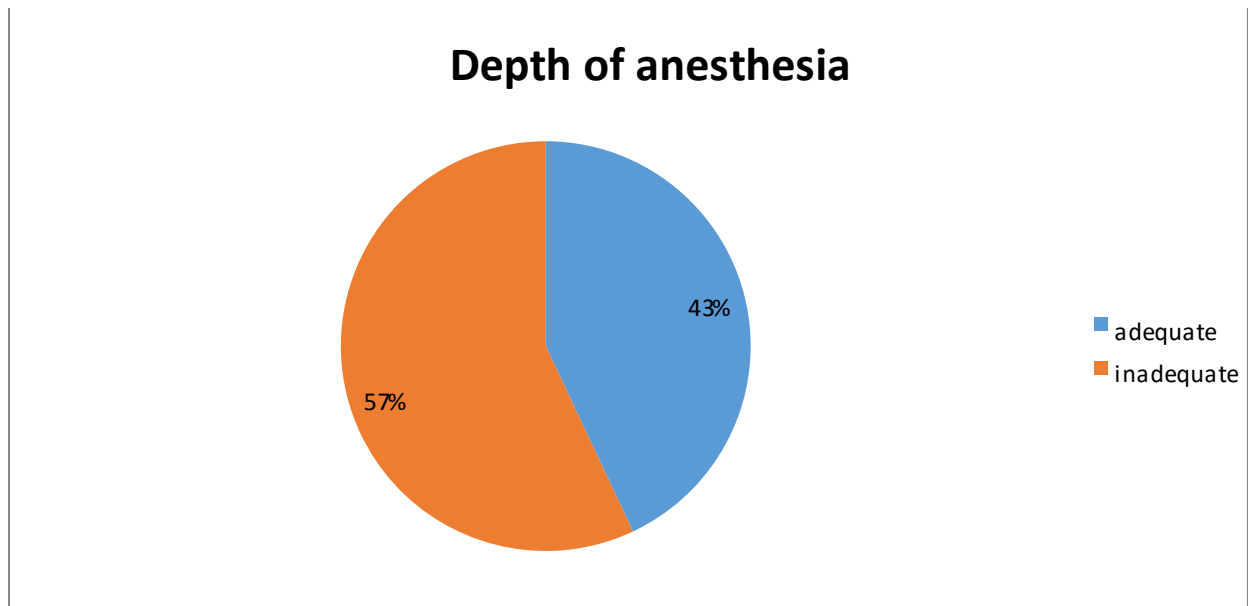


Figure 2: Depth of anesthesia of respondents who underwent elective major surgery under general anesthesia at JMC Jimma, Ethiopia from September to December, 2021 (n=100).

5.3.1 Factors associated with depth of anesthesia

In binary logistic regression about 11 variables (age, sex, educational status, marital status, BMI, ASA status, type of current surgery, premedication used, IV induction agents, mean MAC of isoflurane and substance use) were candidates for multivariate logistic regression for having p-value <0.25.

Finally, five variables (mean MAC of isoflurane (<1.117), sex (female), number of premedication (<2), type of current surgery (cholecystectomy) and IV induction agents (thiopentone) were identified as the predictors of in adequate depth of anesthesia having AOR, CI and p-value of 8.1(1.8-36.2), p=0.006; 4.1(1.1-14.6), p=0.032; 3.4(1.1-10.9),p=0.04; 0.1(0.02-0.6), p=0.016; 0.03(0.002-0.5),p=0.014 respectively.

Table 4: Factors associated with depth of anesthesia among respondents who underwent elective major surgery under general anesthesia at JMC Jimma, Ethiopia from September to December, 2021 (n=100)

Variable	Category	Depth of anesthesia, Number					
		Adequate	In adequate	COR(CI)	Pvalue	AOR(CI)	Pvalue
Age in years	<40	14	33	2.8(1.2-6.5)		2.8(0.8-10.4)	0.112
	≥40	29	24	1	0.013*	1	
Sex	Male	24	24	1		1	
	Female	19	33	1.7(0.78-3.8)	0.176*	4.1(1.1-14.6)	0.032*

Educational status	No formal educations	23	22	0.5(0.24-1.2)	0.140*	0.6(0.2-1.9)	0.393
	Others	20	35	1		1	
Residency	Rural	19	23	1			
	Urban	24	34	0.85(0.38-1.9)	0.701		
Marital status	Married	39	44	2.8(0.8-9.5)	0.084*	1.8(0.3-9.9)	0.502
	Others	4	13	1		1	
BMI	Underweight	3	8	1.86(0.4-7.5)	0.387	2.4(0.3-18.8)	0.376
	Normal	30	43	1		1	
	Overweight	10	6	0.4(0.14-1.3)	0.126*	0.74(0.2-2.9)	0.672
ASA classification	1	14	25	1.6(0.7-3.7)	0.250*	3.1(0.8-10.5)	0.078
	Others	29	32	1		1	
History of previous surgery	Yes	10	16	1.3(0.5-3.2)	0.587		
	No	33	41	1			
Specific type of current surgery	Cholecystectomy	10	7	0.44(0.15-1.3)	0.142*	0.1(0.02-0.6)	0.016*
	Laparotomy	7	9	0.8(0.2-2.4)	0.717	0.5(0.1-2.3)	0.366
	Others	26	41	1		1	
Presence of comorbidity	Yes	12	14	0.84(0.34-2.1)	0.706		
	No	31	43	1			
Number of used premedication	≤2	17	30	1.7(0.76-3.8)	0.195*	3.4(1.1-10.9)	0.04*
	>2	26	27	1		1	
Induction agents	Propofol	23	23	0.4(0.07-2.3)	0.302	0.1(0.01-1.4)	0.102
	Ketofol	7	23	1.3(0.2-8.3)	0.772	0.8(0.07-9.5)	0.902
	Thiopentone	11	6	0.2(0.03-1.4)	0.120*	0.03(0.002-0.5)	0.014*
	Ketamine	2	5	1		1	
Intubated by	Succinylcholine	38	48	0.7(0.2-2.3)	0.554		

	Others	5	9	1			
Intraoperative antipain	Yes	27	37	1			
	No	16	20	0.9(0.4-2.1)	0.827		
Mean MAC of Isoflurane	<1.17	31	47	1.8(0.7-4.7)	0.219*	8.1(1.8-36.2)	0.006*
	≥1.17	12	10	1		1	
Duration of surgery	Continuous			1.01(0.99-1.004)	0.682		
Substance use	Yes	15	10	0.39(0.15-1.0)	0.051*	0.9(0.2-3.5)	0.906
	No	28	47	1		1	
Sleep problems	Yes	17	21	0.9(0.4-2.0)	0.784		
	No	26	36	1			
Appetite loss	Yes	24	32	1.01(0.46-2.3)	0.974		
	No	19	25	1			
Emotional problems	Yes	15	23	1.2(0.56-2.8)	0.577		
	No	28	34	1			
Habit of Physical exercise	Yes	4	4	1			
	No	39	52	1.3(0.3-5.7)	0.697		

CHAPTER SIX: DISCUSSION

The current study aimed to assess depth of anesthesia, accidental intraoperative awareness, quality of recovery, post-operative pain and their associated factors among 100 patients who underwent major surgeries under general anesthesia. The mean age of respondents was 43 ± 14.9 years that ranged from 18-80 years where majority of the them belonged to age ≥ 40 years (53%), females (52%), rural dwellers (52%), married (83%) and Muslims (49%).

Depth of anesthesia was measured intra-operatively by BIS after applying electrodes as per the standards. The BIS outputs that displayed on the monitor were recorded from the incision time to surgery end time. The mean of BIS score during the surgery period was 60.34 ± 10.23 in the present study. But this figure was relatively higher if compared with study of Sravya Adda and Kalpana Kulkarni who reported the mean of BIS score of 43.3 ± 5.17 ²⁸. The difference may be due multifactor like study method which was comparative in the previous study, number of participants (higher in our study) and differences regarding inclusion and exclusion criteria.

Less than half of the patients (43%) had adequate anesthesia depth while the remaining 57% (CI 47.13-66.87%) of surgeries were performed with inadequate depth of anesthesia (either light or deep anesthesia). This finding of the current study for the prevalence of inadequate depth of anesthesia of 57% was higher as per the standard anesthesia monitoring guideline recommends of 100% maintenance of adequate depth of anesthesia to the level of BIS score of 40-60^{9 48}. Because both extremities of BIS score (light anesthesia and too deep anesthesia) is detrimental to patients' health⁴⁹ as the former is associated with AAGA^{50 51} and the latter is associated with postoperative mortality^{21 52}.

The determined factors that affect inadequate depth of anesthesia were mean MAC of isoflurane (<1.117), sex (Female), number of premedication (<2), type of current surgery (cholecystectomy) and IV induction agents (thiopentone).

The effect of dose of isoflurane and depth of anesthesia was inconsistent and paradoxical among available literatures that warrant further studies. Morimoto Y,et.al, reported that MAC of isoflurane between 0.8% and 1.6% didn't affect BIS value.^{5 43}.This is not consistent with our study; which might be due to other inhalational agents like nitrous oxide they are using in addition to isoflurane .

The use of premedication was identified as a factor associated with the depth of anesthesia. This result was supported by study done in Korea (Kil HK,et.al, 2012), Egypt (Doha NM, et.al, 2010) and in Ethiopia (Tadese et al, 2018) which might be by decreasing intra-operative pain or pre-operative anxiety with antipain and anxiolytics, respectively. Regarding induction agents used for this study, thiopental was found to be an induction agent associated with adequate depth of anesthesia; and it was supported by other study done in India(Ramesh VJ,et.al, 2007);it reported that appropriate dosing of thiopental will give adequate depth of anesthesia and as the dose increase the chance of occurrence deep anesthesia is high.^{24 53 54 55}

This study reported that being female was associated with inadequate depth of anesthesia, which was supported by study done in Australia(Buchanan FF, et. al,2011) showing female sex was associated with higher number of BIS and fast recovery from general anesthesia; which might be due to hormonal effect(progesterone) and also (American Society of Anesthesiologists,2006) reported female sex as a risk factor for intraoperative awareness.⁵⁶

Study done in Spain (Casati L,et. al, 2002) concerning the anesthetic requirement for major abdominal surgeries to attain adequate depth of anesthesia (BIS value between 40-60), reported that in addition to inhalational and intravenous anesthetic agents, using regional anesthesia will decrease intraoperative pain on top of decreasing anesthetic doses. Even though cholecystectomy is one of major abdominal surgeries, the fact that current study reported it as a factor associated with adequate depth of anesthesia is not consistent with the previous study; because there is no combination of regional anesthesia used in this study alerting further studies.⁵⁷

CHAPTER SEVEN: CONCLUSION AND RECOMMENDATION

7.1: Limitations

- Inadequate BIS machine for data collection.
- Absence of adequate literature done in the country of the same setup.
- Presence of Covid-19, preventing us from using one BIS for more than one patient.
- Absence of infuser for IV anesthetic drugs and end-tidal concentration detector for inhalational agents.
- We couldn't use BIS machine for procedures involving the neck and above due to accessibility.

7.2: Conclusion

In conclusion, assessing depth of anesthesia using BIS showed that, more than half of patients (57%) underwent surgery with inadequate depth of anesthesia. And it was affected by MAC of isoflurane, sex, number of premedication used, type of surgery and IV induction agents administered. Using BIS alone will not prevent accidental intraoperative awareness suggesting further studies to be conducted.

7.3: Recommendation

- Anesthesia providers may use BIS machine to improve the adequacy of depth of anesthesia for surgery in addition to clinical means of monitoring.
- Anesthesiologists (seniors) can facilitate for assessment of depth of anesthesia for intravenous, inhalational agents and adjuvants separately.
- Anesthesia providers can use this study as base for further research on why the mentioned factors are associated with depth of anesthesia.

- Anesthesia department can ask the responsible body for more machines to cover large number of patients undergoing surgery for monitoring.

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Annexes

Annex-I English Version Questionnaires

Title:	Assessment Of Depth Of Anesthesia And Associated Factors With Bispectral Index In Adult Patients Undergoing Surgery Under General Anesthesia In JUMC, Ethiopia From September 2021 To December 2021. A Prospective Cross Sectional Study.
Ethics Approval Number:	

Part I Information Sheet and Consent Form

Dear Sir/madam;

Good morning/Afternoon, my name is _____. I am research assistant and working with Dr. Diriba Fayisa from Jimma University. He is doing a research on the assessment of depth of anesthesia and associated factors with Bispectral Index among people who are going to have surgery under general anesthesia at Jimma University Medical Center, in partial fulfillment of the requirement for the speciality in anesthesiology, critical care and pain medicine. I am going to give you information and invite you to be part of this research. If you agree to participate, you will be required to fill out a questionnaire. The information that you will obtain using this interview will be used only for research purpose and also I need to assure you that

confidentiality is our main quality. Therefore; I politely request your cooperation to participate in this interview. You do have the right not to respond at all or to withdraw in the meantime, but your input has great value for the success of our objective.

Did you agree _____?

Did not agree _____

Thank you for your cooperation!!

Annex-II Afaan Oromo Version Questionnaires

Kutaa I;unka Odeffannoo fi Waliigaltee

Obboo/Addee;Akkam jirtu Ani maqaan koo_____dha.

Ani hojjataa Giddugala waldhaansa Fayyaa Yuunivarsiitii Jimmaa yommuun ta’u qorannoo kana irratti akka gargaaratti, Dr.Diriba Fayisa wajjin hojjataa jira.Inni barataa digirii 2ffaa yoo ta’u, ulaagaa eebbifamuuf barbaachisu guutuuf qorannoo mataduree “assessment of depth of anesthesia and associated factors with Bispectral Index”.jedhu irratti dhukkubsattoota yaaliin baqaqsanii hodhuu godhamuuf irratti kan hojjachaa jirudha.Akka hirmaataa qorannichaa taataniif ibsaa fi ragaa gahaa ta’e isin biraan gahuun barbaada. Eeyyamamaa yoo taatan gaaffii afaanii armaan gaditti dhiyaataniif akka nuuf hirmaattan isin gaafanna.ragaan isin nuuf laattan barbaachisummaa qorannichaaf yoo ta’u, qaama qorannicha gaggeessu irraa kan hafe qaama biraatti kan hin dabarsine ta’uu keenya ibsina.kanaafuu qorannoo kana irratti akka nuuf hirmaattaniif kabajaa fi ulfinaan isin gaafanna.yeroo barbaaddanitti diduus ta’ee addaan kutuuf mirga guutuu qabdu.haata’u malee hirmaannan keessan kaayyoo qorannichaa galmaan gahuuf gahee guddaa qaba.

Eeyyamamoo dha_____

Eeyyamamoo miti _____

Eeyyamamoo waan taataniif galatoomaa!

Annex IV: Amharic version Information sheet

እኔ _____ እባላለሁ በጅግ ዩኒቨርሲቲ ክምና ማ ስር ከሚከናወኑ ተግባራት አንዱ የተማሪዎች መመረቂያ ማሙያ የሚደረግ ጥናት ነው ስለሆነም ዶ/ር ድረባ ፋይሣ በጅግ ዩኒቨርሲቲ በሚሰጠው የሁለተኛ ዲግሪ ፕሮግራም ትምህርታቸውን በመከታተል ላይ ይገኛሉ። እናም የመመረቂያ ፅሁፋቸውን “assessment of depth of anesthesia and associated factors with Bispectral Index among people who are going to have surgery under general anesthesia at Jimma University Medical Center” ጥናት እያካሄዱ ይገኛሉ። በዚህ ምርምር ውስጥ ያለዎት ተሳትፎ በፈቃደኝነት ላይ የተመሰረተ ነው። ይህ ደብዳቤ በዚህ ጥናት ላይ ለመካፈልዎ ፍቃድ ለመጠየቅ ያገለግላል። ለመሳተፍ ፈቃደኛ ካልሆኑ በእርስዎ ላይ ምንም አይነት ችግር አይደርስብዎትም። በመሳተፍዎ የሚሰጡት ማንኛውም መረጃ በሚስጥር ይያዛል። ስምዎን ወይም ስልክ ቁጥር መስጠት አይጠበቅብዎትም። ቃለ-መጠይቁ ቢበዛ 30 ደቂቃ ይወስዳል። ለመሳተፍ ፈቃደኛ ከሆኑ መረዳትና የስምምነት ቅፅ ላይ መፈረም አለብዎት።

ጥናቱን የሚያካሄድ ስም: ዶ/ር ድረባ ፋይሣ ስልክ+251 967199944

ኢ-ሜል: fayisadiriba@gmail.com

በቃለ-መጠይቁ ላይ ለመሳተፍ ፈቃደኛ ነዎ? አዎ አይደለሁም

እርስዎ የዚህ ጥናት ተሳታፊ በመሆንዎ በጣም እናመሰግናለን።



Ref.No.

Date:

JHRP/81/2021
26/11/2021

To : Dr. Diriba Fayisa


Subject: Ethical Approval of Research Protocol

The IRB of Institute of Health has reviewed your research project "**Assessment of depth of anesthesia and associated factors in adult patients undergoing surgery under general anesthesia in JUMC** "

Thus, this is to notify that this research protocol has presented to the IRB meets the ethical and Scientific standards outlined in national and international guidelines. Hence, we are pleased to inform you that your research protocol is ethically cleared under the following strict conditions:

1. Any significant deviation from the methodological details indicated in the approved protocol must be communicated to the IRB before it has been implemented.
2. Approval shall be only for a period of twelve months. The principal investigator is required to submit an application for the renewal of the ethical approval.
3. The Committee must be notified Determinants of delayed care seeking for TB suggestive Symptoms in Siltie Zone, Southern Ethiopia: A community based unmatched case-control study ed, in writing, of any alteration to the project including unforeseen events/circumstances that might affect the acceptability of the approved protocol.
4. The Principal researcher is required to immediately notify the committee in the event of any adverse effects on participants or of any unforeseen events that might affect continued ethical acceptability or amendment to the original consent form.
5. The inability of the Principal Researcher to continue in that role, or any other change in research personnel involved in the project; should be communicated.

IRB Chairperson


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ANNEXES Three:

Questionnaire

JIMMA UNIVERSITY

INSTITUTE OF HEALTH SCIENCES, DEPARTMENT OF ANESTHESIA

Part I: Socio-demographic information

Directions: Please circle the appropriate number or fill in the blank

1. Age in years _____
2. Gender
 - a) Male
 - b) Female
3. Religion
 - a) Orthodox
 - b) Muslim
 - c) Protestant
 - d) Others
4. Marital status
 - a) Married
 - b) Single
 - c) Divorced
 - d) Widowed
5. Educational status
 - a) Illiterate
 - b) Elementary
 - c) High school Diploma
 - d) Degree & above
6. Residence
 - a) Urban
 - b) Rural
7. ASA classification
 - a) I
 - b) II
 - c) III

Part II: Types of surgery and anesthesia related factors

1. History of Previous surgery
 - a) Yes
 - b) No
2. If “yes” for number 1 question please specify type of previous surgery and anesthesia _____
3. Type of surgery (Specify name of the procedure _____)
 - a) General
 - b) Orthopedics
 - c) Gynecologic
 - d) Oral maxillofacial
 - e) Others (specify?)
3. Is there any comorbidity?
 - a. Hypertension
 - b. DM
 - c. No
 - d. Others specify _____
4. Premedication given name and dose _____
5. Type of anesthesia
 - a) General Anesthesia
 - b) Neuraxial block
 - c) Peripheral nerve block
 - d) Combined

6. Induction agent with dose: _____mg

a. ketamine

b. propofol

c. thiopental

d. ketofol

e) Succinylcholine f) others

7. Relaxation and maintenance with their doses _____mg

a) Halothane

b) Isoflurane

c) Vecuronium

d) Others

8. Antipain given intraoperatively type with its dose _____mg

9. Intraoperative complications A) Yes _____ B) No _____

10. If your answer to No: "14" is yes, which one?

a) Hypertension b) Hypotension c) Tachycardia d) Bradycardia

e) Laryngospasm f) Bronchospasm g) Hypoxia h) others (specify), _____

11. Postoperative complications A) Yes _____ B) No _____

12. If your answer to No: "14" is yes, which one?

a) Hypertension b) Hypotension c) Tachycardia d) Bradycardia

e) Laryngospasm f) Bronchospasm g) Hypoxia h) others (specify), _____

13. Delayed awakening, yes/no; possible cause _____

14. Time of surgery in hours _____

15. Time of anesthesia in hours _____

16. Reversal with its dose; _____mg

Part III: Behavioral factors and other variables

1. History of smoking: A. Yes B. No

2. If yes to smoke, frequency per week: A. Daily B. Sometimes C. Rarely

3. If yes to smoke, number of cigarette smoked per day in average _____

4. History of alcohol drinking: A. Yes B. No

5. If yes to alcohol, frequency per week: A. Daily B. Sometimes C. Rarely
6. If yes to alcohol, number of bottle/glass per day in average _____
7. History of chewing khat: A. Yes B. No
8. If yes to khat chewing, frequency per week: A. Daily B. Sometimes C. Rarely
9. History of smoking shisha: A. Yes B. No
10. If yes to smoke shisha, frequency per week: A. Daily B. Sometimes C. Rarely
11. History of smoking ashis (mariuna): A. Yes B. No
12. If yes to smoke ashis (mariuna), frequency per week: A. Daily B. Sometimes C. Rarely
13. History of sleep problems: A. Yes B. No
14. History of appetite loss: A. Yes B. No
15. History of emotional disturbance (anxiety, depression, frustration, fear, etc): A. Yes
B. No
16. Habit of physical exercise: A. Yes B. No
17. If yes to exercise, frequency per week: A. Daily B. Sometimes C. Rarely
18. If yes to exercise, for how long do you exercise per day _____ in minutes
19. Weight in kg _____
20. Height in cm _____
21. BMI _____

Part IV: Questionnaire for assessing intra-operative awareness and recall

1. Were you expecting to be completely asleep for this operation (please circle)? YES / NO
2. What is the last thing you remember before going to sleep (please tick one box)?

-Being in the pre-op area	<input type="checkbox"/>	-Seeing the operating room	<input type="checkbox"/>
-Being with family	<input type="checkbox"/>	-Hearing voices	<input type="checkbox"/>
-Feeling mask on face	<input type="checkbox"/>	-Smell of gas	<input type="checkbox"/>
-Burning or stinging in the IV line	<input type="checkbox"/>	-Other [Please write below]:	<input type="checkbox"/>

3. What is the first thing you remember after waking up (please tick one box)?

-Hearing voices	<input type="checkbox"/>	-Feeling breathing tube	<input type="checkbox"/>
-Feeling mask on face	<input type="checkbox"/>	-Feeling pain	<input type="checkbox"/>
-Seeing the operating room	<input type="checkbox"/>	-Being in the recovery room	<input type="checkbox"/>
-Being with family	<input type="checkbox"/>	-Being in ICU	<input type="checkbox"/>
-Nothing	<input type="checkbox"/>	-Other [Please write below]:	<input type="checkbox"/>

4. Do you remember anything between going to sleep and waking up (please tick box)?

-No	<input type="checkbox"/>		
-Yes: -Hearing voices	<input type="checkbox"/>	-Hearing events of the surgery	<input type="checkbox"/>
-Unable to move or breathe	<input type="checkbox"/>	-Anxiety/stress	<input type="checkbox"/>
-Feeling pain	<input type="checkbox"/>	-Sensation of breathing tube	<input type="checkbox"/>
-Feeling surgery without pain	<input type="checkbox"/>	-Other [Please write below]	<input type="checkbox"/>

5. Did you dream during your procedure (please tick box)?

-No -Yes

-What about [Please write below]:

6. Were your dreams disturbing to you (please tick box)?

-No -Yes

7. What was the worst thing about your operation (please tick box)?

-Anxiety	<input type="checkbox"/>	-Pain	<input type="checkbox"/>
-Recovery process	<input type="checkbox"/>	-Unable to carry out usual activities	<input type="checkbox"/>
-Awareness	<input type="checkbox"/>	-Other [Please write below]:	<input type="checkbox"/>

Vital signs base line	Time every 5 min																			
	BP																			
MAP																				
PR																				
Spo2																				
BIS																				
MAC (%)																				
BSR																				
TOF																				

