

# Perioperative Dexmedetomidine Reduces Delirium after Coronary Artery Bypass Graft Surgery: A Prospective, Single-blind, Observational Study

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## ABSTRACT

**Background:** Delirium is a commonly seen complication of cardiac surgery. Dexmedetomidine, by its anti-inflammatory properties and other effects, can attenuate postoperative delirium.

**Aims:** The aim of this work was to study the incidence of delirium after coronary artery bypass graft surgery, and to compare the effects of dexmedetomidine and propofol on the incidence of postoperative delirium in coronary artery bypass graft surgery patients.

**Materials and Methods:** A prospective, observational study was conducted on 180 consecutive patients undergoing off-pump or on-pump coronary artery bypass graft surgery. The patients were administered either intravenous dexmedetomidine ( $n = 90$ ) or propofol ( $n = 90$ ) after hemostasis was achieved, till they were ready for weaning from the ventilator. The Confusion Assessment Method was used to assess the incidence of postoperative delirium.

**Measurements and Main Results:** A total of 25 (13.8%) patients developed delirium after coronary artery bypass graft surgery. Sedation with dexmedetomidine was associated with a significantly reduced incidence of postoperative delirium (8.9% v 18.9% propofol,  $P = 0.049$ ). Subgroup analyses showed reduced incidence of postoperative delirium in off-pump patients compared to on-pump coronary artery bypass graft patients (3.3% vs. 20%,  $P = 0.009$  dexmedetomidine group and 11.6% vs. 33.3%,  $P = 0.047$  propofol group respectively). The mean age of the patients who had delirium was significantly more ( $64.9 \pm 8.1$  years vs.  $52.5 \pm 5.8$  years,  $P = 0.046$ ) compared to those who did not have delirium.

**Conclusion:** Administration of dexmedetomidine-based sedation resulted in the reduced incidence of postoperative delirium compared to propofol-based sedation in patients after coronary artery bypass graft surgery.

**Keywords:** Coronary artery bypass graft surgery, dexmedetomidine, postoperative delirium, propofol

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## INTRODUCTION

Delirium is the most commonly seen psychiatric disorder in intensive care unit (ICU) patients, with the reported incidence varying from 16% to 89% depending on the patient population characteristics, type of ICU (medical or surgical), study methodology, and the assessment tool used for the diagnosis of delirium.<sup>[1,2]</sup> The occurrence and

consequences of delirium place a considerable burden on both the patients and the healthcare system. The adverse effects of delirium include prolonged duration of mechanical ventilation, prolonged lengths of stay in the ICU and hospital, increased medical expenses during hospitalization, increased readmission rate, compromised

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long-term cognitive function, and higher mortality rates.<sup>[3-5]</sup> The known risk factors of delirium after cardiac surgery include advanced age, pre-existing cognitive impairment, previous delirium, atrial fibrillation, congestive heart failure, perioperative medications including benzodiazepines and narcotics; and metabolic disorders.<sup>[6]</sup> Also, patients undergoing cardiac surgery are at an increased risk of delirium due to the use of and deleterious effects of cardiopulmonary bypass (CPB), clamping/unclamping of the aorta, perfusion-related factors, and postoperative complications.<sup>[7,8]</sup> Despite the high incidence, delirium is frequently not detected by the ICU staff, and screening is poorly implemented in ICUs.<sup>[9,10]</sup>

Dexmedetomidine, an  $\alpha$ -2 adrenergic agonist with established sedative and analgesic properties, is suggested for procedural and ICU sedation by Food and Drug Administration since 1999. Dexmedetomidine has anti-inflammatory properties, decreases the use of opioids and benzodiazepines that contribute to delirium. It provides sedation very similar to physiologic sleep that can attenuate delirium seen after cardiac surgery.<sup>[11]</sup> There is increasing evidence on the preventive effects of dexmedetomidine and the incidence of postoperative delirium, though the evidence on improvement in outcome with this drug needs further evaluation.<sup>[12-14]</sup> Propofol, another commonly used agent for ICU sedation, has antioxidant and antiapoptotic effects and can promote recovery after surgery.<sup>[15]</sup>

We hypothesized that dexmedetomidine can reduce the incidence of postoperative delirium, and compared this drug with propofol in patients undergoing off-pump and on-pump coronary artery bypass graft surgery (CABG). The primary objective of the study was to assess the occurrence of postoperative delirium in post CABG patients. The secondary objectives were to evaluate the effects of either drug on the incidence of postoperative delirium, duration of mechanical ventilation, lengths of stay in the ICU, and the hospital.

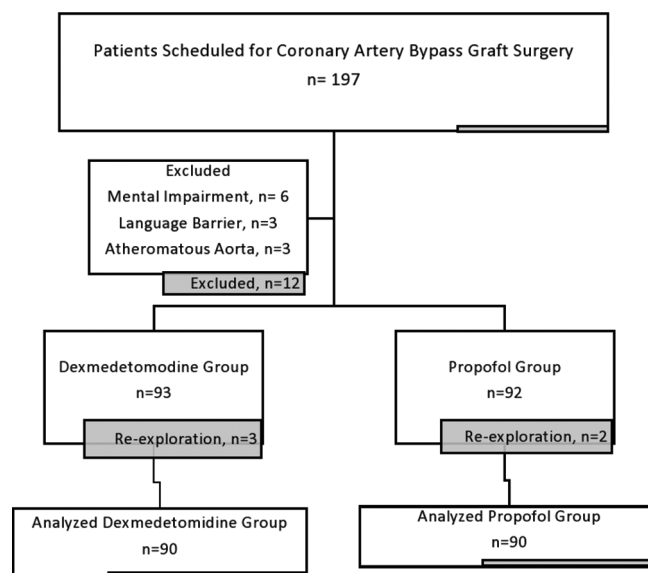
## MATERIAL AND METHODS

This prospective, single-blind, observational study was conducted at our institution to evaluate the incidence of delirium after CABG, and to compare the effects of dexmedetomidine and propofol on the incidence of postoperative delirium. All consecutive patients who underwent isolated, elective, primary CABG between November 2018 and March 2020 were studied. The study protocol was approved by the institutional review board and ethics committee (MIRB No. 919/26<sup>th</sup> Oct 2018,

DNB). Due to the observational nature of the study, the informed consent of the patients was waived off by the ethics committee.

Patients older than 18 years of age, with a left ventricular ejection fraction (LVEF) of more than 35%, undergoing elective CABG were included in the trial. The Confusion Assessment Method (CAM) was used to rule out delirium in the preoperative period. It included focused patient assessment regarding his wakefulness, eye contact, and posture. This was followed by a formal introduction of the name, address, basic orientation, review of preoperative medications particularly antipsychotics, history of substance abuse, and brief cognitive testing if required. Exclusion criteria were (i) neurologic disorders such as pre-existing dementia, delirium, encephalopathy, depression, psychosis, or mental retardation, (ii) hearing or visual impairment, (iii) language barrier, (iv) presence of congestive cardiac failure, significant arrhythmia, intracardiac thrombus, atheromatous aorta, (v) patients who required re-exploration, and (vi) known allergy to the study drug.

The patients were blinded and allocated to either dexmedetomidine (D) or propofol (P) group using open-label sequential numbers with 1:1 allocation [Figure 1]. Under standard cardiac monitoring, anesthesia was induced with intravenous midazolam 0.05 mg/kg, fentanyl 2-5 mcg/kg, thiopentone 3-5 mg/kg, and vecuronium 0.1 mg/kg. Maintenance of anesthesia was achieved with oxygen in air and isoflurane (end-tidal concentration 1%), along with intermittent doses of midazolam, fentanyl, and vecuronium. CABG surgeries were performed either



**Figure 1:** Flow charts of the study groups

off-pump (OPCAB) or conventional on-pump (CCAB) depending upon surgeons' preference. Patients in the OPCAB subgroup were managed with optimization of cardiac positioning to access target coronary arteries, cardiac stabilization by use of tissue stabilizers, and myocardial protection by use of intra-coronary shunts. CPB management in CCAB patients consisted of crystalloid prime, mild hypothermia, flow rate of 2-2.4 L/min/m<sup>2</sup>, and cold-cardioplegic arrest using Plegisol (Hospira, Lake Forest, IL). The patients in group D received a loading dose of intravenous dexmedetomidine 1 µg/kg over 10 minutes followed by 0.5 µg/kg/hr in infusion after hemostasis was achieved, before sternal closure. Dexmedetomidine infusion was continued in the ICU till the patients were ready for weaning from the ventilator. The patients in group P received propofol infusion (25-50 µg/kg/min) till they were ready for weaning from the ventilator. The ICU was equipped with either single or double rooms with physical barriers between two beds, sufficient natural daylight, glass doors to contain noise, windows, and wall clocks. Weaning from mechanical ventilation was commenced once the patients met the following criteria: no neurologic deficit, normal body temperature, urine output ≥0.5 ml/kg/hr, mediastinal drainage <1 ml/kg/hr, hemodynamic stability, absence of significant arrhythmias, PaO<sub>2</sub> >60 mmHg, PaCO<sub>2</sub> <45 mmHg, SpO<sub>2</sub> >98% with FiO<sub>2</sub> ≤0.4, no respiratory distress and respiratory rate <25 breaths/min. The study drugs were discontinued at the commencement of weaning from mechanical ventilation. For pain relief, patients in both groups received intravenous paracetamol 1 gm and tramadol 100 mg, every eight hours since their arrival in the ICU.

The patients were assessed daily for post-operative delirium during their entire ICU and hospital stay. Richmond Agitation Sedation Scale (RASS) was used to assess the level of alertness and the degree of sedation.<sup>[16]</sup> CAM for the ICU (CAM-ICU) score was used to assess the occurrence of delirium once the study drugs were discontinued, till the patients were admitted to the ICU.<sup>[17]</sup> CAM score was used once the patients were shifted to the ward. Evaluation of RASS, CAM-ICU, and CAM score was performed by a dedicated anesthesiologist and trained staff, every eight hours. All patients who had RASS scores of -3 or a lighter level of sedation (-3 to +4) progressed to step two (assessment of delirium). The patients were assessed for the following features of delirium: Feature 1: Change in mental status from baseline or a status that fluctuated, Feature 2: Inattention, Feature 3: Disorganized thinking, and Feature 4: Altered level of consciousness. The diagnosis of delirium was made from the first two features and either feature three or four occurring at least once during

the hospital stay. The type of delirium (hyperactive or hypoactive form) was also noted. Patients with hyperactive delirium were managed with intravenous haloperidol in increments of 1-5 mg if required. The onset and duration of delirium were noted. The secondary outcome measures were the usage of inotropes/intra-aortic balloon pump, duration of mechanical ventilation, positive fluid balance, lengths of stay in the ICU and hospital; and in-hospital mortality.

### Statistical analysis

The sample size was based on the assumption that the incidence of delirium after cardiac surgery is about 25%.<sup>[18]</sup> Based on previously published studies and to account for possible dropouts, a sample size of more than 50 for each group was calculated.<sup>[18,19]</sup> The corresponding α-level of significance was 1.96 and the power of the study (1-β) was 0.84. The patients were profiled based on their demographic and clinical characteristics. Descriptive analysis of continuous variables was expressed as mean with standard deviation. Continuous variables were analyzed using the Student t-test. Categorical data were expressed as absolute numbers and percentages. For comparison of two groups, cross tabs were generated; and the Chi-square test was used for testing of associations. A value of *P* < 0.05 was considered to be statistically significant. All statistical analyses were performed using SPSS Version 24.0 (IBM, Armonk, New York).

### RESULTS

The demographic details of the patients are shown in Table 1. Gender distribution, age, LVEF, body surface area, and body mass index were comparable in both groups. Sub-group analysis of age distribution showed that the majority of the patients who participated in the study were between 61 to 70 years of age (42.2%) followed by 51 to 60 years of age (31.1%). Hypertension and diabetes mellitus were the most common co-morbid conditions [Table 2]. The number of patients who required blood transfusion during surgery was comparable in both groups [Table 3]. Greater number of patients undergoing CCAB required blood transfusion compared to OPCAB subgroup (90% v 58.3%, *P* = 0.002 group D, and 93.3% v 60%, *P* = 0.001 group P). The requirements of midazolam and fentanyl, number of distal anastomoses, duration of surgery, duration of mechanical ventilation, the incidence of low cardiac output, re-intubation, the need for two or more inotropes, and use of intra-aortic balloon pump were comparable in both groups [Table 3]. None of the patients in the OPCAB group required conversion to on-pump CABG. The lengths of stay in the ICU and hospital were

**Table 1: Demographic characteristics of patients (n=180)**

Parameter	Dexmedetomidine group (n=90)	Propofol group (n=90)	Total	Mean±SD Difference (95% CI)	P
Age (years)	60.3±8.1	60.1±10.3		0.2±1.4 (-2.6 to 2.9)	0.932
Age (subgroups)					
<40 years	1 (1.1%)	4 (4.4%)	5 (2.8%)		0.362
41-50 years	10 (11.1%)	11 (12.2%)	21 (11.7%)		0.746
51-60 years	31 (34.4%)	25 (27.8%)	56 (31.1%)		0.249
61-70 years	40 (44.4%)	36 (40%)	76 (42.2%)		0.861
71-80 years	8 (8.9%)	14 (15.6%)	22 (12.2%)		0.644
Male: Female ratio	79: 11	76: 14	155: 25		0.518
LVEF (%)	46.27±7.76	47.84±7.46		-1.6±1.1 (-3.8 to 0.7)	0.768
BSA (m <sup>2</sup> )	1.83±0.20	1.82±0.19		0±0.03 (-0.6 to 0.6)	0.854
BMI (kg/m <sup>2</sup> )	26.4±4.0	26.9±4.8		-0.5±0.7 (-1.8 to 0.8)	0.857

[Table 1]: Data presented as numbers (percentage) for categorical variables and mean±standard deviation (SD) for continuous variables. CI: confidence interval, LVEF: left ventricular ejection fraction, BSA: body surface area, BMI: body mass index

**Table 2: Preoperative risk factors**

Risk factor	Dexmedetomidine Group (n=90)	Propofol Group (n=90)	Total (n=180)	P
Hypertension	55 (61.1%)	52 (57.8%)	107 (59.4%)	0.649
Diabetes Mellitus	51 (56.7%)	56 (62.2%)	107 (59.4%)	0.448
Atrial Fibrillation	3 (3.3%)	2 (2.2%)	5 (2.8%)	0.653
History of Stroke	1 (1.1%)	1 (1.1%)	2 (1.1%)	1.000
History of Smoking	32 (35.6%)	37 (41.1%)	69 (38.3%)	0.443
History of Alcohol consumption	22 (24.4%)	25 (27.8%)	47 (26.1%)	0.611

**Table 3: Intraoperative and postoperative characteristics of the patients**

Parameter	Dexmedetomidine group (n=90)		Propofol group (n=90)		Total (n=180)	Mean±SD Difference (95% CI)	P
	OPCAB	CCAB	OPCAB	CCAB			
Midazolam (mg)	3.5±1.7		3.7±1.3			-0.2±0.5 (0.1 to 0.9)	0.444
Fentanyl (µg)	930.9±208.9		976.7±139.9			-46±15.4 (-28.5 to 77.4)	0.432
Blood transfusion (No. of patients)	62 (68.9%)		52 (57.8%)		114 (63.3%)		0.522
	35/60 (58.3%) 27/30 (90%)		24/40 (60%) 28/30 (93.3%)				0.002* (D) 0.001* (P)
No. of distal anastomoses	3.4±1.2		3.3±1.1			0.14±0.2 (0.0 to 0.7)	0.778
Duration of surgery (hr)	5.1±1.1		5.3±0.8			0.2±0.2 (0.2 to 0.5)	0.757
Low cardiac output	15 (16.6%)		19 (21.1%)		34 (18.8%)		0.873
Inotropes (++) or (>)	7 (7.7%)		11 (12.2%)		18 (10%)		0.766
IABP	2 (2.2%)		0 (0%)		2 (1.1%)		0.158
Duration of ventilation (hr)	10.6±3.7		10.4±2.6			0.18±0.48 (-0.76 to 1.12)	0.709
Mobilization (hr)	20.8±7.6		22.6±7.9			-1.8±1.4 (2.2 to 6.9)	0.643
Re-intubation	1 (1.1%)		1 (1.1%)		2 (1.1%)		0.978
ICU stay (d)	3.2±1.2		2.9±1.3			0.27±0.15 (0.26 to 0.85)	0.797
Hospital stay (d)	6.7±2.8		6.9±3.2			-0.19±0.12 (-0.1 to 3.2)	0.755
Positive Fluid Balance (ml)							
POD 1	442±93		498±92			-56±24.2 (-72 to 274)	0.836
POD 2	582±136		549±111			33±15.8 (27 to 85)	0.835
POD 3	738±180		757±192			-19±11.3 (51 to 105)	0.825
POD 4	944±288		987±305			-43±22.9 (-73 to 134)	0.873
POD 5	1135±297		1038±305			97±55 (59 to 187)	0.827
In-hospital mortality	1 (1.1%)		2 (2.2%)		3 (1.6%)		0.443

[Table 3]: Data presented as numbers (percentage) for categorical variables and mean±standard deviation (SD) for continuous variables.

CI: confidence interval, OPCAB: off-pump coronary artery bypass, CCAB: conventional coronary artery bypass, D: dexmedetomidine, P: propofol, ++ or >: two or more, IABP: intra-aortic balloon pump, ICU: intensive care unit, POD: postoperative day

also comparable in both groups. One patient in group D, and two patients in group P, died in the hospital due to myocardial failure.

The overall incidence of postoperative delirium was 13.8% in our study. The incidence of postoperative delirium was significantly less in group D compared to group P [8.9% v 18.9%,  $P = 0.049$ , Table 4]. The risk of delirium was more

than two times in group P compared to group D (Relative Risk {RR} 2.12 with 95% CI limits 0.97- 4.67). Subgroup analyses revealed a lower incidence of delirium in OPCAB patients compared to CCAB patients (3.3% v 20%,  $P = 0.009$ ; group D, and 11.6% v 33.3%,  $P = 0.047$ ; group P respectively). Of the 25 delirious patients, 19 (76%) had delirium in the ICU, and six (24%) had delirium in the ward. The onset of delirium was delayed in group D compared to group P ( $2.65 \pm 0.46$  d

v  $2.12 \pm 0.33$  d), but it was not statistically significant. Both hyperactive and hypoactive subtypes of delirium occurred with comparable frequencies. The duration of delirium was well-matched in both groups. Of those experiencing delirium, the duration was one day for 35.7%, two days for 37.9%, three days for 16.8%, and four days for 9.6% of patients. The mean age of the patients who had delirium was more compared to those who did not have delirium ( $64.9 \pm 6.1$  years v  $52.5 \pm 5.8$  years,  $P = 0.046$ , Table 5). The lengths of ICU stay and hospital stay were more in patients who had delirium compared to those who did not have delirium [4.3 d vs 2.8 d ICU stay, 12.3 d vs 7.5 d hospital stay, respectively, Table 5], although it did not reach statistical significance.

## DISCUSSION

The primary finding of this study is that the overall incidence of delirium after CABG was 13.8%. We also found that sedation with dexmedetomidine, compared to propofol, was associated with a significantly reduced incidence of postoperative delirium in these patients. Given the increased morbidity and mortality associated with delirium and the increased lengths of stay in the ICU or hospital, these findings may be relevant to the management of cardiac surgery patients.

Delirium is a complex neuropsychiatric syndrome defined by the Diagnostic and Statistical Manual of Mental

Disorders, fifth edition (DSM-V), as an acute onset of a fluctuating disturbance in attention, environmental awareness, cognition, and/or perception.<sup>[20]</sup> Patients with delirium may be agitated and non-cooperative (hyperactive delirium), sluggish/lethargic (hypoactive delirium), or may fluctuate between the two subtypes. The incidence of delirium is often underestimated because it frequently presents in hypoactive form. Environmental factors such as the absence of natural day-light, use of physical restraints, high noise in the ICU, and prolonged immobilization also play an important role in the development of delirium.

Our finding of reduced incidence of delirium with the use of dexmedetomidine is in agreement with the results of a recent, randomized clinical trial by Djaiani *et al.*<sup>[21]</sup> In their prospective trial, delirium was present in 17.5% of patients in dexmedetomidine group v 31.5% patients in propofol group (odds ratio 0.46, 95% CI 0.23 to 0.92;  $P = 0.028$ ). Maldonado *et al.*<sup>[22]</sup> also found a reduced incidence of delirium (3%) with the use of dexmedetomidine in elderly patients undergoing cardiac surgery, compared to propofol and midazolam (50% with either drug). A systemic review and meta-analysis of 13 randomized controlled trials ( $n = 3309$ ) by Duan *et al.*<sup>[23]</sup> found that dexmedetomidine decreased the risk of postoperative delirium (odds ratio 0.41, 95% CI 0.26-0.63;  $P = < 0.01$ ) in a cardiac surgery setting. The beneficial

**Table 4: Incidence, onset, and duration of Delirium**

	Dexmedetomidine group (n=90)		Propofol group (n=90)		P
Incidence	8 (8.9%)		17 (18.9%)		0.049*
	Relative Risk (group P v D) 2.16, 95% Confidence Interval Limits 0.97-4.67				
	OPCAB	CCAB	OPCAB	CCAB	
	2/60 (3.3%)	6/30 (20%)	7/60 (11.6%)	10/30 (33.3%)	0.009* (group D) 0.047* (group P)
Onset (d)	2.65±0.46 (2-4)		2.02±0.33 (2-3)		0.421
	OPCAB	CCAB	OPCAB	CCAB	
	2.8±0.70	2.5±0.51	2.1±0.30	2.0±0.41	0.420 (group D) 0.668 (group P)
Hyperactive/Hypoactive	3/5		8/9		0.768
Duration (d)	1-3		1-4		0.689

[Table 4] Data presented as numbers (percentage) for categorical variables and mean±standard deviation for continuous variables. \*denotes  $P < 0.05$  significant. D: dexmedetomidine, P: propofol, OPCAB: off-pump coronary artery bypass, CCAB: conventional coronary artery bypass

**Table 5: Comparison of patients with or without Delirium**

	Delirium		Mean±SD Difference (95% CI)	P
	Present (n=25)	Absent (n=155)		
Age (Years)	64.9±8.1 (46-77)	52.5±5.8 (28-78)	5.5±1.9 (1.6 to 9.3)	0.046*
Male: Female ratio	Male: 20/155 (13%) Female: 5/25 (20%)	Male: 135/155 (87%) Female: 20/25 (80%)		0.589
CPB Time (Minutes)	89.3±32.3 (67-109)	82.3±29.9 (56-97)	7±2.5 (-23.4 to 37.4)	0.357
Aortic Cross Clamp Time (Minutes)	71.9±18.5 (42-102)	63.8±17.4 (47-104)	8.2±1.8 (-9.4 to 25.8)	0.646
Mechanical Ventilation (hrs)	16.1±3.3 (10-27)	9.4±3.2 (5-12)	6.7±0.7 (-0.6 to 5.1)	0.079
ICU Stay (Days)	4.3±1.4 (2-10)	2.8±1.0 (2-7)	1.4±0.5 (0.0 to 1.9)	0.147
Hospital Stay (Days)	12.3±2.7 (6-22)	7.5±2.0 (6-15)	4.7±1.4 (-0.1 to 9.6)	0.103

[Table 5]: Data (except male: female ratio) presented as mean±standard deviation (SD) with lower and upper range. \*denotes  $P < 0.05$  significant. CI: confidence interval, CPB: cardiopulmonary bypass, ICU: intensive care unit

effects of dexmedetomidine probably result from its unique mechanism of action exhibiting sedative, anxiolytic, and analgesic effects without causing respiratory depression. As an  $\alpha$ -2-adrenergic receptor agonist, it has also been shown to have a significant opioid-sparing effect.<sup>[24]</sup> Moreover, dexmedetomidine improves the quality of sleep in critically ill patients, primarily resembling a non-rapid eye movement sleep pattern.<sup>[25]</sup> Besides, dexmedetomidine lacks clinically significant anticholinergic effects and has been shown to reduce the inflammatory response of CPB.<sup>[26]</sup> However, the exact mechanism of neuroprotection by dexmedetomidine is still not clear. Kim *et al.*,<sup>[27]</sup> in their study in animals, found that dexmedetomidine may inhibit inflammation by inactivation of the Toll-like receptor 4/nuclear factor-kappa B pathway, thus causing reduction of interleukin (IL)-6 and IL-8 levels. Dahmani *et al.*,<sup>[28]</sup> postulated that dexmedetomidine might increase hippocampal phosphorylated extracellular signal-regulated protein kinase 1 and 2 content by an  $\alpha$ -2-adrenoceptor-independent mechanism. These neuroprotective properties can help explain why dexmedetomidine can reduce the incidence of delirium.

We have compared dexmedetomidine with propofol in CABG patients, and each drug was studied in two subgroups (i.e., off-pump and on-pump subgroups) separately as well. The subgroup analyses of our study revealed that reduced incidence of delirium was more evident in the OPCAB patients compared to CCAB cohorts. A similar association between the exposure to CPB and postoperative delirium after cardiac surgery was observed by O'Neal and co-workers as well.<sup>[29]</sup> They found that relative to an off-pump procedure, the risk of delirium was more than two times greater (RR, 2.18; 95% CI, 1.39 to 3.07;  $P = 0.002$ ) among patients who were exposed to CPB for 142 minutes (90<sup>th</sup> percentile of CPB duration). This finding may suggest that the use of CPB with the generation of micro/macro emboli, systemic inflammation, disruption of the blood-brain barrier, perfusion related factors such as mean arterial pressure, flow rate, non-pulsatile flow, temperature, hematocrit, clamping and unclamping of the aorta; and surgical factors play a bigger role than the choice of sedation for the occurrence of delirium. The study by O'Neal *et al.*,<sup>[29]</sup> however, had many limitations such as it was a historical collection of data, sedation protocols were not standardized, the doses of opiates and benzodiazepines were not described, and delirium was not assessed once the patients were shifted to the ward. A recent double-blind, randomized controlled trial by Likhvantsev *et al.*,<sup>[30]</sup> showed a reduced rate of delirium after cardiac surgery when dexmedetomidine was started before initiation of CPB. The authors believed that this timing is

crucial for the prevention of delirium because the action of dexmedetomidine might be mediated by preconditioning properties, which usually require some time to establish.

In the present study, the duration of mechanical ventilation, ICU stay, hospital stay, and mobilization were not significantly different in both groups. The lengths of stay in the ICU and hospital were more in patients who had delirium compared to those who did not have delirium. This finding, however, was not statistically significant. Early mobilization has been recommended as a non-pharmacological intervention aimed to reduce the duration of delirium in a multicenter randomized controlled trial.<sup>[31]</sup> Delayed onset of delirium in group D patients of this study was not statistically significant from group P patients. Djaiani *et al.*,<sup>[21]</sup> however, reported significantly delayed onset of delirium in group D (day 2 v day 1 in group P,  $P = 0.027$ ). They also found the duration of delirium shorter in group D [2 (1–4) days v 3 (1–5) days group P,  $P$  value = 0.04.

In our study, the mean age of the patients who developed delirium was significantly more compared to those who had no delirium ( $64.9 \pm 8.1$  years v  $52.5 \pm 5.8$  years,  $P = 0.046$ ). Although age has been identified as one of the most significant risk factors for delirium outside the ICU, only two studies reported it to be significant in ICU patients, while four studies reported it as insignificant.<sup>[32]</sup> More research is needed to confirm the relationship between age and the development of delirium in ICU patients.

Postoperative pain following cardiac surgery can be moderate to severe in intensity and may contribute to the development of delirium. Ketamine and opiates, such as morphine, may increase the risk of hallucinations and delirium respectively. The use of intravenous acetaminophen (paracetamol) has been shown in multiple studies to reduce the amount of opiate consumption in surgical patients.<sup>[33]</sup> Given its reliable analgesic properties and safety profile, acetaminophen may be a suitable alternative for patients undergoing cardiac surgery.

The primary limitation of the study was the non-randomization of the patients. Other limitations were a single-center study, absence of detailed preoperative cognitive assessment, and impact of delirium on long-term survival and outcome as patients were not followed up beyond hospital discharge. Future studies, aimed to target biomarkers shown to correlate with delirium in non-cardiac surgery patients, should be investigated in cardiac surgery. Another area of research may be to identify patients at higher

risk, pre-emptively treat those patients, and define the severity of disease in patients with delirium.

## CONCLUSION

In conclusion, administration of dexmedetomidine-based sedation regimen resulted in the reduced incidence of postoperative delirium when compared with propofol-based sedation in patients after CABG surgery. This reduction in the proportion of patients developing delirium may translate to decreased inpatient mortality and morbidity, improved patient well-being, and better cognitive functioning. As delirium is found in a considerable proportion of surgical patients, a reduction of its incidence in this population could be beneficial.

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## Conflicts of interest

None.

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