Türk Göğüs Kalp Damar Cerrahisi Dergisi 2013;21(3):683-690
doi: 10.5606/tgkdc.dergisi.2013.7309

Original Article / Özgün Makale

An efficacy comparison of fentanyl and remifentanil during off-pump coronary artery bypass graft surgery

Atan kalpte koroner arter baypas cerrahisinde fentanil ve remifentanilin etkinlik karşılaştırması

Tuğba Aşkın,[1] Ümit Karadeniz,[2] Süheyla Ünver,[3] Ertay Boran,[4] Özcan Erdemli[2]

[1]Department of Anaesthesiology and Reanimation, Afyon State Hospital, Afyon, Turkey
[2]Department of Anaesthesiology and Reanimation, Türkiye Yüksek İhtisas Training and Research Hospital, Ankara, Turkey
[3]Department of Anaesthesiology and Reanimation, Dr. Abdurrahman Yurtaslan
Ankara Oncology Training and Research Hospital, Ankara, Turkey
[4]Department of Anaesthesiology and Reanimation, İzmir Training and Research Hospital, İzmir, Turkey

Background: This study aims to compare the effects of fentanyl and remifentanil on hemodynamic stability, release of troponin-I and early extubation during off-pump coronary artery bypass graft (CABG) surgery.

Methods: Forty patients who were scheduled for elective off-pump CABG surgery were randomly assigned to two groups. The remifentanil group received 1 $\mu g/kg^{-1}$ remifentanil over one minute for induction, followed by 0.1-1 $\mu g/kg^{-1}$ min^{-1} continuous infusion plus midazolam 0.1-0.15 mg/kg^{-1} for maintenance dose. The fentanyl group received 10-15 $\mu g/kg^{-1}$ fentanyl over one minute for induction and 0.1-1 $\mu g/kg^{-1}$ min^{-1} continuous infusion plus midazolam 0.1-0.15 mg/kg^{-1} for maintenance dose. Rocuronium bromide at 0.6-0.8 mg/kg^{-1} was administered to facilitate tracheal intubation. Midazolam infusion at 0.4-1 $\mu g/kg^{-1}$ min^{-1} was initiated for maintenance therapy.

Results: The depth of anesthesia was adjusted to maintain a BIS value between 40-60. Following skin incision and sternotomy, systolic arterial pressure was lower in the remifentanil group compared to the fentanyl group (115±14 mmHg vs. 130±22 mmHg $p<0.05$; 125±14 mmHg vs. 135±19 mmHg, $p<0.05$). Total dose of midazolam was significantly higher in the remifentanil group compared to the fentanyl group (13.9±3.7 mg vs. 11.6±3.7 mg, $p<0.05$). Intraoperative use of beta blockers, nitroglycerine and sodium nitroprusside was similar in both groups. The median time to extubation and the length of stay in the intensive care unit were shorter in the remifentanil group (6.5±3 h vs. 10±3 h, $p<0.05$; 14±6 h vs. 20±6 h, $p<0.05$). The incidence of postoperative electrocardiographic changes and troponin I measurements were similar in both groups.

Conclusion: Although remifentanil infusion offers a better intraoperative hemodynamic stability and postoperative recovery, both agents have similar effects on myocardial injury during off-pump CABG surgery.

Key words: Anesthesia; myocardial protection; off-pump surgery; remifentanil.

Amaç: Bu çalışmada atan kalpte koroner arter baypas greft (KABG) cerrahisinde fentanil ve remifentanilin hemodinamik stabilite, ameliyat sırası troponin-I salınımı ve erken ekstübasyona etkileri karşılaştırıldı.

Çalışma planı: Atan kalpte elektif KABG cerrahisi planlanan 40 hasta randomize olarak iki gruba ayrıldı. Remifentanil grubuna indüksiyonda bir dakika boyunca 1 $\mu g/kg^{-1}$ remifentanili takiben 0.1-1 $\mu g/kg^{-1}$ $dk.^{-1}$ sürekli infüzyon artı midazolam 0.1-0.15 mg/kg^{-1} idame dozu uygulandı. Fentanil grubuna indüksiyonda 10-15 $\mu g/kg^{-1}$ fentanili takiben 0.1-1 $\mu g/kg^{-1}$ $dk.^{-1}$ sürekli infüzyon artı midazolam 0.1-0.15 mg/kg^{-1} idame dozu uygulandı. Trakeal entübasyonu kolaylaştırmak için rokuronyum bromür 0.6-0.8 mg/kg^{-1} verildi. İdame tedavisinde 0.4-1 $\mu g/kg^{-1}$ $dk.^{-1}$ midazolam infüzyonuna başlandı.

Bulgular: Anestezi derinliği BIS 40-60 değerleri arasında olacak şekilde ayarlandı. Cilt insizyonu ve sternotomi sonrası sistolik arter basıncı remifentanil grubunda fentanil grubundan daha düşük bulundu (130±22 mmHg'ye kıyasla 115±14 mmHg, $p<0.05$; 135±19 mmHg'ye kıyasla 125±14 mmHg, $p<0.05$). Toplam midazolam dozu, remifentanil grubunda fentanil grubuna göre anlamlı olarak daha yüksekti (11.6±3.7 mg'ye kıyasla 13.9±3.7 mg, $p<0.05$). Ameliyat sırası beta bloker, nitrogliserin ve nitroprussid kullanımı her iki grupta benzerdi. Ortalama ekstübasyon zamanı ve yoğun bakımda kalış süresi, remifentanil grubunda daha kısaydı (10±3 saate kıyasla 6.5±3 saat, $p<0.05$; 20±6 saate kıyasla 14±6 saat, $p<0.05$). Ameliyat sonrası elektrokardiyografik değişiklik insidansı ve troponin-I ölçümleri iki grupta benzerdi.

Sonuç: Atan kalpte KABG cerrahisinde remifentanil uygulaması daha iyi ameliyat sırası hemodinamik stabilite ve ameliyat sonrası derlenme sağlamasına karşılık, her iki ajanın miyokardiyal hasar üzerine etkileri benzer bulundu.

Anahtar sözcükler: Anestezi; miyokardiyal koruma; atan kalpte cerrahi; remifentanil.

Available online at
www.tgkdc.dergisi.org
doi: 10.5606/tgkdc.dergisi.2013.7309
QR (Quick Response) Code

Received: June 22, 2012 *Accepted:* August 31, 2012

Correspondence: Ümit Karadeniz, M.D. Türkiye Yüksek İhtisas Eğitim ve Araştırma Hastanesi Anestezi ve Reanimasyon Kliniği, 06230 Sıhhiye, Ankara, Turkey.
Tel: +90 312 - 306 17 15 e-mail: ukaradeniz2003@gmail.com

Off-pump coronary artery bypass graft (CABG) surgery is increasingly being performed, especially for high-risk patients,[1] and vasopressors or beta blockers used during the displacement and stabilization of the heart, monitorization and management of myocardial ischemia during coronary occlusion, and management of hypothermia are important modalities for patients during this surgical procedure.[2] The findings of elevated inflammatory markers and the release of cardiospecific enzymes in individual patients imply an ongoing need to develop more effective strategies for myocardial protection during off-pump CABG.[3]

The coronary blood flow during anastomosis can be compromised due to hemodynamic disturbances even in the presence of intracoronary shunts this procedure. There is also evidence that the level of intraoperative analgesia may influence the risk of postoperative myocardial infarction (MI) in all patients undergoing cardiac surgery.[4,5] Therefore, choosing the appropriate opioid and prescribing the proper dosage in order to maintain a stable heart rate and blood pressure by using the least possible vasoactive medication during surgery is a great challenge for every cardiac anesthesiologist.

Remifentanil is a potent, synthetic opioid with an ultra-short duration of action. It has a stable, context-sensitive half-time compared with other opioids, and its rapid elimination allows for the depth of analgesia to be adjusted according to the phase of the operation, thus successfully blocking the stress response.[6]

The goal of this prospective randomized study was to compare the effects of fentanyl and remifentanil as they related to hemodynamic stability, troponin I release, and early extubation in off-pump CABG surgery.

PATIENTS AND METHODS

This clinical study was performed at Türkiye Yüksek İhtisas Education and Research Hospital with the approval of the ethics committee and the informed consent of the participants. Forty patients, aged 40 to 75 years, with the American Society of Anesthesiologists (ASA) physical status II and III who were to undergo off-pump CABG surgery were enrolled in the study. The exclusion criteria were the following: an ejection fraction (EF) of less than 40%, the preoperative use of inotropic agents and/or an intraaortic balloon pump, major organ failure [creatinine >1.5 mg/kg^{-1}, serum glutamic oxalacetic transaminase (SGOT) >40 IUL^{-1}, serum glutamic pyruvic transaminase (SGPT) >40 IUL^{-1}, hematocrit (Htc) <30%], opioid intolerance, a history of neurological diseases, or a cerebrovascular event.

The patients were premedicated with 10 mg diazepam (Diazem, DEVA Holding, Istanbul, Turkey) orally the day before surgery and with 0.1-0.15 mg/kg^{-1} morphine hydrochloride (HCL) (Biosel İlaç Sanayi ve Ticaret A.Ş., Istanbul, Turkey) intramuscularly on the day of surgery. Monitorization of all patients was done via electrocardiogram (ECG), arterial oxygen saturation, and nasopharengeal and rectal temperature. The patients' blood pressure was also monitored via a left arterial line, and a catheter was inserted in the right internal jugular vein to observe the central vein pressure. The depth of anesthesia was measured using the Bispectral Index™ (BIS™) brain function monitoring system (Covidien, Mansfield, MA, USA). The baseline blood pressure was recorded before instrumentation, and a baseline blood sample was collected for cardiac enzyme analysis.

Before the induction of anesthesia, each of the 40 patients scheduled for elective off-pump CABG was given 100% oxygen for at least three minutes and randomly assigned to either the remifentanil group (group R), which received 1 $\mu g/kg^{-1}$ remifentanil (Ultiva™, GlaxoSmithKline, Istanbul, Turkey) over one minute for induction and 0.1-1 $\mu g/kg^{-1}$ min^{-1} continuous infusion for maintenance, or the fentanyl group (group F), which received 10-15 $\mu g/kg^{-1}$ fentanyl (Abbott Laboratories, Istanbul, Turkey) over one minute for induction and 0.1-1 $\mu g/kg^{-1}$ min^{-1} continuous infusion for maintenance. Rocuronium bromide 0.6-0.8 mg/kg^{-1} and 0.1-0.15 mg/kg^{-1} midazolam (Zolamid, Defarma, Ankara, Turkey) were administered to facilitate tracheal intubation and continued as 0.3 mg/kg^{-1} every 30-45 minutes. Midazolam maintenance infusion 0.4-1 $\mu g/kg^{-1}$ min^{-1} was also started, and the depth of anesthesia was adjusted to maintain a BIS™ value of between 40-60.

In addition, the patients were ventilated with oxygen and air, with the ventilation being adjusted to maintain an end-tidal carbon dioxide (CO_2) of between 30-35 mmHg. Adjustments were also made with regard to the hypnotic (midazolam), analgesic, and antihypertensive treatments as they related to the intraoperative response (Tables 1 and 2).

The mean arterial pressure, heart rate and BIS™ index were recorded before induction, after induction, five minutes after intubation, after the skin incision and sternotomy, during the left internal mammary artery (LIMA) dissection, and at coronary anastomosis and skin closure.

All patients underwent coronary revascularization using the LIMA. For additional grafts, a saphaneus

Table 1. Bispectral index™ guided anesthetic management

Intraoperative response	BIS™	Treatment
Increased BP, HR, and autonomic or somatic response	>60	Increase use of hypnotics and analgesics; identify strong stimuli
Stable	>60	Rule out artifact; increase use of hypnotics
Hypotension or instability	>60	Support BP, decrease use of analgesics and consider amnesia
Increased BP, HR, and autonomic or somatic response	40-60	Increase use of analgesics; maintain use of hypnotics; possible use of paralytics or antihypertensives (β-blocker, nitroglycerin, and sodium nitroprusside)
Stable	40-60	Optimum safety and cost-effectiveness
Hypotension or instability	40-60	Support BP (volume and ephedrine); decrease use of analgesics
Increased BP, HR, or autonomic and somatic response	<40	Decrease use of hypnotics, increase use of analgesics (if continuing β-blocker, nitroglycerin, and sodium nitroprusside)
Stable	<40	Decrease use of hypnotics; possible decrease in use of analgesics
Hypotension or unstable	<40	Support BP (volume and ephedrine); decrease use of hypnotics and analgesics

BIS™: Bispectral Index™; BP: Blood pressure; HR: Heart rate.

vein was used. All patients received a single dose of intravenous heparin (Vasparin, Defarma, Ankara, Turkey), 75-150 IU/kg^{-1} after the LIMA dissection, and the activated coagulation time was measured to ensure the appropriate heparin effect and reversal.

The anastomosis, anesthesia, and surgery durations were recorded, and blood samples for troponin I analysis were obtained at the baseline and six hours after the surgery.

Postoperatively, the patients were followed up until discharge from the intensive care unit (ICU). Intramuscular diclofenac sodium and intravenous paracetamol (Parol, Atabay, İstanbul, Turkey) were used for postoperative pain control, and the duration of tracheal extubation and ICU discharge times along with any postoperative complications (nausea, vomiting, arrythmias, reintubation, awareness, bleeding, and myocardial ischemia), and the use of inotropics and antihypertensive drugs were recorded.

Data analysis was performed via the SPSS version 11.5 for Windows software program (SPSS Inc., Chicago, IL, USA). Student's t-test was used to determine whether or not there was a statistically meaningful difference between the two groups regarding the commonly distributed variables with continual measurement. If there was a difference, the Mann-Whitney U test was then employed to determine if there was any connection with the abnormally distributed variables. The Friedman test was used to evaluate whether there was a statistically meaningful difference between more

Table 2. Procedure times

	Group R	Group F	
	Mean±SD	Mean±SD	*p*
Anesthesia time (min.)	173.2±33.4	178.5±47.7	0.968
Surgery time (min.)	140.1±29.0	146.5±42.8	0.738
Extubation time (hrs.)	6.5±3.2*	10.3±3.7	0.001
Intensive care unit time (hrs.)	14.6±6.7*	20.7±6.5	0.014
Drainage (ml)	718.8±27	730±214	0.478

SD: Standard deviation; * p<0.05 between the two groups.

Table 3. Demographic data

	Group R			Group F			
	n	%	Mean±SD	n	%	Mean±SD	*p*
Age (years)			52±12			58±15	0.191
Gender							
Females	5			5			0.642
Males	15			15			0.642
Weight (kg)			74±13			75±7	0.640
Additional diseases	13	65		15	75		0.490
Preoperative β-blocker usage	16	80		11	55		0.091
Ejection fraction			56.35±7.77			57±7.38	0.512

SD: Standard deviation.

than two concurrent measurements within the groups If there was, then the Wilcoxon signed-rank test for multicomparison was performed and the measurement times that caused the difference were determined. In cases in which there was a second concurrent measurement, the significance in the difference between the measurements was evaluated via a dependent ttest or Wilcoxon signed-rank test. Nominal variables were compared using Pearson's chi-square or Fisher's probability tests with complete results, and a p value of <0.05 was considered to be significant. During all possible in-group or multiple comparisons, the Bonferroni correction was applied so as to take into account the type I fault.

RESULTS

Of the original 40 patients enrolled in this study, one was excluded because of the need to switch to on-pump coronary artery bypass grafting (CABG). The patients in group F and group R were comparable with respect to age, gender, weight, additional diseases, preoperative use of beta (ß) blockers, and left ventricular ejection fraction (LVEF). Thirteen patients in group R and 15 patients in group F had additional diseases [hypertension, diabetes mellitus (DM), hyperlipidemia, malignancy, epilepsy, and rheumatoid arthritis (RA)]. Furthermore, 27 patients were on preoperative ß blocker therapy, (Table 3). The mean BIS™ values of the patients during the surgery are shown in Figure 1.

The heart rate measurements were significantly lower in group R than in group F after sternotomy (67±8 vs. 79±12; p<0.05) (Figure 2). After the skin incision and sternotomy, the mean arterial blood pressures was also lower in group R than in group F (80±14 mmHg vs. 92±22 mmHg; p<0.05; 86±14 mmHg vs. 94±19 mmHg, respectively; p<0.05) (Figure 3).

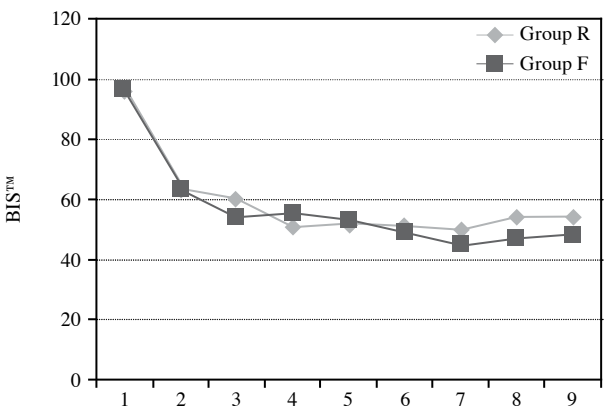

Figure 1. 1. Before induction; 2. After induction; 3.5. Five minutes later after intubation; 4. After skin incision; 5. After sternotomy; 6. During left internal mammary artery dissection; 7. At coronary anastomosis; 8. At chest closure; and 9. At skin closure. BIS™: Bispectral Index™.

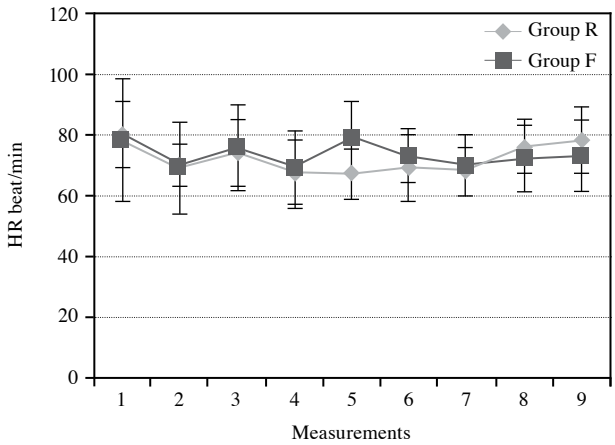

Figure 2. 1. Before induction; 2. After induction; 3. Five minutes later after intubation; 4. After skin incision; 5. After sternotomy; 6. During left internal mammary artery dissection; 7. At coronary anastomosis; 8. At chest closure; and 9. At skin closure. HR: Heart rate.

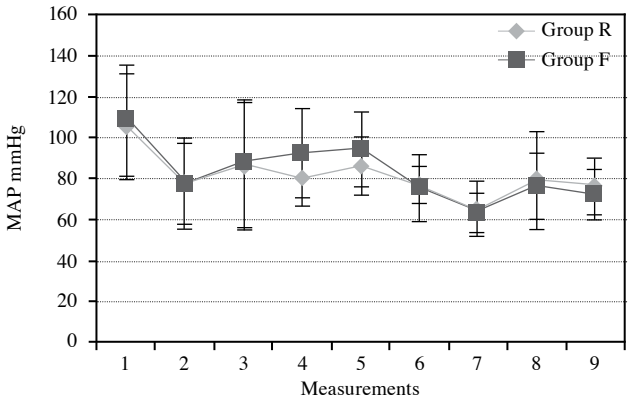

Figure 3. 1. Before induction; 2. After induction; 3. Five minutes later after entubation; 4. After skin incision; 5. After sternotomy; 6. During left internal mammary artery dissection; 7. At coronary anastomosis; 8. At chest closure; and 9. At skin closure. MAP: Mean arterial pressure.

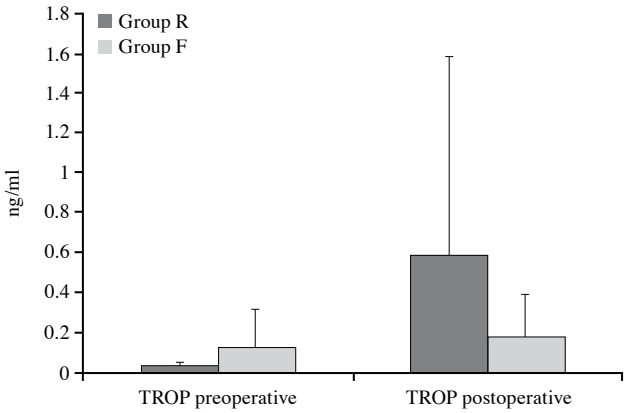

Figure 4. Pre- and postoperative troponin-I values.

A total of 4.6±1.2 mg fentanyl and 8.8±2.5 mg remifentanil were used in the groups during the surgery. The amount of midazolam was significantly higher in group R than group F (13.9±3.7 mg vs. 11.6±3.7 mg, respectively; $p<0.05$), but the intraoperative use of ß blockers, nitroglycerin, and sodium nitroprusside were similar between the two groups (Table 4).

The median durations of anesthesia, surgery, and bypass were also comparable. The median time to extubation and length of ICU stay were shorter in group R (6.5±3 hours and 10±3 hours, respectively; $p<0.05$) than in group F (14±6 hours and 20±6 hours, respectively; $p<0.05$) (Table 2).

The incidence of postoperative ECG changes [atrial fibrillation (AF) in one patient in group R and T-wave changes in the second-fifth vertebrae in another patient in group F) and troponin I measurements were similar between the groups (Figure 4).

Nitroglycerin and sodium nitroprusside were needed in 18 patients in group R and 16 in group F postoperatively ($p<0.05$), and the postoperative side effects, such as nausea, vomiting, emphysema, arrhythmia, convulsions, and reintubation due to hypercarbia, are shown in Table 5.

DISCUSSION

In the last 20 years, interest in performing CABG without the use of CPB has emerged in order to reduce postoperative complications associated with CPB and aortic manipulation, including generalized systemic inflammation, cerebral injury, myocardial injury, hemodynamic instability, and renal dysfunction. However, the initial enthusiasm over off-pump CABG has decreased with concerns about the completeness of revascularization, the rate of perioperative MI, and long-term graft patency.

As with conventional CABG, the overall goal of off-pump CABG is to preserve hemodynamic stability throughout the surgery while also maintaining an adequate level of anesthesia.

In cardiac surgery, patient comorbidity and periods of hemodynamic instability make it difficult to avoid occasional instances of light anesthesia. Furthermore, unrecognized inadequencies in depth of anesthesia may occur during CPB, which can alter the pharmacokinetics and pharmacodynamics

Table 4. Use of opioids, midazolam, and other drugs during the surgery

	Group R	Group F	
	Mean±SD	Mean±SD	*p*
Opioid (mg)	8.75±2.51* (R)	4.58±1.61 (F)	0.000
Midazolam (mg)	13.92±3.77*	11.62±3.76	0.038
Esmolol (mg)	1324.33±778.14	1270.38±652.15	0.821
Metoprolol (mg)	5±0.81	5.68±2.93	0.933
Nitroglycerin (mg)	5.38±4.01	3.70±3.59	0.184
Sodium nitroprusside (mg)	7.8±4.24	2.4±1.69	0.333

SD: Standard deviation; * $p<0.05$. between the two groups.

Table 5. Postoperative complications

	Group R		Group F	
	n	%	n	%
Nausea/vomiting	5	25	4	20
Reintubation	–	–	1	5
Emphysema	1	5	–	–
Seizure	1	5	–	–
Arrhythmia	1	5	–	–
Electrocardiography change	–	–	1	5

of prescribed medications, resulting in considerable changes in the drug concentrations. In addition, the oxygenator and tubing may bind large amounts of drugs. In addition, there is high risk involved with the rewarming process when restoration of brain normothermia coupled with decreased anesthetic concentrations could result in inadequate depth of anesthesia and potential for awareness.

There are potential limitations associated with processed electroencephalography (EEG) instruments such as the relative unresponsiveness to certain hypnotic agents like opioids, the proclivity of interference from other sources (which affects signal acquisition), the high cost of routine use, the inability to distinguish sleep from anesthetic-induced unconsciousness, and the unvarying nature of the indices (beyond loss of responsiveness) over a wide range of anesthetic drug concentrations. Although these limitations exist, the sensible use of a processed EEG tool like BIS™ to assess depth of anesthesia may help reduce the chances of intraoperative awareness. Vigilance is required, especially during intubation or intense surgical stimulation, instances of hemodynamic instability, and the rewarming phase of CPB.[7]

In our study, the efficacy of remifentanil and fentanyl regarding intraoperative hemodynamic changes, the use of ß-blockers, nitroglycerin, and sodium nitroprusside, extubation time, ICU length of stay, and the impact on perioperative troponin I release was evaluated.

One way to suppress the sympathetic response to a direct laryngoscope and orotracheal intubation is the use of high doses of opioids, but this may cause respiratory depression, indicating the need for long, postoperative ventilatory support. It is understood that remifentanil, with its rapid elimination, is responsible for the depth of analgesia. This leads to the successful prevention of the stress response that forms during procedures such as orotracheal intubation, skin incision, and sternotomy.[8]

Möllhoff et al.,[9] in their study that compared the effectiveness of remifentanil and fentanyl during on-pump CABG found a higher response to tracheal intubation in the group fentanil. Additionally, Mekis et al.[8] reported higher stability during intubation and sternotomy with 0.5 mg/kg^{-1} remifentanil and propofol compared with 5 μg/kg^{-1} fentanyl and propofol.

In adult anesthesia, remifentanil has a reputation for causing cardiovascular instability. Although the administration of a crystalloid solution or a vagolytic drug may minimize the incidence of bradycardia and hypotension, it appears to be more appropriate to use smaller doses of remifentanil.[10] In children, in particular neonates, remifentanil is known to cause bradycardia, but there is not much evidence of this in the pediatric literature. Some authors have suggested parasympathetic activation as a mechanism for bradycardia, but direct negative chronotropic effect and pretreatment with atropine or glycopyrrolate may also play a role in this condition.[11] Shinohara et al.[12] attempted to elucidate the cause of the hemodynamic effects of remifentanil in two groups of anesthetized rabbits using single doses of 1, 2, 5 µg/kg and found that it had a central vagotonic action which caused bradycardia and hypotension; however, it also was responsible for a corresponding increase in sympathetic activity.

In our study, no significant differences were found between the two groups regarding the heart rate and mean arterial pressures related to intubation ($p>0.05$). We believe this is related to the nitroglycerin added to the induction and the difference in the drug doses and combinations. The mean artery pressure values after the skin incision and sternotomy were lower in group R, but changes in both groups remained within the clinically acceptable rate of 20%. Asystole and serious bradycardia were reported after remifetanil induction during cardiac surgery and simultaneously administered sevoflurane and propofol, but the lack of the use of anticholinergic agents was found to be responsible.[13,14] However, others have proposed that remifentanil has a direct negative chronotropic effect.[15]

The reason for the different results in our study might be that we administered midazolam instead of propofol along with the fact that nitroglycerin increases the heart rate.

Off-pump CABG surgery is associated with hemodynamic changes that result from positioning and stabilizing the heart during distal anastomosis.[16] In addition, vessel occlusion associated with the distal anastomosis may cause ischemia, which may add to the hemodynamic changes. Several possible

treatment methods can be used to counteract the hemodynamic changes during off-pump CABG surgery. Volume loading is helpful for increasing the preload. Additionally, placing the patient in the Trendelenburg position with the feet raised by 20-30° is also beneficial, both for increasing the preload and for assisting in cardiac displacement. The use of inotropes, vasopressors during grafting, and nitroglicerin for ischemia are other potential treatment options.

Kessler et al.,[17] compared three different anesthesia techniques used in off-pump CABG surgery in connection with the significant increase in heart rate during coronary anastomoses and discovered that n the general anesthesia group, intravenous esmolol administration was required for seven patients. In our study, no statistically significant difference was found between the two groups in connection with the intraoperatively administered ß-blocker, nitroglycerin, and sodium nitroprusside doses. We did observe that there were more hypnotic (midazolam) drugs needed in the group R from the induction of anesthesia until the completion of the operation in order to maintain the same BIS™ values. This may be because the remifentanil had less of an effect on the change in the BIS™ than the fentanyl. Similarly, there were no significant differences noted between the two groups of patients regarding the need for antihypertensive treatment in the postoperative ICU.

Although anesthesia affects cardiac surgery patients postoperatively, the therapeutic strategies used during this period are the primary factors that determine the extubation time and length of ICU stay. A significant difference was observed between the duration in ICU in both groups in connection with the mean extubation periods, and shorter ICU stays were seen in the group R. There were no significant differences between the groups with regard to gender and age, and no patient needed intraoperative or postoperative inotropic agents. Both anesthetic regimes were well tolerated in our study, and similar postoperative complications were seen in the two groups (35% in group R and 30% in group F).

The hemodynamic changes that occur with displacement and stabilization of the heart often happen within seconds and end within five minutes; however, progressive decreases in systemic pressure may occur from ischemia during distal anastomosis. Typically, some degree of new-onset ST-segment elevation or depression can be found. Bein et al.[18] reported echocardiographic evidence of preserved myocardial function with sevoflurane in patients undergoing minimal invasive bypass surgery. Furthermore, Hemmerling et al.[19] recently compared isoflurane and sevoflurane and concluded that both the agents provided similar myocardial protection during off-pump CABG. In one study.[20] sevoflurane or propofol was administered to maintain the BIS™ between 40 and 60, but a cardioprotective effect could not be demonstrated since the cardiac troponin I levels and hemodynamics were comparable in both groups. Similar to the results of the Law-Koune et al.[21] study in which they compared the myocardial protective effects of the sevoflurane/remifentanil and propofol/remifentanil anesthesia techniques associated with BIS™ in off-pump CABG surgery, we did not find any differences related to the troponin I levels between the remifentanil and fentanyl groups.

As suggested by Glass et al.[22] we adjusted the hypnotic and analgesic doses according to the BIS™. In this way, we administered the analgesics and anesthetics with equipotent doses in both groups. Due to the small sample size of our groups, the negative cardiac results are open to debate, and wider series and multi-central evaluations are necessary to confirm our findings.

In conclusion, although remifentanil infusion provides better intraoperative hemodynamic stability and postoperative weaning than fentanyl, both agents appear to have similar effects on myocardial injury during off-pump CABG bypass surgery. Therefore, either can be used during off-pump CABG surgery.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Tempe DK, Dutta D, Garg M, Minhas H, Tomar A, Virmani S. Myocardial protection with isoflurane during off-pump coronary artery bypass grafting: a randomized trial. J Cardiothorac Vasc Anesth 2011;25:59-65. doi: 10.1053/j.jvca.2010.03.002.
2. Huffmyer J, Raphael J. The current status of off-pump coronary bypass surgery. Curr Opin Anaesthesiol 2011;24:64-9. doi: 10.1097/ACO.0b013e328341ccf5.
3. Conzen PF, Fischer S, Detter C, Peter K. Sevoflurane provides greater protection of the myocardium than propofol in patients undergoing off-pump coronary artery bypass surgery. Anesthesiology 2003;99:826-33.
4. Mangano DT, Siliciano D, Hollenberg M, Leung JM, Browner WS, Goehner P, et al. Postoperative myocardial ischemia.

Therapeutic trials using intensive analgesia following surgery. The Study of Perioperative Ischemia (SPI) Research Group. Anesthesiology 1992;76:342-53.
5. Mangano DT. Perioperative cardiac morbidity. Anesthesiology 1990;72:153-84.
6. Lison S, Schill M, Conzen P. Fast-track cardiac anesthesia: efficacy and safety of remifentanil versus sufentanil. J Cardiothorac Vasc Anesth 2007;21:35-40.
7. Serfontein L. Awareness in cardiac anesthesia. Curr Opin Anaesthesiol 2010;23:103-8. doi: 10.1097/ACO.0b013e328334cb75.
8. Mekis D, Kamenik M. A randomised controlled trial comparing remifentanil and fentanyl for induction of anaesthesia in CABG surgery. Wien Klin Wochenschr 2004;116:484-8.
9. Möllhoff T, Herregods L, Moerman A, Blake D, MacAdams C, Demeyere R, et al. Comparative efficacy and safety of remifentanil and fentanyl in 'fast track' coronary artery bypass graft surgery: a randomized, double-blind study. Br J Anaesth 2001;87:718-26.
10. Guignard B, Menigaux C, Dupont X, Fletcher D, Chauvin M. The effect of remifentanil on the bispectral index change and hemodynamic responses after orotracheal intubation. Anesth Analg 2000;90:161-7.
11. Marsh DF, Hodkinson B. Remifentanil in paediatric anaesthetic practice. Anaesthesia 2009;64:301-8. doi: 10.1111/j.1365-2044.2008.05731.x.
12. Shinohara K, Aono H, Unruh GK, Kindscher JD, Goto H. Suppressive effects of remifentanil on hemodynamics in baro-denervated rabbits. Can J Anaesth 2000;47:361-6.
13. Wang J, Winship S, Russell G. Induction of anaesthesia with sevoflurane and low-dose remifentanil: asystole following laryngoscopy. Br J Anaesth 1998;81:994-5.
14. Reitan JA, Stengert KB, Wymore ML, Martucci RW. Central vagal control of fentanyl-induced bradycardia during halothane anesthesia. Anesth Analg 1978;57:31-6.
15. Tirel O, Chanavaz C, Bansard JY, Carré F, Ecoffey C, Senhadji L, Wodey E. Effect of remifentanil with and without atropine on heart rate variability and RR interval in children. Anaesthesia 2005;60:982-9.
16. Bainbridge D, Cheng DC. Minimally invasive direct coronary artery bypass and off-pump coronary artery bypass surgery: anesthetic considerations. Anesthesiol Clin 2008;26:437-52. doi: 10.1016/j.anclin.2008.03.007.
17. Kessler P, Aybek T, Neidhart G, Dogan S, Lischke V, Bremerich DH, et al. Comparison of three anesthetic techniques for off-pump coronary artery bypass grafting: general anesthesia, combined general and high thoracic epidural anesthesia, or high thoracic epidural anesthesia alone. J Cardiothorac Vasc Anesth 2005;19:32-9.
18. Bein B, Renner J, Caliebe D, Scholz J, Paris A, Fraund S, et al. Sevoflurane but not propofol preserves myocardial function during minimally invasive direct coronary artery bypass surgery. Anesth Analg 2005;100:610-6.
19. Hemmerling T, Olivier JF, Le N, Prieto I, Bracco D. Myocardial protection by isoflurane vs. sevoflurane in ultra-fast-track anaesthesia for off-pump aortocoronary bypass grafting. Eur J Anaesthesiol 2008;25:230-6.
20. Law-Koune JD, Raynaud C, Liu N, Dubois C, Romano M, Fischler M. Sevoflurane-remifentanil versus propofol-remifentanil anesthesia at a similar bispectral level for off-pump coronary artery surgery: no evidence of reduced myocardial ischemia. J Cardiothorac Vasc Anesth 2006;20:484-92.
21. Law-Koune JD, Raynaud C, Liu N, Dubois C, Romano M, Fischler M. Sevoflurane-remifentanil versus propofol-remifentanil anesthesia at a similar bispectral level for off-pump coronary artery surgery: no evidence of reduced myocardial ischemia. J Cardiothorac Vasc Anesth 2006;20:484-92.
22. Glass PSA, Johansen J. The Bispectral index monitor. Surgical Services Management 1998;4:50-2.