

EFFECT OF PERIOPERATIVE DEXMEDETOMIDINE ON CARDIAC SURGERY OUTCOME

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Abstract: *This retrospective study was designed to assess the impact of perioperative dexmedetomidine on the outcome of open-heart surgery. This study was conducted at the Faisalabad Institute of Cardiology Faisalabad from 01 Jan 2022 to Dec 2022. A total of 350 fulfilled the inclusion criteria and were included in the study. Informed consent of the participants was taken. The ethical board of the hospital approved the study. Subjects were divided into the dexmedetomidine group (who were administered dexmedetomidine peri operatively, 179 (51%)) and non-dexmedetomidine group (who were not helped dexmedetomidine peri operatively, 171(48.8%).0.24-0.6 µg/kg/h was infused intravenously after cardiopulmonary bypass. The was continued for more than twenty-four hours postoperatively.10 out of 350 subjects (2.8%) died in hospital, and 14 (4%) died within thirty days. Perioperative dexmedetomidine infusion resulted in a significant reduction in hospital and 30-day mortality. In-hospital mortality in the dexmedetomidine and non-dexmedetomidine group were 1.22% and 4.6%, respectively (P=.008). 30-day mortality in the dexmedetomidine and non-dexmedetomidine groups was 1.8% and 5.2%, respectively (P=.002). Perioperative dexmedetomidine significantly reduced post-operative sepsis (0.8% vs. 2.2%, P=.043) and other complications (46.19% vs. 56.07%, P=.0205). There was no difference in the duration of hospital stay, ICU stay, post-operative ventilation time, and incidence of delirium and MACEs. So, it can be concluded that perioperative intravenous dexmedetomidine results in improved hospital and thirty-day survival and is associated with a decrease in post-operative delirium and overall complications.*

Keywords: Dexmedetomidine, cardiac surgery, α -2 agonists, myocardial infarction

Introduction

A large number of invasive cardiac procedures are done each year globally (Bangalore et al., 2021). According to the Society of Thoracic Surgeons (STS) reports, the complication rate of coronary artery bypass graft (CABG) is up to 30% (Kurlansky et al., 2022). Major post-operative complications include acute renal failure, infection, delirium, and cardio cerebral events (MACEs) like cardiac arrest, heart block, myocardial infarction(MI), coma, or stroke (Nicola and Ho, 2019). Such complications result in increased hospital stays and mortality. There are multifactorial reasons for such difficulties; however, the surgical stress response is the primary factor. It results in increased epinephrine and norepinephrine levels which cause an imbalance in the supply and demand of myocardial oxygen (Gideon et al., 2022). Currently, α -2 receptor agonists, dexmedetomidine and clonidine, are used clinically. They have various desirable effects like anxiolysis, and analgesia, reducing the release of systematic norepinephrine, inhibiting central sympathetic outflow, and providing myocardial

infarction by positively affecting the supply and demand of myocardial oxygen (Basavaraddi, 2022). Dexmedetomidine is a short-acting, highly selective α -2 agonist. Studies have shown that post-operative cardiovascular complications can be reduced through α -2 agonists. These studies included use of dexmedetomidine for noncardiac and vascular surgery n ad clonidine for cardiac surgery (Koutsaki et al., 2019; Roth et al., 2021). However, there are limited studies on the effect of perioperative α -2 agonists on cardiac surgery outcomes. Different studies have shown that dexmedetomidine positively impacts the lungs, kidneys, brain, and heart (Duncan et al., 2018; Kartal et al., 2020). Additionally, dexmedetomidine is reported to attenuate plasma cytokine levels, has `anti-inflammatory properties, and decreases mortality (Carnicelli et al., 2022). Therefore, in this study, more definitive outcomes like death or MI effect of dexmedetomidine on acute renal failure, infection, delirium, stroke, arrhythmia, and congestive heart failure after cardiac surgery are evaluated. The aim of this study is to assess the

impact of perioperative dexmedetomidine on the outcome of open-heart surgery.

Methodology

The retrospective study was conducted at Faisalabad Institute of Cardiology Faisalabad from Jan 2022 to Dec 2022. The patients undergoing valve surgery, CABG alone, or other procedures were included in this study. Those undergoing surgery that involved thoracic aorta or required deep hypothermic circulatory arrest and emergency surgery were excluded. A total of 350 fulfilled the inclusion criteria and were included in the study. Informed consent of the participants was taken. The ethical board of the hospital approved the study. Subjects were divided into the dexmedetomidine group (who were administered dexmedetomidine perioperatively, 179 (51%)) and non-dexmedetomidine group (who were not helped dexmedetomidine perioperatively, 171(48.8%)). Demographic data, medical history, pre-operative medications, risk factors, perioperative data, and post-operative data, including acute renal failure, MACEs, and in-hospital and 30-day mortality. For surgery, general anesthesia was performed. Respiratory rate and tidal volume were adjusted for controlling ventilation. Cardiac function and hemodynamics were monitored by transesophageal echocardiography, arterial catheter, and pulmonary artery catheter. 0.24-0.6 µg/kg/h was infused intravenously after cardiopulmonary bypass. The was continued for more than twenty-four hours postoperatively. SPSS version 23:00 was used for data analysis. Continuous variables were represented as mean and standard deviation and compared using a t-test. Categorical variables were expressed as percentages and compared using X²test. Association between clinical outcome, therapeutic and demographic variables were assessed by univariate and multivariate logistic regression analysis. The propensity score was calculated to mitigate selection bias in subjects administered dexmedetomidine. Kaplan Meier analysis was performed for subjects who were administered dexmedetomidine versus those who were not. $P < 0.05$ were considered statistically significant.

Results

The differences between both the groups' sex, age, body mass index (BMI), history (hypertension, diabetes mellitus, peripheral vascular disease, chronic lung disease, cerebrovascular disease, and smoking), and pre-operative drug therapy (aspirin, inotropes, Coumadin, antiplatelet drug, nitrates, and β-blockers) was not significant. However, the dexmedetomidine group had a higher incidence of previous congestive heart failure (32.61% vs.

7.24%, $P < .0001$), MI (42.46% vs. 31.75%, $P = .0002$), low ejection fraction ($48.7 \pm 13.7\%$ vs. $53.6 \pm 12.9\%$, $P = .0004$), use of lipid-lowering drugs (64.49% vs. 52.2%, $P < .0001$), dyslipidemia (68.16% vs. 43.6%, $P < .0001$), renal failure (5.64% vs. 2.74%, $P = .010$).

Procedural characteristics, like the type of surgery and the number of bypassed vessels, were the same in both groups. Aortic cross-clamp time (129.8 ± 64.8 vs. 145.7 ± 63.6 min, $P < .0001$), cardiopulmonary bypass time (182.9 ± 75.7 vs. 198.9 ± 82.7 min, $P = .001$) and intra-aortic balloon pump use (6.78% vs. 15.14%, $P < .0001$) was significantly higher in the non-dexmedetomidine group (Table I). 10 out of 350 subjects (2.8%) died in hospital, and 14 (4%) died within thirty days. Perioperative dexmedetomidine infusion resulted in a significant reduction in hospital and 30-day mortality. In-hospital mortality in the dexmedetomidine and non-dexmedetomidine group were 1.22% and 4.6%, respectively ($P = .008$). 30-day mortality in the dexmedetomidine and non-dexmedetomidine groups was 1.8% and 5.2%, respectively ($P = .002$). Perioperative dexmedetomidine significantly reduced post-operative sepsis (0.8% vs. 2.2%, $P = .043$) and other complications (46.19% vs. 56.07%, $P = .0205$). There was no difference in the duration of hospital stay, ICU stay, post-operative ventilation time, and incidence of delirium and MACEs (Table II).

The multivariate analysis was used to assess MACEs, including age, BMI, smoking status, diabetes mellitus, family history of coronary artery disease, type of surgery, and use of Intra-aortic balloon pump. After propensity adjustment, reduction in hospital (adjusted OR 0.33, 95% CI 0.18–0.63, $P < .0001$) and 30-day (adjusted OR 0.38, 95% CI 0.22–0.67, $P < .0001$) mortality in dexmedetomidine group persisted. The revised rate of delirium (adjusted OR 0.52, 95% CI 0.38–0.76, $P = .0030$) and post-operative complication (adjusted OR 0.81, 95% CI 0.67–0.87, $P = .0136$) between both groups were statistically significant. The rate of post-operative renal failure (adjusted OR 1.4, 95% CI 1.13–2.61, $P = .00945$) in the dexmedetomidine group increased significantly. The incidence of sepsis ($P = .3349$) and cardiac arrest ($P = .4681$) between both groups did not differ statistically.

Discussion

This study showed that perioperative dexmedetomidine improves survival in cardiac surgery patients. In hospitals, mortality in the dexmedetomidine and the non-dexmedetomidine group were 1.22% and 4.6%, respectively. 30-day mortality in the dexmedetomidine and non-dexmedetomidine group was 1.8% and 5.2%,

respectively. The improvement persisted after the adjustment of propensity scores. It was also found that perioperative dexmedetomidine is associated-

with a reduction in overall complications of cardiac surgery

Table I Demographic characteristics of groups

Characteristic	Dexmedetomidine group n=179	Non- dexmedetomidine group n=171	P value
Aortic cross-clamp time (minutes)	129.8±64.8	145.7±63.6	<.0001
Perfusion time (minutes)	182.9±75.7	198.9±82.7	.001
Intra-aortic balloon pump use (n,%)	12 (6.78%)	26 (15.2%)	.0001
Type of surgery (n,%)			
CABG	98 (54.7%)	92(53.8%)	.766
CABG and valve	37 (20.6%)	35 (20.4%)	.77
CABG and other	4(2.2%)	9(5.2%)	.21
Valve and valve/other	27(15%)	36 (21%)	.18
Number of bypassed vessels (n)	3.81±1.17	4.02±1.07	.33

Table II Post-operative outcomes

Findings	Before adjustment			After risk adjustment		
	Dexmedetomidine group	Non dexmedetomidine group	P value	Dexmedetomidine group	Non dexmedetomidine group	P value
Post-operative ventilation (hour)	30.1±84.3	41.6±134.4	.085	34.7	34.8	.961
Duration of ICU stay (hour)	111.3±163.0	113±158.1	.790	103.2	121.7	.050
Duration of hospital stay (day)	9.2±10.7	9.1±8.8	.668	8.9	9.7	.145

The effect of perioperative dexmedetomidine on sepsis and MACEs was not statistically significant; however, odds ratios favored dexmedetomidine perioperatively. In our study, 2.8% of subjects died in the hospital, and 4 % died within thirty days. The in-hospital and 30-day mortality was similar to those reported by previous studies (2.67% to 4.5%)(Aboul-Hassan et al., 2020; Schubert et al., 2019). Dexmedetomidine is used for analgesia, anxiolysis, sedation, and anesthetic premedication. A study reported that dexmedetomidine was used in 17% of non-cardiac surgeries intraoperatively or pre-operatively (Arnold et al., 2018). Another study found that it was used as after surgery sedative in 12% of cardiac surgery patients(Lee, 2019). In the current study, dexmedetomidine was administered to more than half of the study sample. It can be postulated that perioperative dexmedetomidine is associated with early post-operative recovery in

cardiac surgery, considering its anti-delirium, anti inflammatory and sympatholytic effects. In the current study, though, evidence on the beneficial impacts of dexmedetomidine use on myocardial function is insufficient, yet MACEs trend suggests this effect. The previous study shows that dexmedetomidine preconditioning is associated with reduced reperfusion injury and risk of myocardial ischemia through activating pro-survival kinases(He et al., 2019). In our study, the incidence of delirium was significantly lower in cardiac surgery. The prevalence was lower than reported in the previous study (He et al., 2019). This may be because only the cases of hyperactive delirium were included in the study. The rate of delirium post-cardiac surgery is high, but hyperactive delirium is lower than emotional delirium(Novotny et al., 2022). This study shows that dexmedetomidine reduced post-operative complications of cardiac surgery. However, it was

associated with an increased prevalence of post-operative renal failure. A previous study reported that α 2-adrenoceptor agonists have a protective effect on renal function (Ma et al., 2020). The contrary finding of our research may be attributed to the timing of administration, as dexmedetomidine should be administered before the renal injury. The limitation of this is that though the rate of perioperative dexmedetomidine infusion was higher in a previous study (Arnold et al., 2018), more randomized, multi-center studies are needed to confirm the results.

Conclusion

Perioperative intravenous dexmedetomidine results in improved hospital and thirty-day survival and is associated with decreased post-operative delirium and overall complications.

Conflict of interest

The authors declared absence of conflict of interest.

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