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ORIGINAL ARTICLE

Effects of dexmedetomidine and propofol on sedation in patients after coronary artery bypass graft surgery in a fast-track recovery room setting

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Abstract
Purpose We aim to compare the effects of propofol and dexmedetomidine infusions on extubation times, hemodynamic and respiratory functions, complication rates and patient satisfaction scores in patients undergoing coronary artery bypass graft (CABG) surgery using a fast-track anesthesia regimen for early extubation.
Methods We enrolled 64 patients who underwent CABG surgery. Dexmedetomidine (min 0.2 μg/kg/h–max 1.0 μg/kg/h) and propofol (min 1.0 mg/kg/h–max 3.0 mg/kg/h) infusion doses were titrated to give bispectral index values between 60 and 90 and a Ramsay sedation score (RSS) between 3 and 4. Postoperative extubation times, patient satisfaction and postoperative adverse events were recorded.
Results The mean times to extubation were 265.94 ± 43.1 min for the dexmedetomidine group and 322.52 ± 39.2 min for the propofol group ($P < 0.001$). In all recordings, RSS median values for the propofol group were significantly lower than the dexmedetomidine group ($P < 0.05$). There were no differences in the incidence of postoperative adverse events between the dexmedetomidine and propofol groups. There was a statistically significant difference between patient satisfaction median values of the two groups—7 (5–9) and 9 (7–10) (min–max) for the propofol and dexmedetomidine groups, respectively ($P < 0.001$).
Conclusion Our results show that dexmedetomidine can easily be preferred over propofol in fast-track cardiac anesthesia due to its significant advantages of shorter extubation time and higher postoperative patient satisfaction scores.

Keywords Fast-track extubation · Dexmedetomidine · Propofol · Coronary artery bypass grafting surgery

Introduction

Fast-track is defined as the extubation of open cardiac surgery patients in the first six postoperative hours. Early extubation performed in applicable patients provides early mobilization and lowers the incidence of delirium. Furthermore, the total time spent in the intensive care unit (ICU) and the hospital is reduced, decreasing the medical costs [1]. The importance of postoperative optimal sedation in patients who undergo coronary artery bypass graft (CABG) and who are scheduled to have a fast-track cardiac anesthesia is increasing. Although it was first performed in the 1970s, there is still no net protocol for the sedative agent and dose that are to be used in the fast-track postoperative period.

Although propofol is commonly used as a sedative agent in operating rooms and ICUs, it may lead to hypotension, bradycardia, respiratory depression and even apnea depending on the infusion dose [2, 3].

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Dexmedetomidine is a selective α_2 receptor agonist. Its use in the fast-track procedure is increasing because it does not cause respiratory depression in addition to its other benefits, i.e., sedative, analgesic and anxiolytic properties. The sedative effect of dexmedetomidine resembles physiological sleep electroencephalographically; therefore, the cognitive functions are preserved. Patients can easily be woken up and cooperation can be established; however, it may result in hypotension and bradycardia depending on the infusion dose [4, 5].

A previous review of a randomized controlled trial showed that remifentanil could be beneficial in cardiac surgery with a reduced time on mechanical ventilation, cardiac biomarker release, and hospital stay [6]. Although many studies have been performed to compare the efficacies, advantages and disadvantages of propofol and dexmedetomidine, their superiority to each other with regard to the fast-track method is still under debate [7–9]. Our aim in this first prospective study is to compare the effects of propofol and dexmedetomidine as sedative agents of the fast-track regimen in patients undergoing CABG surgery using remifentanil anesthesia.

Materials and methods

This study was peformed after obtaining approval from the local ethics committee (29.01.2011/23–4), and receiving signed informed consent forms from patients who were willing to take part.

The study was performed on 70 patients who had elective CABG surgery, were between the ages of 40–75 years and who had an American Society of Anesthesiologists (ASA) physical condition score of <IV. Exclusion criteria in the preoperative stage were chronic renal failure, liver failure, congestive heart failure, valvular heart disease, respiratory system disorder (FEV1/FVC <60 %), allergy towards propofol and dexmedetomidine, dementia and Alzheimer's disease, a left ventricle ejection fraction of ≤40 %, body mass index (BMI) of ≥30 kg m^{-2}, anticonvulsive, antidepressant and psychoactive drug use, a cardiopulmonary bypass time of ≥120 min, and re-operated and emergency patients. The postoperative stage exclusion criteria were bleeding (chest tube drainage >100 mL/h), renal insufficiency (urine output <0.5 mL/kg/h in first 6 h), increase in serum creatinine level (>50 % of initial level), prolonged support of inotropic and vasodilating drugs due to cardiac problems and patients who cannot be extubated within the first 6 h because of pulmonary problems that prohibit weaning. Two patients were excluded during the postoperative period due to bleeding, a further 3 patients due to prolonged support of inotropic and vasodilating drugs, and 1 patient because of pulmonary problems, leaving 64 patients in the study (Fig. 1).

Premedication was performed with 25–50 μg/kg intravenous (IV) midazolam 1 h before surgery. Anesthetic gas and end-tidal CO_2, peripheric oxygen saturation, noninvasive and invasive arterial blood pressure, central venous pressure (CVP) monitorization and a 5-lead electrocardiography was routinely performed on all patients taken to the operating room. Pulmonary artery catheterization was not performed.

Remifentanil infusion (1 μg/kg/min) was given to the patients 3 min before anesthesia induction and preoxygenization was performed. Intubation was sustained with 0.25 mg/kg etomidate and 0.1 mg/kg vecuronium. Maintenance of anesthesia following intubation was achieved by 1–2 % sevoflurane end-tidal concentration, 1 μg/kg/min remifentanil infusion and intermittent 0.05 mg/kg vecuronium IV bolus. Sevoflurane and remifentanil infusion was continued until the end of the operation. When the perioperative systolic artery pressure (SBP) increased by >20 % of its preoperative level or the mean arterial pressure (MBP) was ≥90 mmHg and the heart rate (HR) was >100 beats/min, the first step was to increase remifentanil infusion by 0.5 μg/kg/min and the sevoflurane end-tidal concentration by 50 %. If there was no response within 3 min, remifentanil infusion was increased by a further 0.5 μg/kg/min. If the hemodynamic stability could still not be controlled, either nitroglycerine or β-blocker infusions were started.

When the perioperative SBP decreased by >20 % of its preoperative level or MBP was <60 mmHg, the first step was to start fluid infusion if it was thought to be due to hypovolemia. If there was no response within 3 min, remifentanil infusion was decreased by 0.5 μg/kg/min and the sevoflurane end-tidal concentration by 50 %.

Vasopressors were used in patients when hemodynamic stability was still not under control. Anticolinergic agents were used if the heart rate was <55 beats/min. Fluid infusions were carried out to maintain the CVP level between 3 and 8 mmHg during perioperative and postoperative stages.

The actual time intervals for the multiple hemodynamic and laboratory measurements were taken during surgery.

After the skin was closed, sevoflurane was stopped. Remifentanil infusion was decreased to 0.5 μg/kg/min and the patients were transferred to the ICU. The time of transfer to the ICU was regarded as the start of the study. All patients received bispectral index (BIS) monitorization (Aspect Medical Systems®, The Netherlands). By using sealed envelopes, one group of patients received 0.6 μg/kg/h dexmedetomidine IV infusion (Group D) and the other group received 2 mg/kg/h propofol IV infusion (Group P) in a random fashion. Ten minutes after their arrival at the ICU, the remifentanil infusion was reduced to 50 % (0.25 μg/kg/min). In the postoperative

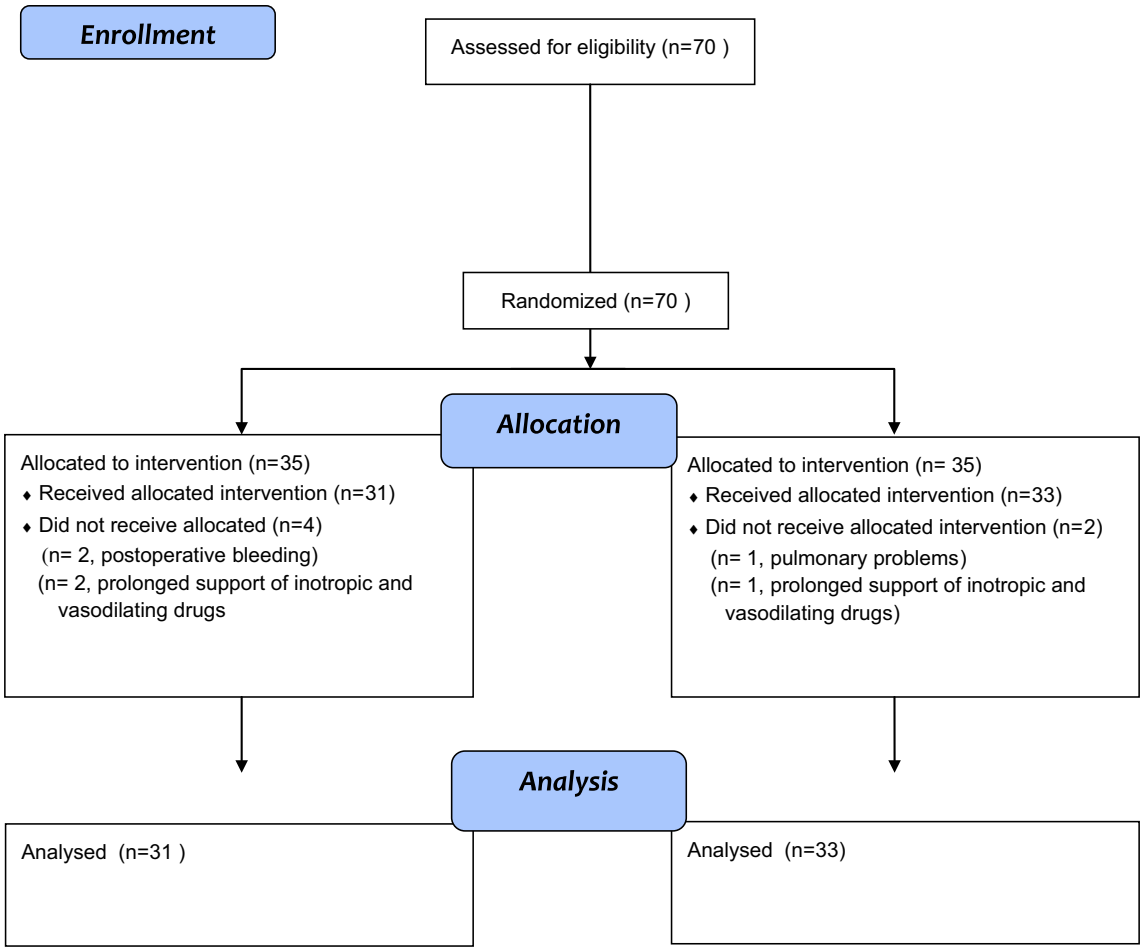

Fig. 1 Flow chart

20th min, remifentanil infusion was reduced by a further 50 % (0.125 μg/kg/min) and was completely stopped at the 30th min. Analgesia was provided by paracetamol (1 g IV every 6 h) and dexketoprofen trometamol (25 mg IV every 8 h). Opioid analgesics that can affect the respiratory functions were not used in postoperative analgesia.

The sedation levels of the patients were evaluated with BIS and RSS every 15 min until the 6th postoperative hour and hourly levels were recorded. Dexmedetomidine (0.2–1.0 μg/kg/h) and propofol (1.0–3.0 mg/kg/h) infusion doses were titrated to keep BIS values between 60 and 90 and RSS values between 3 and 4. It was decided that the patients in both groups would receive extra analgesics (25–50 mg pethidine hydrochloride IV) and would be excluded from the study if BIS was >90 and RSS was <3 in spite of the maximum doses. It was also decided that the patients in both groups would be excluded from the study and propofol infusions stopped if BIS was <60 and RSS was >5 in spite of the minimum doses.

The weaning procedure was started in patients who were hemodynamically stable and did not have pulmonary problems. Extubation criteria were body temperature of >36 °C, chest tube drainage <100 mL/h, urine output >0.5 mL/kg/h, F_IO_2 <0.5, SpO_2 >%95, pH >7.25–7.3, and $PaCO_2$ <55 mmHg. Patients were evaluated for extubation with extubation criteria at hourly intervals.

Infusions of dexmedetomidine and propofol were stopped with the extubation. The duration of time between the postoperative arrival at the ICU and extubation was recorded along with the postoperative adverse events. All patients enrolled in the study were evaluated on the surgical wards at 24 h postoperatively using a 10-point scale test for patient satisfaction (0, no satisfaction; 1–4, mild satisfaction; 5–7, moderate satisfaction; 8–9, satisfaction; 10, extreme satisfaction) [10].

The aim of the study was to evaluate the effects of dexmedetomidine-based sedation in postoperative cardiac surgery patients in clinical practice. The primary objective measured by this study was the achievement of early extubation, defined as postoperative extubation of $\leq$6 h.

A similar study on the subject was conducted on 56 patients in two groups of 28 patients [8]. We determined

our total patient number of 70 based on this similar study; however, as 6 patients were excluded from our study, we performed a power analysis to test the sufficiency of the sample size. After the study was completed with 64 patients, post hoc power analysis was performed to test the strength of the hypothesis that would be founded upon the 20 % difference between the mean duration of postoperative extubation times. As a result, it was observed that 29 patients from each group were adequate to differentiate the difference between the groups with 100 % certainty.

Results are expressed as mean ±SD or median (min–max) or number of patients (%). Proportions and means were compared using Student's *t* test, chi-squared test and Fisher's exact test where appropriate. Times to extubation were estimated by Kaplan–Meier and *P* values by log rank analysis. All *P* values were 2-tailed and statistically significant at an alpha of <0.05. Statistical analysis was performed with SPSS version 18.0 for Windows.

Results

There were no differences between the groups regarding demographic data and baseline characteristics (Table 1).

Extubation time was found to be statistically shorter in Group D compared to Group P ($P < 0.001$) (Fig. 2). The mean times to extubation were 265.94 ± 43.1 min for Group D and 322.52 ± 39.2 min for Group P.

When the groups were evaluated for sedation scores, a statistically significant difference was observed regarding the RSS median values of Group P which were shorter at all measurement times compared to Group D ($P < 0.05$) (Table 2).

When the groups were evaluated for patient satisfaction, the median (min–max) values of Group P [7 (5−9)] were significantly lower than Group D [9 (7–10)] ($P < 0.001$]. The number of patients with a satisfaction score of ≥8 was 27 (87 %) in Group D and 16 (48.5 %) in Group P ($P = 0.002$).

SBP mean values in both groups were close to baseline values (±5 mmHg) in all measurements. There was an average of 10 mmHg increase in SBP in both groups following extubation; however, no significant difference was observed between the groups (Fig. 3). Median heart rate was similar in both groups (Fig. 4).

There were no differences in the incidence of postoperative adverse events in both groups (Table 3). Postoperative adverse events were noted in 9 patients in Group D (29 %) and 11 patients in Group P (33.3 %); however, no significant differences were detected between the groups. The most common postoperative adverse event in both groups was hypotension (12.1 % in Group D vs 15.1 % in Group P) ($P = 0.796$). Two patients in Group D and seven

Table 1 Demographic data and baseline characteristics

Variable	Group D ($n = 31$)	Group P ($n = 33$)	*P* value
Age (year)	62.5 ± 6.8	63.9 ± 7.1	0.42
BMI (kg/m^2)	26.9 ± 1.8	27.1 ± 1.9	0.65
Ejection fraction (%)	54.8 ± 3	53.5 ± 3.1	0.1
ASA Score	3 (2–3)	2 (2–3)	0.61
Operation time	267.2 ± 55.2	282.75 ± 60.2	0.43
Gender			0.72
Male	26 (83.8 %)	29 (87.9 %)	
Female	5 (16.2 %)	4 (12.1 %)	
Medical history			
Hypertension	20 (64.5 %)	19 (57.5 %)	0.61
COPD/asthma	4 (12.9 %)	2 (6 %)	0.41
Diabetes mellitus	11(35.5 %)	13 (39.3 %)	0.8

Data are presented as mean ± SD or median (min–max) or number of patients (%). There were no differences between the groups

BMI body mass index, *ASA* Score American Society of Anesthesia Score, *COPD* chronic obstructive pulmonary disease

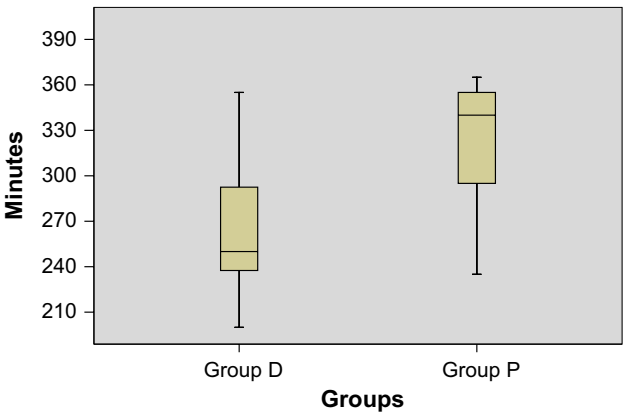

Fig. 2 Times to extubation by treatment box and Whisker plot. Median, IQR and extremes are shown. Statistical difference was detected between the two groups ($P < 0.001$)

Table 2 Postoperative Ramsay Sedation Scores

Time (h)	Group D ($n = 31$)	Group P ($n = 33$)
1	3 (2–4)*	3 (2–4)
2	4 (2–4)*	3 (2–4)
3	4 (3–4)*	3 (2–4)
4	4 (3–4)*	3 (2–4)
5	3 (3–4)*	3 (2–4)
6	3 (3–4)*	3 (2–4)

Data are presented as median (min–max)

* $P < 0.05$ vs propofol

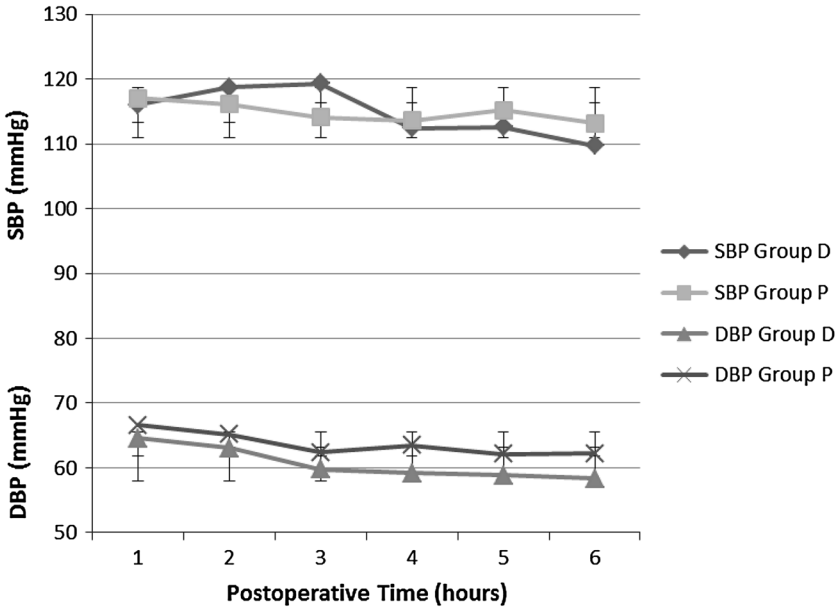

Fig. 3 Changes in systolic and diastolic blood pressure (mean ± SD). No statistical difference was detected between the two groups ($P > 0.05$)

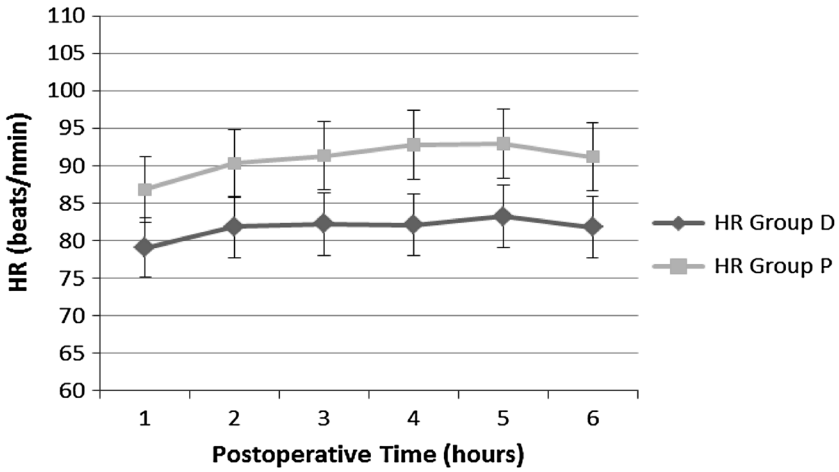

Fig. 4 Changes in heart rate (HR) in beats/min (mean ± SD). No statistical difference was detected between the two groups ($P > 0.05$)

Table 3 Postoperative adverse events

	Group D ($n = 31$)	Group P ($n = 33$)	P value
Patients reporting at least 1 adverse event	9 (29 %)	11 (33.3 %)	0.711
Hypotension	4 (12.1 %)	5 (15.1 %)	0.796
Bradycardia	2 (6.4 %)	1 (3 %)	0.518
Tachycardia	1 (3.2 %)	3 (9 %)	0.333
Bronchospasm	2 (6.4 %)	2 (6 %)	0.949
Atrial fibrillation	2 (6.4 %)	1 (3 %)	0.518
Hyperglycemia	1 (3.2 %)	2 (6 %)	0.592

Data are presented as number of patients (%). There were no differences between the groups

patients in Group P had extra analgesic requirements and there were no statistically significant differences between groups ($P = 0.89$). The mean analgesic dose administered was 2.4 mg (±9.9) in Group D and 7.58 mg (±15.9) in Group P. There were no statistically significant differences between groups ($P = 0.128$).

Discussion

Propofol and dexmedetomidine are commonly used for sedation in the ICU (doses of 1–3 mg/kg/h and 0.2–1.0 μg/kg/h, respectively) [3, 7–9]. The dosage of both agents is usually determined by evaluation of the sedation level by

subjective methods such as RSS. In our study, we performed BIS monitorization for all patients in addition to RSS in order to be able to compare the effects of propofol and dexmedetomidine in fast-track cardiac anesthesia in an objective manner.

The primary aim of our study is to compare the effects of dexmedetomidine and propofol on extubation time in fast-track cardiac anesthesia. We observed a significantly shorter extubation time in Group D compared to Group P. Other similar studies have been conducted in the literature with an extensive group of patients as in our study. A recent study of 582 patients in the cardiovascular surgery intensive unit by Curtis et al. [11] also found a shorter extubation time in the dexmedetomidine group compared to the propofol group. However, this was a retrospective study and patients with valvular surgery, congestive heart failure, obesity and emergency ward patients were also enrolled. There were no standard protocols in preoperative patient selection, intraoperative and postoperative anesthesia, analgesia and sedation. Their study was not performed using a fast-track anesthesia protocol and only postoperative extubation times were screened. Herr et al. [7] also studied 295 patients who underwent CABG surgery and found extubation time to be shorter in the dexmedetomidine group compared to the propofol group; however, the primary outcome of the study was to compare the sedative efficacy of propofol and dexmedetomidine by checking the amount of morphine consumption. The study was not performed according to the fast-track protocol and the infusion levels of dexmedetomidine and propofol were determined only by RSS evaluation. Compared to other studies, our study was performed in a well-defined patient group with a uniform anesthetic, analgesic and sedative plan using a one-type cardiac surgery group under RSS and BIS sedation data and with fast-track cardiac anesthesia protocol taken into account. When the data is evaluated, it may be hypothesized that dexmedetomidine, with its spontaneous respiration and cognitive function protective features that are not present in propofol, enables a shorter extubation time.

In our study, RSS was recorded to be significantly lower in Group P at all measurement times when compared to Group D. In the literature, there are reports with varying results on which drug should be chosen by the clinicians for sedation. A study by Okawa et al. [12], which was performed in healthy subjects, reported that the subjective evaluation of the patients was more favorable in the propofol group. Thus, they concluded that propofol was a more appropriate agent for sedation. A study by Lin et al. [13] on patients who underwent elective cardiac surgery, compared dexmedetomidine with placebo and concluded that dexmedetomidine was a better sedative agent. Venn et al. reported that the only disadvantage of dexmedetomidine when compared to propofol was the fact that it caused bradycardia [13]; however, they also reported that this could be an advantage in certain patient groups due to protection against myocardial ischemia. In our study, the fact that RSS was found to be significantly lower in Group P at all measurement times when compared to Group D can be interpreted as the ability of dexmedetomidine to provide better sedation conditions in the postoperative period when compared to propofol.

When current research and meta-analysis are assessed, it is observed that dexmedetomidine provides significantly increased patient satisfaction compared to propofol [9, 15]. Stein-Parbury et al. [16] reported that patients who receiving dexmedetomidine had far better moderate approaches to annoying factors in the ICU such as pain, noise, mechanical ventilation and entubation. Venn et al. [14] also observed that patients receiving dexmedetomidine had more optimistic ICU experiences. In our study, we performed patient satisfaction assessments 24 h postoperatively and determined that dexmedetomidine patients gave more positive replies than propofol patients. It can be deduced that the analgesic features of dexmedetomidine, as well as its ability to conserve cognitive functions and to produce a sedation that resembles physiological sleep, all contribute to it receiving better patient satisfaction scores than propofol.

We did not observe statistically significant hemodynamic changes between the groups. In studies that assessed the hemodynamic effects of dexmedetomidine there were many outcomes such as inevident hypotension and bradycardia evident hypotension, evident bradycardia, and evident hypotension and tachycardia [7, 8, 14, 17]. The most common side-effects of α_2 receptor agonists are hypotension and bradycardia in compliance with their mechanisms of effect. This effect of dexmedetomidine usually develops during bolus. The hypertension and tachycardia effect is regarded as a compensatory response of α-2b receptors to the effects of α-2a receptors. The fact that other studies determined different hemodynamic effects is because of the different applications and patient groups involved in the studies. Some patient groups received the bolus dose while others did not. Some patient groups received high bolus and infusion doses while others received low doses. Apart from patient groups who had undergone various surgical operations, studies were also conducted on ICU patients who had no previous surgery and healthy volunteers. In some studies, patients were enrolled who used inotropic agents, vasodilatators and opioids that could affect postoperative hemodynamics. On the other hand, we performed this study on patients who were administered no bolus, who had infusion doses determined with certain criteria, and who were hemodynamically stable and had no complications. Our results showed no evident effect of dexmedetomidine and propofol on hemodynamics.

One limitation of our study is that overall cost and hospitalization times in the ICU and ward were not calculated. However, the primary aim of our study was to analyze the effects of dexmedetomidine and propofol on extubation times in fast-track cardiac anesthesia. Therefore, we conducted our study on a homogeneous patient group whose preoperative patient selection, perioperative and postoperative anesthesia, analgesia and sedation practices were well defined and who had elective CABG surgery. The surgery for the patients in our study started at approximately 08.30–09.00 am and ended between 01.00 and 02.00 pm. In order to increase the accuracy of the data obtained during the study, we tried to the best of our ability to provide similar circumstances and used objective tests. Another limitation of our study was that the sedative drugs were not blinded due to the unique physical properties of propofol. However, we think we avoided a possible bias by evaluating patients using both BIS and RSS.

According to our study, dexmedetomidine has apparent advantages in fast-track cardiac anesthesia compared to propofol such as shorter extubation time and higher postoperative patient satisfaction scores. Moreover, it does not have the disadvantage of a side-effect unlike propofol. Thus, we are of the opinion that clinicians can easily prefer dexmedetomidine over propofol in fast track-cardiac anesthesia.

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