

# Intraoperative Awareness and Post Operative Recall and Cognitive Dysfunction in Patients Undergoing Off Pump Coronary Artery by Pass Grafting with Intravenous Propofol v/s Dexmedetomidine - A Randomised Control Study

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**Abstract:** Background: Awareness during general anesthesia is unanticipated patient wakefulness during surgery or recall of intraoperative events. Incidence of awareness in patients undergoing cardiac surgery is significantly higher than the overall incidence of 1% during general surgery. Awareness during cardiac surgery can be prevented by supplemental, intraoperative use of sedative agents. Propofol has been shown to reduce the incidence of awareness. Dexmedetomidine is also being considered for maintaining intraoperative depth of anesthesia. Postoperative cognitive dysfunction (POCD) is a regular and well known complication after prolonged surgeries that can prolong recovery from surgery and impair quality of life in the longer term. The purpose of this study was to evaluate the effect of dexmedetomidine on depth of anesthesia and to compare it with the effect of propofol in cardiac surgery. Methodology: This was a prospective, randomized, double-blind study conducted in a tertiary-care hospital. 69 patients with ASA - PS I - III planned for elective open heart surgery were randomized into three groups of 23 patients each. Each patient of the dexmedetomidine group received an initial bolus dose of dexmedetomidine at 1 mcg kg<sup>-1</sup> over 10 minutes followed by infusion at the rate of 0.2–0.6 mcg kg<sup>-1</sup> hr<sup>-1</sup>. Patients of the propofol group received infusion at the rate of 0.25 - 1 mg kg<sup>-1</sup> hr<sup>-1</sup> and the control group were administered only isoflurane. An identical technique—of standard general anesthesia and routine physiological monitoring—was used in the three groups. Bispectral scores were recorded at predetermined intervals during surgery. The patients were assessed for awareness and recall 24 hours after tracheal extubation. Results: Intraoperative BIS scores remained within the target range; however, the BIS scores showed variable trends between the groups and were significantly lower in the dexmedetomidine group ( $p < 0.001$ ). None of the patients in the three groups had recall of intraoperative events. MMSE scores on POD 1 were found to be significantly higher in the dexmedetomidine group, suggesting lesser incidence of POCD. Conclusion: Administration of dexmedetomidine was as effective in reducing awareness and recall in cardiac surgery compared to propofol. Thus, dexmedetomidine can be used as an alternative agent to prevent awareness and recall in cardiac surgery. It was found that dexmedetomidine administration will also reduce the incidence of POCD when compared to propofol.

**Keywords:** awareness, postoperative cognitive dysfunction, dexmedetomidine, propofol, OPCABG

## 1. Introduction

Cardiovascular disease is considered as a major problem in our society, and is one of the major causes of death. The cardiac surgical patients are at an increased risk for intraoperative awareness and recall, especially due to intentional avoidance of the cardiac depressant volatile anaesthetics in the presence of hemodynamic instability, mostly caused by surgical manipulations of the heart and great vessels, leading to intervals of light planes of anaesthesia.

Awareness during anaesthesia is an uncommon but serious drawback with potential long-term psychological consequences for the patient and medico-legal consequences for the anaesthetist. Awareness is a degree of consciousness occurring during the period in which the patient is assumed to be under general anaesthesia. It has been disclosed by patients after the surgery by explicit memory; the ability of the patient to remember events that occurred during anaesthesia. Intraoperative awareness and post-operative recall continues to be a matter of clinical significance and neurobiological inquisitiveness.

Intra-operative awareness can be identified postoperatively by obtaining information directly from the patient as there

are reliable methods for the detection of intraoperative awareness.

Newer techniques for detecting intraoperative awareness focus on measuring brain activity. The use of such monitoring techniques during general anaesthesia will decrease the likelihood of awareness. Of these, the bispectral index (BIS) has been most widely accepted in clinical practice. The BIS monitor integrates a proprietary algorithm that analyses signals from scalp EEG electrodes. The monitor shows a dimensionless number between (0) and (100), with lower numbers indicating deeper planes of anaesthesia.

Postoperative cognitive dysfunction (POCD) is a regular and recognized complication after prolonged surgeries. But due to the modest nature of POCD, this complication might be recognized only by the patient's relatives. Accordingly, neuropsychological testing is needed for its detection.

Its clinical manifestations include cognitive function disorder, personality change and memory impairment; in severe cases, Alzheimer's disease (AD) may occur. Postoperative cognitive dysfunction can delay recovery from surgery and impair quality of life in the longer term. The Mini-Mental State Examination (MMSE) is commonly

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used to evaluate cognitive function in patients postoperatively.

## 2. Methodology

After Institutional Ethics committee's approval and obtaining written informed consent, this randomized controlled study was conducted on sixty nine American Society of Anaesthesiologist's (ASA) Physical Status I - III adults scheduled for elective Off - pump Coronary Artery By - pass Grafting (OPCABG) at A. J. Institute of Medical Sciences and Research Centre Hospital, Mangalore, between December 2019 and June 2021.

A thorough pre anaesthetic evaluation was done where a detailed history of medical illnesses, anaesthesia in the past was taken.

Laboratory test to assess the functions of vital systems such as hepatic, renal, coagulation was done prior to planning the surgery. Preoperative transthoracic echocardiography, chest X ray, and ECG served as baseline investigations.

All patients of both genders undergoing off pump coronary artery bypass grafting under general anaesthesia were included in this study.

Exclusion criteria comprised of -

- 1) Patients who had to undergo on - pump coronary artery bypass grafting
- 2) Patients who developed post - operative delirium or psychosis
- 3) Patients with renal/liver dysfunction, or allergic to propofol or dexmedetomidine

Preoperative optimization of diabetes, hypertension and reactive airway was done. Low molecular weight heparin and unfractionated heparin were with - held 12 hours and 6 hours prior to surgery.

Patients were advised NPO for 8 hours prior to the procedure. Pre - anaesthetic medication consisted of T. Ranitidine 150mg BD and T. Diazepam 10mg HS or T. Alprazolam 0.25mg HS.

After arrival to the anaesthetic room, patients were administered oxygen by facemask and monitoring of ECG (5 lead) with automated ST segment analysis and pulse oximetry and non - invasive blood pressure monitors were connected and monitoring was initiated. A 20G and 18G (9cm) BD intra - arterial cannula was inserted into the right radial artery and right femoral artery respectively for monitoring of the arterial pressure and obtaining arterial blood for analysis.

A triple lumen 11 Fr Central venous catheter was inserted into right internal jugular vein for monitoring of central venous pressure.

Non - invasive monitoring device - the BIS monitor was applied. BIS was obtained using disposable sensors (Covidien IIC, MA, USA). EEG electrodes were placed in a

bifrontal montage. The EEG signal acquired and the BIS scores displayed on the monitor were recorded.

General anaesthesia was induced, while patients breathed 100% O<sub>2</sub> by facemask, using a combination of fentanyl 2 µg/kg, midazolam 100 µg/kg, Inj. Etomidate 0.2mg/kg and endotracheal intubation was performed after administration of Inj. Rocuronium 0.15 mg/kg and mechanical ventilation was initiated. Low - flow technique (fresh gas flow of 1 L/min) using anaesthesia workstation to achieve end - tidal carbon - dioxide tensions of 35 ± 3 mm Hg was used. Inspired and expired gas concentration of oxygen, carbon dioxide (CO<sub>2</sub>) and Isoflurane was measured using smart anaesthetic gas monitoring system. Muscle relaxation was maintained with vecuronium bromide (0.01–0.02 mg kg<sup>-1</sup>). Haemodynamic parameters were maintained within 25% of the basal values with dopamine, phenylephrine, and glyceryltrinitrate, as required. Intraoperative hypothermia was prevented by the use of warm airflow, warming blanket and warm intravenous fluids.

Patients were randomly divided into three groups using lottery technique:

Group P: In this group, anaesthesia was maintained using Isoflurane in oxygen; Along with this patients received intravenous propofol infusion at 0.25 mg/ kg/ hr.

Group D: In this group, anaesthesia was be maintained using Isoflurane in oxygen; Along with intravenous dexmedetomidine 1mcg/kg bolus over 10 minutes and 0.2 - 0.6mcg/kg/hr infusion.

Group C: In this group, anaesthesia was maintained using Isoflurane in oxygen.

BIS scores were recorded during surgery at the following time points: prior to induction; postintubation; at sternotomy; before and after partial aortic cross clamping; after closure of thorax; and at the end of surgery.

Patients received heparin in a dose of 300 units/kg prior to anastomosis so as to maintain an activated coagulation time of greater than 300 seconds. After skin closure, the dexmedetomidine / propofol infusion was stopped.

All patients were ventilated postoperatively for 2 - 4 hours and tracheal extubation performed after satisfying the criteria for extubation.

An intensive care unit resident interviewed all patients at 24 hours after extubation. After an initial introduction, the interview, which was very structured, was begun. Each patient was asked the following standard set of questions.

- 1) What was the last thing you remember before surgery?
- 2) What was the first thing you remember after waking after the operation?
- 3) Do you remember anything in between these two periods?
- 4) Did you have any dreams during your operation?
- 5) What was the most unpleasant thing you remember from your operation and anaesthesia (noises/ voices, feeling anything, or waking up)?

If the patient indicated that he or she had explicit memory of intraoperative events while answering the questions, the following sub - questions were asked:

- 1) What did you notice; sounds, touch, pain, paralysis?
- 2) How long did it last?
- 3) Did you try to alert anything?
- 4) Have there been any consequences for you?

Awareness was defined by the presence of explicit memory of any event from induction of anaesthesia to recovery of consciousness in the cardiac surgical intensive therapy unit (ITU).

The baseline cognitive functions will be assessed by an examiner blinded to patient's allocation, for each patient, a day before surgery and repeated 24 h postoperatively and one week later. Patients with MMSE score <24 post operatively were considered to have cognitive dysfunction.

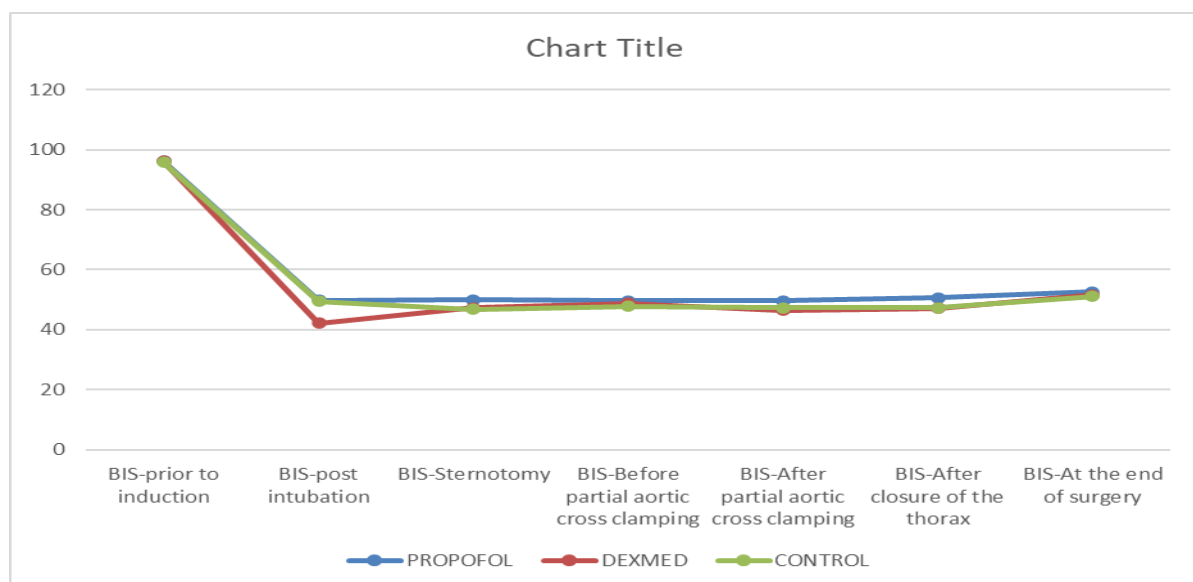
### 3. Discussion

In our study we found monitored intraoperative anaesthetic depth at specific time intervals using Bispectral Index. Mean

BIS scores before induction was  $96.09 \pm 1.13$  in the dexmedetomidine group and  $94.87 \pm 1.74$  in the propofol group and  $95.83 \pm 0.78$  in the control group. The scores were comparable and statistically insignificant. BIS scores in the post - intubation period and throughout the surgery remained within the target range of 40 - 60.

The difference between the scores among patients in the three groups was statistically significant (Fig.1) (Fig.2) On Post hoc analysis, the dexmedetomidine group was found to have recorded significantly lower BIS scores compared with the propofol group in the post - intubation period (p value < 0.001), at sternotomy (p value 0.004), after partial aortic cross - clamping (p value - 0.001) and after the closure of the thorax (p value < 0.001). None of the patients who were interviewed postoperatively gave responses suggestive of awareness under anaesthesia.

We studied incidence of awareness among 69 patients with ASA physical status 3, scheduled for elective off - pump coronary artery bypass grafting. The patients were randomly allocated into 3 groups of 23 each - Propofol group, Dexmed group and Control group.



**Figure 1:** Comparison of BIS scores between the three groups at various intervals of the surgery

The three groups were comparable for age, sex, weight, ASA PS and LVEF. No patients were excluded from the study.

Explicit memory' is assessed by the patient's ability to recall specific events that took place during general anaesthesia.

The unintended experience and memory of surgical or procedural events can be devastating for patients and remains a dynamic area of investigation. Intraoperative awareness, with or without explicit episodic recall, is relevant to patient safety, standards for intraoperative monitoring, and the search for the neural correlates of consciousness.

None of the patients included in our study reported intraoperative awareness of being interviewed. Their BIS values monitored were all within the target range. This absence of awareness under anaesthesia in our study can be attributed to the use of a balanced anaesthesia technique. The control group which received only the volatile agent in higher concentrations without any intravenous infusions also showed no evidence of awareness. A possible factor for a low frequency of awareness could also be due to a lack of accurate feedback from the patients.

**Figure 2:** Comparison of BIS scores between the three groups at various intervals of the surgery

	PROPOFOL	DEXMED	CONTROL	ONE WAY ANOVA		POSTHOC TUKEY TEST		
				Welch Statistics (*)/F (ANOVA)	P VALUE	PROPOFOL vs DEXMED difference (p value)	PROPOFOL L vs CONTROL difference (p value)	DEXMED vs CONTROL difference (p value)
<b>BIS-prior to induction</b>	96.13±1 .18	96.09± 1.13	95.83±0 .78	0.57 3	0.566	0.04 (0.989)	0.3 (0.586)	0.26 (0.674)
<b>BIS-post intubation</b>	49.74±4 .81	42.13± 1.84	49.43±3 .31	57.1 88*	<b>&lt;0.001</b>	7.61 (<0.001)	0.3 (0.954)	-7.3 (<0.001)
<b>BIS-Sternotomy</b>	49.91±3 .58	47.35± 1.58	46.83±2 .33	6.19 4*	<b>0.005</b>	2.57 (0.004)	3.09 (0.001)	0.52 (0.78)
<b>BIS-Before partial aortic cross clamping</b>	49.57±3 .88	48.87± 1.46	47.91±3 .4	1.23 4*	0.303	0.7 (0.727)	1.65 (0.174)	0.96 (0.549)
<b>BIS-After partial aortic cross clamping</b>	49.57±4 .08	46.52± 1.47	47.3±2. 25	5.87 6*	<b>0.006</b>	3.04 (0.001)	2.26 (0.022)	-0.78 (0.616)
<b>BIS-After closure of the thorax</b>	50.61±3 .82	47.22± 1.54	47.3±2. 01	7.94 2*	<b>0.001</b>	3.39 (<0.001)	3.3 (<0.001)	-0.09 (0.993)
<b>BIS-At the end of surgery</b>	52.65±3 .8	51.65± 2.01	51.22±2 .71	1.07 3*	0.351	1 (0.484)	1.44 (0.229)	0.44 (0.87)

MMSE scores were used to assess postoperative cognitive dysfunction among all the patients undergoing OPCABG. According to the Mini Mental-State Examination score: 24 - 30 - No cognitive impairment; 18 - 23 - Mild cognitive impairment; 0 - 17 - Severe cognitive impairment.

Preoperative and postoperative scores were recorded. Preoperatively MMSE scores between the three groups were statistically insignificant and hence comparable. The scores were significantly reduced after surgery, as compared to before surgery especially in the control group. On postoperative day 1 (POD 1), the scores were 23.7±0.93 in the propofol group, 24.13±0.82 and 22.7±1.22 in the Dexmedetomidine group and control group respectively. On post hoc analysis, the incidence of POCD was significantly lower in Dexmedetomidine group than that in control group. The patients in the propofol group had significantly higher scores compared to the control group. However, on comparing the scores between the propofol and dexmedetomidine group, there was no statistically significant difference observed. Assessment done on POD 7, showed improvement in the scores and no significant difference between the groups.

POCD is usually short-lived and resolves in a few weeks to 6 months. Its pathogenesis is multifactorial, with the inflammatory stress response to surgery and anaesthesia probably acting as a trigger.

In our study, the neuropsychological test used to define POCD was a simple screening method (Mini - Mental State Examination), and there might be confounding factors due to other anaesthetics used during anaesthesia (eg: benzodiazepines, propofol, inhalation anaesthetics) that could alter patients neuropsychological states.

It has been widely speculated that as an anaesthetic adjuvant, dexmedetomidine decreases the need for opioids, inhalational anaesthetics, and also intravenous anaesthetics. It is known to have MAC sparing effects.

Hemodynamic parameters were within normal range among all the patients throughout the surgery, however significantly lower values were recorded in the Dexmed group.

#### 4. Conclusion

Patients in the dexmedetomidine group were found to have lower BIS scores than propofol group and control group. It can thus be used as an alternate anaesthetic adjuvant to maintain adequate depth of anaesthesia and prevent awareness among patients undergoing off pump coronary artery bypass grafting. Dexmedetomidine was also found to be beneficial in preventing POCD compared to propofol.

## MMSE Scores

**Table 16:** Comparison of MMSE scores between the groups

	PROPOFOL	DEXMED	CONTROL	ONE WAY ANOVA		POSTHOC TUKEY TEST		
				Welch Statistics (*)/F(ANOVA)	P VALUE	PROPOFOL vs DEXMED difference (p value)	PROPOFOL vs CONTROL difference (p value)	DEXMED vs CONTROL difference (p value)
<b>MMSE-preop</b>	26.52±0.99	26.3±1.11	26.57±1.2	0.369	0.693	0.22 (0.783)	-0.04 (0.99)	-0.26 (0.703)
<b>MMSE-POD1</b>	22.13±0.69	24.13±0.82	22.7±1.22	39.994*	<b>&lt;0.001</b>	-2 (<0.001)	-0.57 (0.11)	1.44 (<0.001)
<b>MMSE-POD7</b>	26.74±0.86	26.22±1.28	26.17±1.23	1.753	0.181	0.52 (0.273)	0.57 (0.219)	0.04 (0.991)

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