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The Effect of BIS Usage on Anaesthetic Agents Consumption in High-risk Patients for Coronary Artery-bypass Grafting Off-pump Surgery

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A B S T R A C T

The aim of this study was to compare whether the Bispectral Index (BIS) reduces anaesthesia consumption and improves recovery time in coronary artery bypass grafting-off-pump (CABG) surgery without awareness during surgery (ADS). The study was a prospective, randomised and double-blind comparative study of ASA3 patients enrolled for elective CABG surgery under general anaesthesia (GA). Patients received either propofol or isoflurane anaesthesia and their consumption was calculated and compared. Conventional groups CPG-1 and CIG-3 received propofol and isoflurane, and haemodynamic parameters (± 20% of baseline values) were considered for anaesthesia. Groups BPG-2 and BIG-4 received propofol and isoflurane, and the BIS (value 50±5) was used for maintenance of anaesthesia. Haemodynamic parameters, wake-up conditions, duration of intubation, hospital stay and drug consumption were also recorded. For explicit ADS, patients were interviewed 24 hours after extubation. The amount of propofol used was 178 ± 11 ml in CPG-1 and 117 ± 6 ml in BPG-2, with a 34.26% reduction in BIS. The amount of isoflurane used was 39 ± 8 ml in CIG-3 and 25 ± 6 ml in BIG-4, corresponding to a 35.89% reduction in isoflurane requirements. This difference was statistically significant in BIS monitored anaesthesia compared to conventional anaesthesia. The duration of intubation was 2.2 ±1.27 and 2.3 ±1.49 hours in the BPG-2 and BIG-4 groups, respectively ($p<0.05$). BIS-assisted CABG surgery with adequate depth of anaesthesia (BIS 50 ± 5) prevents ADS, reduces anaesthetic need for anaesthetics and facilitates ultrafast (UFT) extubation.

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1. Introduction

Coronary artery bypass grafting off-pump (CABG-OP) is an old technique first used in 1960 by Goetz [1]. CABG-OP is a minimally invasive surgery performed without cardiopulmonary bypass (CPB). Neither needs cross-

clamping of the aorta nor its cannulation. However, many studies have recognised the role of the systemic inflammatory response (SIR) caused by CPB in recent years, leading to substantial postoperative dysfunction of organs [2]. CABG-OP is a minimally invasive surgery that reduces perioperative morbidity and mortality such as stroke, renal failure, large blood transfusion, and coagulation disorders caused by CPB [3-5]. Also, OP surgery reduces the risk of cognitive changes that have been reported in many CPB-CABG cases [5, 6]. Encouraged with outcomes of CABG-OP, approximately 65% of CABG procedures are currently performed OP in Japan. In contrast, approximately 15% of CABG-OP is performed in Western countries [7]. Too deep anaesthesia leads to hypotension, delayed awakening, increased morbidity and mortality, and light anaesthesia leads to the risk of awareness during surgery (ADS) [8]. ADS has many long-term psychological consequences, such as depression, post-traumatic stress, insomnia, and anxiety [6, 9, 10]. Unintended accidental ADS reported 0.2% to 2% during general surgery [11, 12]. However, ADS is significantly higher in cardiac surgery, up to 23% [13]. ADS has been a concern among anaesthesiologists and the subject of numerous studies during the past few decades in cardiothoracic surgeries. Bispectral Index (BIS) monitors the depth of general anaesthesia, and values range from a hundred to zero. A BIS value of a hundred means a fully awake state, and zero means the absence of brain activity. A BIS value below 60 decreases the incidence of awareness during anaesthesia [14]. One anaesthetic agent may be less sedated than another, and combining drugs responds differently. Certain anaesthetics influence BIS values abnormally, for example, nitrous oxide and ketamine [14, 15]. After administration of neuromuscular blocking drugs (NMBDs), patients are immobile during surgery but provide evidence of ADS after surgery. Many previous studies proved the association between NMBD and awareness during surgery [16, 17]. BIS monitoring decreases anaesthetics requirements during surgery, as reported with sevoflurane, desflurane, alfentanil, and propofol anaesthesia [18, 19]. On the contrary, Karaca *et al.* reported that injection propofol consumption was more in the BIS group than without BIS (control) group in patients operated on for supratentorial mass under general anaesthesia [20]. Literature reviews initiate an academic debate on the utility of the BIS in reducing the requirement of anaesthetic agents in critically ill high-risk patients without ADS [18-20]. In CABG-OP surgeries, general anaesthesia (GA) is usually administered by an intravenous (IV) agent and then maintained with an inhalational agent till the end of surgery. However, a recent trend is to maintain GA solely with an intravenous agent, such as etomidate, propofol or dexmedetomidine [9]; this delivery method is called total intravenous anaesthesia (TIVA). Propofol (2,6-diisopropyl phenol) is a γ aminobutyric acid (GABA) receptor agonist used intravenously for sedation and hypnosis of patients during procedures. It has a fast onset and offset and demonstrated that a continuous infusion of the standard rate of propofol reduces the occurrence of ADS [21]. Isoflurane, a volatile anaesthetic used to induce and maintain general anaesthesia, halogenated ether compounds, in the central nervous system inhibits neurotransmitter-gated ion channels, including N-methyl-d-aspartate (NMDA), GABA, and glycine receptors. Due to weak -adrenergic stimulation, it has little effect on left ventricular function (LVF) and lowers systemic vascular resistance. However, it causes coronary dilation and the coronary steal phenomenon but is overlooked due to its cardioprotective effect by ischemic preconditioning [22]. This study compares conventional anaesthesia without BIS and BIS guided anaesthesia in terms of the use of anaesthetic drugs, blood pressure parameters, anaesthesia recovery time, length of intubation, awareness during anaesthesia, duration of stay (DOS) in the cardiac care unit (CCU) and DOS in hospital among patients undergoing CABG-OP surgery.

2. Materials and methods

The study was conducted in the Department of Anesthesiology and Intensive Care after approval by the Ethical Clearance Committee on Human Research (Number: AH/127/C/2021-22) SAMSRI, Lucknow, India, in accordance with the Declaration of Helsinki and the revised guidelines of 2000. All operations were performed under anesthesia and every effort was made to minimize suffering. SAMSRI is the second-largest referral hospital with a bed capacity of more than 1000 beds in the capital of Uttar Pradesh (UP), Lucknow. UP is India's largest state, with a population of >200 million. This was a single centre, prospective, randomised, and double-blind comparative research that recruited 100 patients from August 2021 to February 2022 of both genders below the age of 60, belonging to physical status (PS) 3 of the American Society of Anaesthesiologists (ASA) for elective CABG-OP surgery under GA. After explaining research protocols, informed written consent was obtained from participants. Exclusion criteria for the study were patients with left ventricular ejection fraction (LVEF) < 40%, New York Heart Association (NYHA) class IV, LV aneurysms, carotid stenosis, recent/unstable angina, cerebrovascular accident (CVA), emergency surgery, body mass index (BMI)> 40, on catecholamines or

vasodilators before anaesthesia, hepatic/ renal dysfunction, psychological/ neurological disorders, allergy to propofol, with alcohol intake and drug abuse. In addition, patients requiring perioperative Intra-aortic balloon pump (IABP) were also excluded from the study. We hypothesised that the anaesthetic requirement would be less in the BIS group than in the conventional (non-BIS) group. We derived a mean difference of 8.3% with a standard deviation of 10.5% from the pilot study. Two-sided α error of 0.05 and power of 0.8 with G*power 3.1 (flexible statistical power analysis program) calculated a sample size of 21 patients per group [26]. We included a drop-out rate of 15% to make up for withdrawals or surgeries converted to on-pump CABG, which is calculated 3.15. Therefore, the required sample size for each study group is (21 + 3.15 = 24.15) = 25 patients per group. A study nurse, with the help of a computer-generated randomisation programme, distributed participants to any one group from the conventional propofol infusion group (CPG-1), BIS guided propofol infusion group (BPG-2), conventional isoflurane group (CIG-3), and BIS guided isoflurane group (BIG-4) of 25 each. The drug, patient, and BIS allocation were concealed in an envelope. This envelope was opened on the day of surgery before the procedure. The patient and outcome assessor were blinded regarding drug allocation and the BIS monitoring group. The anaesthesiologist who anaesthetised and monitored the patient had all information. In groups (CPG-1 and CIG-3) and (BPG-2 and BIG-4), the depth of anaesthesia was maintained with conventional haemodynamics monitoring and BIS monitoring, respectively. The anaesthesiologist provided anaesthesia according to the research protocol. The patients were advised to take antihypertensive and antianginal medications as prescribed during the night with tablet diazepam 10 mg and on the morning of the operation with tablet diazepam 5 mg as premedication. Patients were kept nil per os after dinner on the night before surgery. After arrival in the operating room on the day of surgery, intravenous (IV) access was obtained. Non-invasive blood pressure (NIBP), electrocardiography (ECG), pulse oximetry (SpO_2), temperature, urine output, BIS and neuromuscular monitoring were performed. Baseline haemodynamics such as systolic (SBP), diastolic (DBP), mean arterial blood pressure (MAP), SpO_2 and heart rate (HR) were recorded. BIS was obtained with disposable sensors of BISTM Covidien Nellcor Medtronic, Minneapolis, USA monitoring system. BIS monitor was used in all study groups, but anaesthesia was maintained with BIS values in BPG-2 and BIG-4 groups. In the conventional propofol infusion group (CPG-1), anaesthesia was maintained with injection (inj) propofol 1mg/kg as a bolus, then infusion at 7–8 mg/kg/hr was maintained till sternotomy and after that maintained 5-6 mg/kg/hr while keeping blood pressures and HR within the range of ± 20% of baseline values as per the research protocols. In BIS guided propofol infusion group (BPG-2), anaesthesia was maintained with inj propofol 1mg/kg as a bolus, then titrated to a BIS of 50 (±5). Propofol used from Claris Life Sciences Limited (Gujarat, India)-Profol. In the conventional isoflurane (CIG-3) group, isoflurane and oxygen (O_2) were used, and isoflurane end-tidal concentration (Et iso) was adjusted to 1 or 2 minimum alveolar concentration (MAC) during the procedure while keeping haemodynamic changes within the range of ± 20% of baseline values. In the BIS guided Isoflurane group (BIG-4), isoflurane and O_2 were used to maintain anaesthesia to a BIS of 50 (±5). Isoflurane was administered in CIG-3 and BIG-4 groups through a calibrated isoflurane anaesthetic vaporizer-Jupitar (MNLife Care Products Private Limited, Kolkata, West Bengal, India). Isoflurane USP was used in our study from Piramal Healthcare (Andhra Pradesh, India). The total dose of isoflurane as liquid consumed was calculated using formula [23]: Total dose isoflurane as liquid (mL) = Fresh gas flow (mL/min) X volatile anesthetic concentration (Vol%) X Anaesthesia duration (min) / Saturated vapor volume (mL/ml) X 100 (Vol%)

Anaesthesia was induced with fentanyl 2µg/kg, midazolam 0.1mg/kg, lignocaine 50mg, propofol (1–2.5 mg/kg), isoflurane with MAC 1, and for tracheal intubation vecuronium dose, 0.1–0.2 mg /kg was used. For ventilation of the lungs, the intermittent positive pressure ventilation (IPPV) technique was used with 100% O_2. The end-tidal CO_2 ($EtCO_2$) of 33 (±3) mmHg was maintained by adjusting tidal volume (Vt) and respiratory rate (RR). Diclofenac sodium 100mg suppository was administered for perioperative analgesia. An arterial line and central venous catheter were inserted to monitor invasive blood pressure (IBP) and central venous pressure (CVP). Anaesthesia during the procedure was maintained with propofol or isoflurane as per study protocols. Phenylephrine, glyceryl trinitrate, and dopamine were used to maintain haemodynamics within 15% of the baseline value. To prevent intraoperative hypothermia warming blanket and warm airflow at 35°C- 40°C (Bear Hugger warmer EP, MN, US) was used. The total amount of fentanyl use was restricted to 10 µg/kg during the entire procedure. Vecuronium (0.01–0.02 mg/kg) was repeated for muscle relaxation. The patient received heparin 100-200 IU/Kg, so activated coagulation time (ACT) maintained greater than 300 seconds (secs) before graft anastomosis. Every 30 min, the ACT is repeated during the procedure, and heparin is added if ACT is recorded

below 300secs. During surgery, ST-segment analysis was carried out in I, II, and V5 ECG leads; any elevation or depression >1.0mm of ST-segment was considered significant. BIS scores were recorded throughout the surgery, but the BIS values were not considered during electrocautery. Patients were reversed with inj neostigmine 25 µg /kg at the end of the operation, and reversal was confirmed after achieving a TOF ratio > 0.9. Propofol/ isoflurane administration was stopped as per study protocol. Patients were mechanically ventilated and monitored for 2-3 hours before tracheal extubation in CCU. Removal of the endotracheal tube after ensuring haemodynamic stability, temperature 36 °C, no bleeding, and sufficient spontaneous ventilation indicated by Vt >6 ml/kg and negative inspiration pressure <-20 cmH_2O. The patient's observer assessment alertness and sedation (OAA / S) score of more than two was recorded [24]. Awareness is the presence of memory of any event from induction of anaesthesia to the time of emergence from GA. Using the Brice Questionnaire, a structured interview was conducted to rule out ADS after 24 hrs of tracheal extubation in the CCU [25]: 1. The last thing remembered after anaesthesia for the surgery? 2. The first thing remembered after the operation? 3. Is anything recalled between these two periods? While answering these questions, if the patient stated, "had no specific memory of event during surgery," further patients were not questioned. If the patient indicated memory of intraoperative events, then detailed information was gathered by a senior anaesthesiologist to assess the patient and answer their questions and, if required, then refer them for psychological counselling. In this study, statistical tests such as the Chi-squared test, Student's t-test, Wilcoxon-Mann-Whitney U test and ANOVA test are used to analyse the data. The study data are expressed as mean ± SD, median (interquartile range)/ percentage/and absolute numbers. In this analysis, a p-value <0.05 was considered significant. SPSS -23.0; IBM, Armonk, NY, the USA for Windows was used for statistical analyses.

3. Results and Discussion

One hundred patients were enrolled in this study as per our study's inclusion criteria. Study participants were randomly divided into four groups conventional propofol infusion group (CPG-1), BIS guided propofol infusion group (BPG-2), conventional Isoflurane group (CIG-3), and BIS guided Isoflurane group (BIG-4) of 25 each. These four groups were comparable, the study age 57±13.17 years, weight 82.9±9.21 kg, height 165±5.21 cm, body mass index 30.2±4.43 kg/m^2, and gender ratio of 1:18 between females and males (Table 1).

Table 1: Demographic profile.

Parameters (mean ± SD)	Study (n=100)	CPG-1 (n=25)	BPG-2 (n=25)	CIG-3 (n=25)	BIG-4 (n=25)	p-value
Age (Yrs)	57±13.17	57 ±13.41	57±13.25	56±13.64	58±12.38	0.914
Weight (Kg)	82.9±9.21	83.5±9.13	82.3±9.41	83.2±8.92	82.7±9.37	0.527
Height (cm)	165±5.21	166±5.38	164±4.83	165±5.16	165±5.47	0.382
BMI(Kg/m^2)	30.2±4.43	30.1±4.37	30.5±4.81	30.4±4.62	30.1±3.94	0.856
Sex F:M/percent	1:18/36%:64%	1:2.6/28%:72%	1:1.5/40%:60%	1:2.1/32%:68%	1:1.3/44%:56%	0.174

Patients' preoperative characteristics such as left ventricular ejection fraction, the number of grafts, and previous myocardial infarction showed no difference between the groups. In addition, the prevalence of comorbidities like hypertension and diabetes mellitus were 60% and 27%, respectively, in this study (Table. 2). These were comparable in all four groups.

Table 2: Distribution of patient's preoperative characteristics.

Clinical Variables	Study (n=100)	CPG-1 (n=25)	BPG-2 (n=25)	CIG-3 (n=25)	BIG-4 (n=25)
LV Ejection Fraction (mean) ± SD	50±6.1	51±5.7	50±6.2	49±5.8	51±6.7
Number of grafts (mean) ± SD	1.83±1.17	1.75±1.32	1.90±0.94	1.85±1.16	1.80±1.29
Previous MI n (%)	(43) 43	(11) 44	(13) 52	(10) 40	(9) 36
Hypertension n (%)	(60) 60	(16) 64	(15) 60	(14) 56	(15) 60
Diabetes mellitus n (%)	(27) 27	(7) 28	(9) 36	(6) 24	(5) 20

No difference was noticed between the groups regarding preoperative antihypertensive medications received. Patients on β-blockers, calcium channel blockers, and ACEI were 93%, 35%, and 21% in the study. None of the study participants was on digoxin or diuretics. There was also no difference between the groups receiving oral hypoglycaemic medications and insulin, and in the study were 85% and 15%, respectively (Table. 3).

Table 3: Distribution of patient's preoperative medications:

Preoperative medications	Study	CPG-1	BPG-2	CIG-3	BIG-4
Hypertensives on β-blockers n (%)	(56) 93	(15) 94	(13) 87	(14)100	(14) 93
Hypertensives on Calcium channel blockers n (%)	(21) 35	(6) 37	(4) 26	(6) 42%	(5) 33
Hypertensives on Digoxin n (%)	(0) 000	(0) 000	(0) 000	(0) 000	(0) 000
Hypertensives on Diuretics n (%)	(0) 000	(0) 000	(0) 000	(0) 000	(0) 000
Hypertensives on ACEI n (%)	(13) 21	(3) 19	(5) 33	(3) 21	(2) 13
Diabetics on Oral Hypoglycaemic Medications n (%)	(23) 85	(6) 85	(7) 77	(5) 83	(5) 100
Diabetics on Insulin n (%)	(4) 15	(1) 14	(2) 22	(1) 17	(0) 000

The study groups BPG-2 and BIG-4 average mean arterial pressure (MAP) prior to induction and after extubation (85.45±8 and 87.62±6mmHg) and post-intubation and after sternum closure were (76.47±7 and 74.51±8 mmHg), respectively (Fig.1). The study groups mean BIS values prior to induction, post-intubation, skin closure, and after extubation were 95.64±6.75, 51.32±11.92, 54.16±10.25, and 83.10±13.14 (Fig. 2). In addition, the mean BIS values during CABG-OP surgery in the groups CPG-1, BPG-2, CIG-3, and BIG-4 were 38±8, 49±5, 32±12, and 51 ±6, which were statistically significant in both the study groups with BIS monitoring compared to conventional anaesthesia during CABG-OP surgeries (Tables 4 and 5).

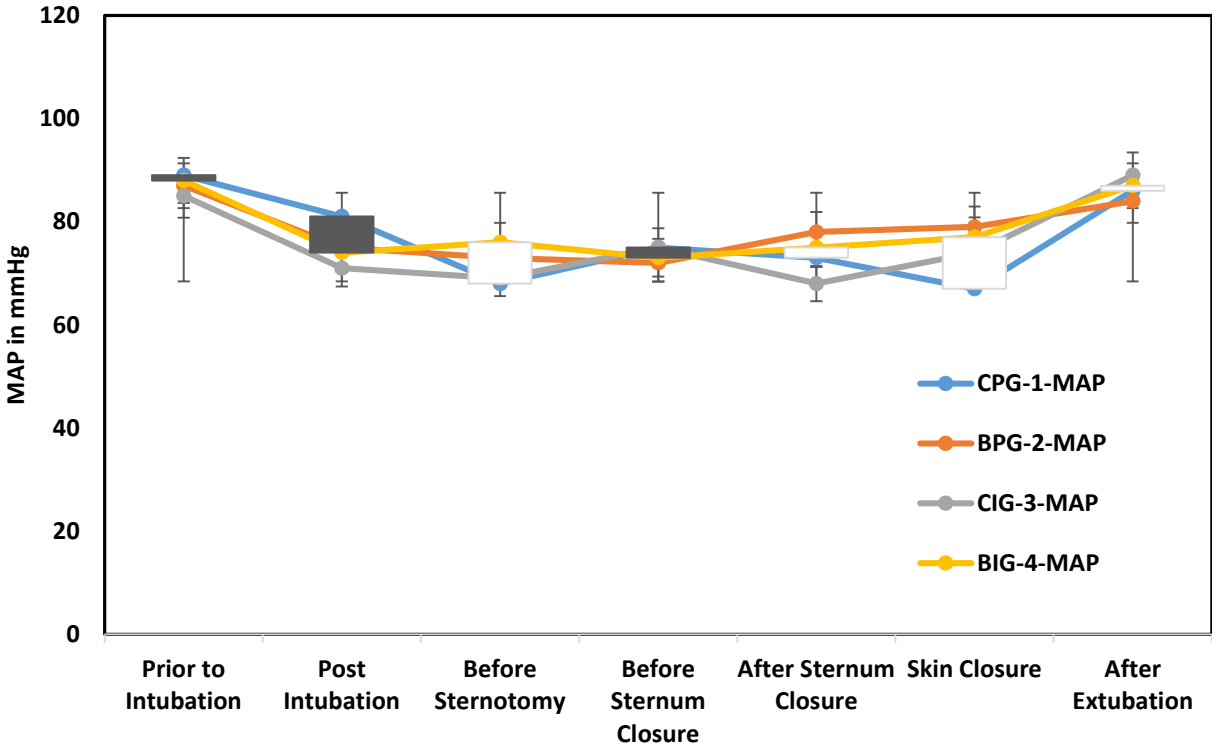

Figure 1: Mean arterial pressure (MAP) between study groups.

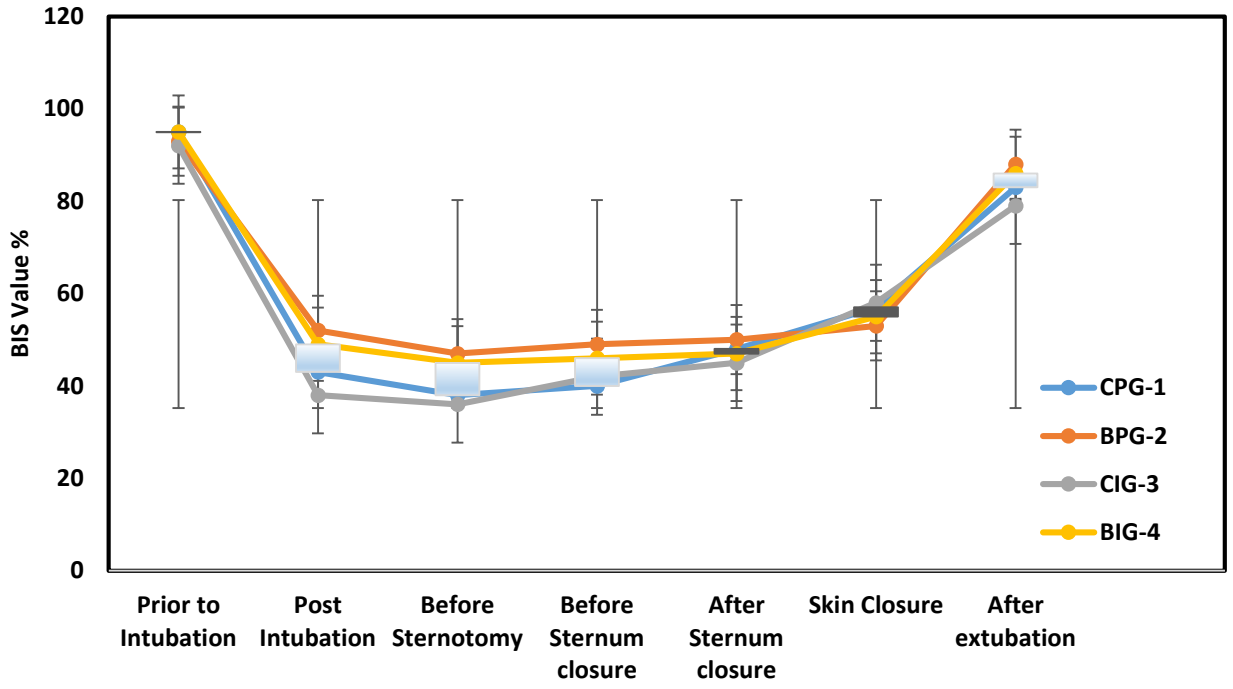

Figure 2: BIS scores between study groups.

The mean quantity of propofol used for CABG-OP surgery was 178 ± 11 mL in CPG-1 and 117 ± 6 mL in BPG-2. On calculating, there was a reduction of 34.26% in propofol requirements with BIS guided anaesthesia for CABG-OP surgeries compared to conventional anaesthesia for CABG-OP surgeries, which was statistically significant in both the study groups (Table 4).

Table 4: BIS value and propofol used in study groups.

Anaesthetic Agents Used	CPG-1 (n=25)	BPG-2 (n=25)	p-value
Mean BIS value during CABG-OP surgery	38±8	49±5	<0.0001
Total quantity of propofol (mean ± SD) mL	178 ± 11	117 ± 6	<0.0001
Propofol mL/hr (mean ± SD)	35.3 ± 8	23.6 ± 5	<0.0001

Standard deviation =SD, p-value significant <0.05.

The quantity of isoflurane used to perform CABG-OP (the formula to derive the amount of isoflurane in mL is mentioned in methods) was 39 ± 8 mL in CIG-3 and 25± 6ml in BIG-4. On calculating, there was a reduction of 35.89% in isoflurane requirement with BIS monitored anaesthesia compared to conventional anaesthesia for CABG-OP, and this difference was statistically significant with the use of BIS (Table 5).

Table 5: BIS value and isoflurane used in study groups.

Anaesthetic Agents Used	CIG-3 (n=25)	BIG-4 (n=25)	p-value
Mean BIS value during CABG-OP surgery	32±12	51 ±6	<0.0001
Total quantity of propofol (mean ± SD) mL	39 ± 8	25 ± 6	<0.0001
Isoflurane mL/hr (mean ± SD)	7.2 ± 6	4.5 ±3	<0.0001

All patients completed CABG-OP surgeries without converting them into an on-pump procedure. In groups, BPG-2 and BIG-4 lengths of endotracheal intubation were 2.2 ±1.27 and 2.3 ±1.49 hours, respectively. The extubation time was reduced by 37% and 50% for propofol and isoflurane with BIS, which was statistically significantly lower for the BIS groups. The Observer assessment of alertness and sedation score (OAA-S) >2, DOS in CCU, and DOS in the hospital had no significant difference among the four groups. None of our participants had ADS when interviewed 24 hours after extubation in CCU.

Table 6: Distribution of patient's postoperative characteristics in propofol groups.

Clinical Variables	CPG-1 (n=25)	BPG-2 (n=25)	p-value
Observer assessment of alertness and sedation (OAA/S) score >2	248±93	241±85	0.728
Length of intubation (hrs)	3.5 ±4.51	2.2 ±1.27	0.041*
Duration of stay in CCU (hrs)	42±9.3	41±7.6	0.653
Duration of stay in hospital (days)	6.3±1.42	6.4±1.57	0.742
Explicit recall	0 (000%)	0(000%)	1.000

Table 7: Distribution of patient's postoperative characteristics in isoflurane groups.

Clinical Variables	CIG-3 (n=25)	BIG-4 (n=25)	p-value
Observer assessment of alertness and sedation (OAA/S) score >2	248±93	241±85	0.728
Length of intubation (hrs)	3.5 ±4.51	2.2 ±1.27	0.041*
Duration of stay in CCU (hrs)	42±9.3	41±7.6	0.653
Duration of stay in hospital (days)	6.3±1.42	6.4±1.57	0.742
Explicit recall	0 (000%)	0(000%)	1.000

Nowadays, many anaesthesiologists monitor haemodynamic responses and or measure minimum alveolar concentrations of inspired inhalation anaesthetics to adjust the doses of anaesthetic agents during general anaesthesia. However, these adjustments do not always reflect anaesthesia's hypnotic component and lead to ADS. Deep anaesthesia may develop complications such as delayed awakening, hypotension, increased morbidity and mortality, and awareness may occur through superficial anaesthesia [8]. The ADS reported in the literature and incidence of ADS varies between 0.2 to 2% [11, 12]. The incidence of ADS, especially in cardiac surgery, is significantly higher, with an older report of up to 24% [13]. In cardiac surgeries, the incidences of awareness are more common due to the longer duration of surgery and frequent use of muscle relaxants. The heart's compression and displacement are ubiquitous during CABG-OP, resulting in a significant increase in atrial pressures and a marked decrease in cardiac output. Patients with low cardiac output and pulmonary arterial hypertension (PAH) become vulnerable to haemodynamic compromise with deep anaesthesia. Anaesthesiologists, therefore, try to minimise anaesthetic drug utilisation among these patients resulting in ADS. The exact amount of the anaesthetic required to guarantee lack of recall is unknown. A reliable monitor that can ensure unconsciousness is highly desirable in high-risk patients. Many electroencephalographies (EEG) based machines have been marketed for this purpose, and the most common are M-entropy (G.E. Health-care), Narcotrend (MonitorTechnik) and Bispectral Index (Medtronic Ltd). The most broadly studied and FDA approved is the BIS, used to titrate anaesthetic agents to maintain a loss of consciousness and prevent ADS [18, 19]. While comparing ADS in the BIS group and without the BIS (conventional) group patients, the B-Aware study reported that BIS utilisation reduces the risk associated with the incidence of ADS by 82% [27]. However, Avidan *et al.* performed a more extensive BAG-RECALL study and could not demonstrate BIS's superiority over end-tidal anaesthetic gas concentration (ETAC) in preventing ADS [11]. Karaca *et al.* compared the effects of BIS monitoring with the conventional anaesthesia approach and reported no incidence of awareness in their study [20]. These differences may be due to differences in the study designees, the dose of anaesthetic drugs used, and the patients' condition. In addition, Karaca *et al.* under-reported cases of ADS, as they ruled out awareness of intra-operative events at 20 minutes after surgery in the recovery unit, which was too early. Although previous literature has acknowledged that the structured postoperative interview is the most appropriate method to investigate ADS, the interview's actual timing is debatable. Some studies advocated interviewing patients as soon as they regain consciousness. Others suggest

interviewing patients after 24 hours or even as long as 30 days after surgery [3]. However, most patients will be drowsy during the early interview and may give unreliable information. Interviewing after one week would eliminate patients already discharged from the hospital with an ultra-fast-track (UFT) strategy involving early hospital discharge for more cost-effective quality health care [28]. Interview 24 hours after extubation was the interview timing in our study due to the UFT extubation strategy. In a study, Leslie *et al.* disclosed that a BIS value <40 maintained for five minutes during surgery increases morbidity and mortality of patients [8]. Also, Monk *et al.*, in a retrospective study, reported deep hypnotic time with a BIS <45 as a significant risk for one-year mortality [29]. Therefore, to reduce the deep hypnotic time and avoid ADS, we used BIS monitoring in these high-risk patients going for OP-CABG and kept the BIS value 50 ± 5. On the other hand, Karaca *et al.* compared the effects of BIS monitoring with the conventional anaesthesia approach and reported that BIS monitoring does not bring much benefit [20]. This was maybe due to the wide range of BIS values used in their study, from 40 to 60. BIS monitoring enables one to titrate anaesthesia to meet patients' requirements without awareness, especially in high-risk patients with cardiovascular disease, haemodynamic instability, or renal failure. In our study groups, BPG-2 and BIG-4 showed average MAP prior to induction and after extubation (85.45±8 and 87.62±6mmHg) with average BIS values (92±6 and 87±11) and post-intubation and after sternum closure showed average MAP (76.47±7 and 74.51±8 mmHg) and average BIS values (52± 4 and 54 ±3), respectively. BPG-2 and BIG-4 reductions in MAP were noticed in groups along with BIS values. Our haemodynamic findings are inconsistent with Thomas *et al.*, who reported hypotension incidences correlated with low BIS values [30]. Our study recorded no hypotension as a BIS value of 50 ± 5was titrated with blood pressure. Many researchers compared BIS versus conventional anaesthesia practices (18-20). The use of propofol in the BIS and control groups varied between 2.8 to 8.0 mg/kg/hour and 4.9 to 11.9 mg/kg/hour, respectively. Using BIS monitoring during CABG-OP surgery, we reduced the requirement of propofol by 34.26% and isoflurane by 35.89%. Our findings support Gan *et al.* that the BIS monitoring reduces the quantity of anaesthetic drugs (9, 19). In contrast, Karaca *et al.* reported that propofol consumption was more in the BIS group than in the conventional group [20]. However, in their study difference between the two groups was statistically insignificant. We believe that the disparity in results is related to methodological discrepancies, as they used a BIS value of 40 compared to our 50. Likewise, titrating anaesthetic agents with BIS monitoring decreases anaesthetic drug requirements. The reduced use of anaesthetic drugs during CABG-OP in patients with poor LV function causes less myocardial depression and reduces the requirement for inotropic support and arrhythmias. In a study, Gan *et al.* compared BIS to the conventional anaesthesia practice and reported BIS reduces propofol requirement and that leads to faster recovery [19]. The length of postoperative intubation in the groups BPG-2 and BIG-4 were (2.2 ±1.27) and (2.3 ±1.49) compared to the groups CPG-1 and CIG-3 were (3.5 ±4.51) and (4.6 ±3.72), respectively. The length of postoperative intubation was significantly less in BIS groups BPG-2 and BIG-4 in our study, supporting the study of Gan *et al.* [19]. The authors believe that the extubation time was impacted by factors other than the propofol or isoflurane dose.

4. Conclusions

Our study raised an important question: high-risk OP-CABG patients get more anaesthetic drugs than required without BIS monitoring. In this era of UFT anaesthesia with early extubation and CCU discharge, minimising unnecessary exposure to anaesthetic agents using BIS monitoring is crucial. Furthermore, many anaesthesiologists would prefer to limit excessive use of anaesthetic agents due to their myocardial depressing property, particularly while grafting the distal vessels when haemodynamic instability is typical. Thus, BIS monitoring aids CABG-OP surgeries by monitoring the depth of anaesthesia (BIS value 50 ± 5), preventing ADS (0%), reducing anaesthetic requirement (propofol 34.26% and isoflurane 35.89%), reducing myocardial depression (MAP >74mmHg), and aiding ultra-fast-track (UFT) extubation (37 and 50% reduction in the duration of intubation in propofol and isoflurane with BIS).

Conflict of Interest

The authors declare that they have no conflict of interest.

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