

## PROPOFOL VERSUS DEXMEDETOMIDINE SEDATION REDUCES DELIRIUM AFTER CARDIAC SURGERY

Muhammad Adnan Khan<sup>1</sup>, Muhammad Usman<sup>2</sup>, Israr Hussain<sup>3</sup>, Sayyed Nadar Shah<sup>4</sup>, Omar Khattab<sup>5</sup>, Bashir Ul Haq<sup>6</sup>, Siti Khuzaiyah<sup>7</sup>, Muhammad Tayyeb<sup>8</sup>

### Correspondence

<sup>8</sup>Muhammad Tayyeb, Lecturer Anesthesia, Department of Anesthesia, College of Medical Technology, Medical Teaching Institution, Bacha Khan Medical College, Mardan

☎: +92-313-9936972

✉: [tayyabm851@gmail.com](mailto:tayyabm851@gmail.com)

<sup>1</sup>Department of Anaesthesiology, Afridi Medical Complex, Peshawar

<sup>2</sup>Department of Anaesthesiology, Afridi Medical Complex, Peshawar

<sup>3</sup>Department of Anaesthesiology, Institute of Health Sciences, Peshawar

<sup>4</sup>Department of Intensive Care Unit, Hayatabad Medical Hospital, Peshawar

<sup>5</sup>Department of Anaesthesiology, Afridi medical complex AMC, Peshawar

<sup>6</sup>Respiratory Therapist, Lady Reading Hospital, Peshawar

<sup>7</sup>Department, Faculty of Health Sciences, Universitas Muhammadiyah Pekajangan Pekalongan, Central Java, Indonesia

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### INTRODUCTION

Delirium is a serious neurological condition that causes disruptions in awareness, concentration, cognition, and perception. Between 20 and 50 percent of individuals after heart surgery experience postoperative delirium (POD), and the risk is much higher in the elderly.<sup>1,2,3</sup> POD is associated with higher healthcare expenses, higher care home admission rates, higher morbidity and death rates, and may have unfavourable effects on patients and their families.<sup>4</sup> Whereas POD's risk factors and effects are well understood, no pharmaceutical treatment for this illness has been recommended.<sup>5</sup> The frequency of POD in patients following cardiac surgery is decreased by dexmedetomidine, according to a series of recent meta-

### ABSTRACT

#### OBJECTIVES

*Postoperative delirium (POD) is a serious complication after cardiac surgery. Use of dexmedetomidine infusion to prevent delirium is controversial. We hypothesized that dexmedetomidine sedation after cardiac surgery would reduce the incidence of POD.*

#### METHODOLOGY

*After the approval from institutional ethics review board and informed consent, a comparative cross sectional study was conducted in 100 patients scheduled for cardiac surgery. Patients suffering from consequential psychological issues, delirium, and grievous dementia were excluded. Delirium was evaluated by confusion assessment method for ICU (CAM-ICU). Normality and homogeneity of data were analyzed using Kolmogorov-Sminorv and saphiro wilk. The factors related to delirum status were analyzed using Logistic Regression.*

#### RESULTS

*The mean age among propofol group was 55.14±9.6 while among Dexmedetomidine was 55.96±12.1. POD was present in 24 of 50 (48%) and 4 of 50 (8.%) patients in propofol and dexmedetomidine groups, respectively. variables which had significance values <0.05 were patient age (0.000), associated disease (p<-0.003). In regards to other variables like patient gender (p value: 0.660), pre-operative medication (p value: -0.090), different type of surgery (p value: -0.239), had no correlation with POD.*

#### CONCLUSION

*In comparison with propofol, dexmedetomidine postoperative sedation minimized the occurrence and abbreviated the time span of POD in patients who had to undergo cardiac surgery.*

**KEYWORDS:** Cardiac Surgery, Delirium, Dexmedetomidine, Propofol, Sedation Procedure, Intensive Care Unit

analyses of randomised clinical studies.<sup>6,7</sup> Dexmedetomidine, however, was not shown to be effective in preventing POD following cardiac surgery in a number of recent well-designed large-scale randomised controlled studies.<sup>8</sup> Keeping in mind, the ultimate goal of this study is to discuss the assumed etiologies which are hypothesized to lead to the manifestation of the delirium syndrome since that model then provides the framework for the rationale of the various pharmacologic strategies that have been employed for its treatment.<sup>9</sup> These investigations raise significant doubt on earlier studies findings regarding the perioperative usage of dexmedetomidine following cardiac surgery. In order to investigate the combined effects of dexmedetomidine in patients having cardiac surgery, We hypothesized that dexmedetomidine-based

sedation strategy would reduce the incidence of POD.

## METHODOLOGY

A cross-sectional study was carried out in patients undergoing cardiac surgery from November 2021 to June 2022 who were scheduled for the single coronary revascularization or single-valve repair/replacement surgery using cardiopulmonary bypass (CPB), After taking formal ethical approval from Afridi Medical Complex [R/SC/165]. The purpose and benefits of the study was explained to the patients both oral and written informed consent were obtained and maintain the anonymity of patients. This study strictly followed the highest level of ethical standards proposed by Helsinki Declaration (Revised 2013), and the International Ethical Guidelines for Human Research in Health (2016). Patients having a history of severe dementia, delirium, or major mental disease were not allowed to participate. This was a single-center research study conducted at the Afridi Medical Complex Peshawar, Pakistan. To reduce any potential effects that anaesthetic type could have on neurological outcomes, anaesthesia management was standardised. Premedication with 0.07 to 0.15 mg per kilogram intramuscular midazolam was optional. Fentanyl (10–12 g/kg), etomidate (0.2–0.3 mg/kg), and cisatracurium (0.15 mg/kg) were used to induce anaesthesia. Isoflurane (0.5–2.0%) was used to maintain it. The blood pressure and heart rate were maintained within 25% of the pivot point. Heparin was used to achieve anticoagulation to keep the active clotting time over 470 seconds. 50 ml of 20 percent mannitol and 1.8 l of lactated Ringer's solution were used to prime the CPB circuit. Systemic temperature shift to 34°C, alpha-stat pH control, a marked mean perfusion pressure of 60 to 80 mmHg, and pump flow rates of 2.0 to 2.4 l/min/m<sup>2</sup> were all used to control CPB. Fragmentary antegrade and rarely retrograde blood cardioplegia was used. By dropping the temperature to 20°C with antegrade cerebral perfusion, deep hypothermic circulatory arrest was obtained. The body temperature of the patients was elevated to 36°- 37°C before being weaned from CPB. The maximum influx warmth of the body was confined to 37°C during rewarming. Protamine sulphate was used to counterbalance heparin, 1 mg/100 U heparin, after being weaned from CPB to get an active clotting time that was within 10% of the baseline value. After surgery, all patients were shifted to the ICU. After comparison to propofol sedation, it was expected that using dexmedetomidine would help to depreciate delirium level after cardiac surgery. Using simple random sampling, patients were assigned at random to receive either propofol or dexmedetomidine. Patients lying in the dexmedetomidine group were given a

bolus of 0.4 µg kg<sup>-1</sup> min<sup>-1</sup> dexmedetomidine (after a period of 10 to 20 min), then an infusion of 0.2 to 0.7 µg kg<sup>-1</sup> min<sup>-1</sup> following their admission to the ICU. Bolus doses were skipped in cases when patient's hemodynamic stability was precarious. Dexmedetomidine infusion was maintained for a maximum of 24 hours. Before the tracheal Extubation, patients present in the propofol were given an infusion of 25 to 50 µg kg<sup>-1</sup> min<sup>-1</sup> of propofol. According to institutional best practices, patients present in the dexmedetomidine group were converted to propofol sedation if mechanical breathing was required for longer than the 24-hour period. The Richmond Agitation-Sedation Scale (RASS) was used to measure the level of sedation.<sup>9</sup> Dexmedetomidine and propofol infusions were titrated to provide light sedation, resulting in a patient who was calm and compliant (RASS score of 0). Every 4 hours, or more frequently, if necessary (e.g., the patient's situation changed), RASS was carried out. Both groups received a combination of non-opioid adjuvants and opioid analgesics for the treatment of postoperative pain. Using a standard 10-cm visual analogue scale, pain was evaluated (0, no pain; 10, worst and unbearable pain). Patients administered 2 mg of morphine intravenously or, if pain was assessed at 4 or higher on the analogue scale, 2 to 4 mg orally. Delirium was evaluated preoperatively (baseline) and postoperatively at the intervals of 12-h or as per the patient's condition demanded using the confusion assessment method (CAM) for ICU.<sup>10</sup> CAM was used to evaluate delirium in patients who were shifted from the intensive care unit to the surgical ward. During the first five postoperative days, patients were evaluated for delirium. Patients were labelled as delirious until they tested negative for CAM. Both ventilated and extubated patients were treated in the CAM-ICU. A four-step algorithm was used to determine the following: I) a sudden beginning of mental state changes or fluctuations, II) inattention, III) disorganized thinking, and IV) changed levels of awareness. Patients were deemed delirious if they displayed both symptoms (I) and (II) as well as either characteristic (III) or (IV). Patients were classified as delirium-positive (CAM positive) or delirium-negative (CAM negative) (delirium absent). All the data was entered and analyzed in SPSS version 25.0. Mean ± SD was calculated for quantitative variables like age, premedication and comorbidities. Frequency and percentages were calculated for categorical variables like infusion type. Normality and homogeneity of data were analyzed using Kolmogorov-Sminorv and saphiro wilk One Way Anova, respectively. The effect of the propofol and dexmedetomidine was analyzed using Mann-Whitney test. The factors related to delirium

status were analyzed using Logistic Regression. All results were presented in the form of tables and graphs.

## RESULT

Total of 100 patients were included in the study and were evaluated for the incidence Post operative delirium (POD). The mean age of the sample observed was  $55.14 \pm 9.6$  years,  $55.96 \pm 12.1$  years in propofol and dexmedetomidine respectively. Furthermore, demographic information, preoperative medicines, comorbidities, and surgical features, both groups were compared Table 1.

**Table 1: Baseline Demographics and Surgical Characteristics of Study Population**

	Propofol n=50	Dexmedetomidine n=50
Age years mean (SD)	55.14+9.6	55.96+12.1
Ejection Fraction (EF)	52.4+7.2	53.26+6.7
Male n(%)	38 (76%)	41(82%)
Associated diseases n(%)		
Coronary Artery Disease	24(48%)	15(30%)
Congestive Heart Failure	01(2%)	04(8%)
Congenital heart disease	03(6%)	01(2%)
Coronary Artery diseases, Valvular heart diseases	01(2%)	08(16%)
Coronary Artery Disease, Hypertension, Diabetes Mellitus	10(20%)	01(2%)
Coronary Artery Disease, Hypertension	08(16%)	03(6%)
Coronary Artery Disease, Diabetes Mellitus	02(4%)	13(26%)
Other	01(2%)	05(10%)
Preoperative medication n(%)		
Beta Blockers	25(50%)	11(22%)
ACE inhibitors	01(2%)	01(2%)
Statins	02(4%)	01(2%)
Antidepressant	01(2%)	01(2%)
Anxlyotics	01(2%)	05(10%)
Beta Blockers, Statins	05(10%)	12(24%)
Diuretics, Insulin, Nitrate, Beta blocker	04(8%)	04(8%)
Nitrate, Digoxin	07(14%)	12(24%)
Beta Blocker, Nitrate, Statins, Aspirin, Clopidogrel	03(6%)	02(4%)
Beta Blocker, Diuretics	01(2%)	01(2%)
Type of Surgery n(%)		
Coronary artery bypass graft	41(82%)	45(90%)
Mitral valve replacement	03(6%)	01(2%)
Ventricular septal defect	01(2%)	01(2%)
Coronary artery bypass graft+ Mitral valve replacement	03(6%)	02(4%)
Aortic valve replacement	01(2%)	01(2%)
Left arterial myxoma	01(2%)	0(0%)

The data had been analyzed using Kolomogorov-

smirnov and saphiro wilk to identify the normality of the data. By using Kolmogorov Sminorv, the statistic result for infusion type was 0.340 and those for delirium status was 0.435. while, based on Saphiro Wilk tets, the statistic of infusion type was 0.636 and delirium status was 0.562. This results show that the data was normal ( $>0.05$ ).

**Table 2: Normality of Data**

Variables	Statistic (Kolmogorov – Sminorv)	Statistic (Saphiro Wilk)
Infusion type	0.340	0.636
Delirium Status	0.453	0.562

b. data were analyzed using Kolmogorov Sminorv and saphiro wilk

The researcher had been analyzed the homogeniti of the data using one way anova. The result show that the significance was 0.00 ( $p < 0.05$ ). It means that the data heterogene.

**Table 3: Homogeneity of Variances**

Variables	Df	Means Square (between group)	F	Sig
Infusion type	99	4.960	24.257	0.000
Delirium Status	99	4.000	24.257	0.000

c. data were analyzed using One Way Anova

Although the data was normal, but it was heterogen. Thus, researcher used Nonparametric test to analyze the difference between independent variables to dependent variable. Then, Mann Whitney test was applied because it was possible to be used without considering whether the data are homogen or not.

**Table 4: Effect of Propofol and Dexmedetomidine on Delirium Status**

Variables	N	Means Rank	Mann-Whitney	Sig (2-tailed)
Delirium - Propofol	50	60.50	750.000	0.000
Delirium – Dexmedetomidine	50	40.50	24.257	0.000

d. data were analyzed using Statistic non Parametric (Mann-Whitney)

Table 4 shows that p-value of both group was 0.000, this means that propofol and dexmedetomidine are significant to delirium status. However, the means rank of delirium scores of dexmedetomidine group was lower (40.50) than propofol group (60.50). This means rank indicates that the dexmedetomidine is better to reduce delirium status than propofol. To analyze factors influencing delirium status, we applied Logistic Regression. The result can be seen in the table 5.

**Table 5: Logistic Regression for Factors Related to Delirium Score**

S.No	Variables	Sig
1	Patient age	0.000
2	Patient gender	0.660
3	Percentage of Ejection Fraction	-0.011
4	Associated disease	-0.003
5	Pre-operative medication	-0.090
6	Different type of surgery	-0.239
7	Level of consciousness	1.423

e. data were analyzed using Logistic regression

Factors influencing delirium status can be seen at the variables with sig value  $<0.05$ . Based on table 5., variables which had significance values  $<0.05$  were patient age (0.000), associated disease ( $p < -0.003$ ), and percentage of ejection fraction (-0.011). Patient age had positive correlation with delirium status; the older age, the higher score of delirium. Meanwhile, percentage of ejection fraction (EF) had negative correlation with delirium status; the higher of EF percentage, the lower of delirium score. In regards to other variables such as patient gender (p value: 0.660), pre-operative medication (p value: -0.090), different type of surgery (p value: -0.239), and the level of consciousness (p value: 1.423) had no correlation with delirium status because the sig value  $p > 0.05$ .

## DISCUSSION

The goal of the current study is to find out the postoperative delirium POD in patients scheduled for cardiac surgery by comparing propofol with dexmedetomidine-based postoperative sedation. The intensive care unit (ICU) frequently uses anesthetics or analgesics for sedation to keep patients relaxed, and pain-free. Most intense conditions need sedation and analgesia to permit assisted respiration, promote natural sleep, and control physiological reactions to stress (such as tachycardia and hypertension). Benzodiazepines, propofol, morphine, dexmedetomidine, clonidine, and other sedative drugs are frequently prescribed. When compared to propofol, dexmedetomidine's anti-sympathetic activity lowers serum catecholamine, slows heart rate, improves blood flow to the left ventricle's coronary arteries by lengthening diastole, and lowers myocardial oxygen consumption.<sup>11,12,13</sup> The incidence of delirium was decreased by using a post operative dexmedetomidine-based sedative regimen. The findings of our study are corroborated by meta-analysis, which finds that Dexmedetomidine can lower the frequency of POD in adult patients after cardiac surgery when compared to other anesthetics.<sup>14</sup> Moreover, this strategy achieved significant cost savings, mostly as a result of the POD's decreased incidence and shorter duration. In order to achieve a more balanced regimen of hypnotic-

and analgesia-based sedation, postoperative sedation procedures have undergone an evolution process. After heart surgery, a compact section of patients should not necessitate any sedation, and the patients might be extubated quickly and safely in the operating room or after the arrival in the intensive care unit (ICU). While having high-risk heart surgery, individuals with several comorbidities may still need sedation need sedation and postoperative mechanical ventilation. Dexmedetomidine offers a compelling alternative to postoperative sedation with propofol, which has been a standard of care for cardiac surgery for more than ten years. Dexmedetomidine differs on the basis of mode of action from other sedatives that are frequently used in the patients will some critical illness, demonstrating sedative, anxiolytic, and analgesic effects without resulting in respiratory depression.<sup>15</sup> Furthermore, dexmedetomidine improves the quality of sleep in critically ill patients primarily resembling a nonrapid eye movement sleep pattern. It has also been demonstrated to have a strong opioid-sparing effect when used as an agonist for the 2-adrenergic receptor.<sup>16,17</sup> Dexmedetomidine has also been proven to lessen the inflammatory response of CPB and lacks clinically significant anticholinergic effects.<sup>15,18</sup> The decreased frequency and duration of POD might have been attributed to a combination of all dexmedetomidine's special characteristics.<sup>19</sup>

## LIMITATIONS

There is some limitation to our study as there was the factors related to delirium status were analyzed using Logistic Regression.

## CONCLUSION

After the comparison of propofol with dexmedetomidine, dexmedetomidine postoperative sedation reduced incidence, delayed onset, and shortened duration of Postoperative delirium POD in patients schedule for cardiac surgery.

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## CONTRIBUTORS

1. **Muhammad Adnan Khan** – Concept & Design; Supervision; Final Approval
2. **Muhammad Usman** – Data Acquisition; Drafting Manuscript; Final Approval
3. **Israr Hussain** – Drafting Manuscript; Critical Revision; Final Approval
4. **Sayyed Nadar Shah** – Drafting Manuscript; Critical Revision; Final Approval
5. **Omar Khattab** – Drafting Manuscript; Critical Revision; Supervision; Final Approval
6. **Bashir Ul Haq** – Drafting Manuscript; Critical Revision; Final Approval
7. **Siti Khuzaiyah** – Data Analysis/Interpretation; Final Approval
8. **Muhammad Tayyeb** – Concept & Design; Data Acquisition; Data Analysis/Interpretation; Drafting Manuscript; Critical Revision; Supervision; Final Approval



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