Original Article

Fentanyl - Based Cardiac Anesthesia Provides Higher Recovery Compared with Morphine in Elective CABG Surgery Patients

Hasan AMK[1], Ahmed Niaz[2], Ahmed S[3], Haider MZ[4], Kabir MAAM[5], Nine SMAZ[6], Khan A[7], Hasan MS[8]

[1-5]Registrar- Cardiothoracic Anaesthesia and critical care, Apollo Hospitals, Dhaka; [2]S.Consultant & Co-Ordinator- Cardiothoracic Anaesthesia and critical care, Apollo Hospitals, Dhaka; [3,4]Senior Consultant, Cardiothoracic and vascular surgery, Apollo Hospitals, Dhaka; [6]Specialist- Cardiothoracic and vascular surgery, Apollo Hospitals, Dhaka; [7]S. Medical Officer-CTVS, Apollo Hospitals, Dhaka [8]Assistant Professor, Dept. of Anaesthesia, Rangpur Medical College.

***Correspondence:** Dr. A. M. Kamrul Hasan. email: dramkamrulhasan@gmail.com*

Abstract:

***Background :** High-dose opioid anesthesia during cardiac surgery has been the mainstay of cardiac anesthesia for decades due to its ability to preserve hemodynamic stability and attenuate hormonal and metabolic response to surgical stress. The hypothesis of this study is that the use of fentanyl as part of a balanced anesthetic would lead to improved patient health status and recovery during the first 3 days after cardiac surgery with CPB compared with morphine. Quality of recovery was assessed using the QoR-40 questionnaire administered preoperatively and daily on postoperative days 1–3. Hemodynamic variables, duration of tracheal intubation, organ morbidities, intensive care unit (ICU) and hospital length of stay were evaluated.*

***Methods:** This comparative randomized double blind study was conducted in the department of cardiothoracic vascular anaesthesia and critical care of Apollo Hospitals,Dhaka on 100 patients undergoing elective CABG. Study period was (January-July), 2019. The study was approved by the institutional review board, and informed consent was obtained from all subjects. One hundred patients presenting for elective CABG surgery, between the ages of 18 and 79, were enrolled in the study. Exclusion criteria included (1) concurrent valvular surgery or the presence of valvular disease, (2) reoperative procedures, (3) unstable angina or elevated cardiac enzymes within 48 hours of surgery, (4) morphine or fentanyl allergy, (5) the need for an intra-aortic balloon pump or inotropic agents preoperatively, (6) psychiatric or central nervous system disturbances precluding completion of the QoR-40.*

***Results:** Compared with patients given morphine, those receiving fentanyl had higher global QoR-40 scores on postoperative days 1 (174.8 vs 162.5,* P *0.001), 2 (175 vs 166.1,* P *0.001), and 3 (178.1 vs 167.3,* P *0.001). Differences between the groups were observed in the QoR-40 dimensions of emotional state, physical comfort, and pain . Postoperative visual analog scale pain scores, use of pain medication in the ICU and surgical ward, and postoperative febrile reactions were reduced significantly in the fentanyl group . No differences between the groups were noted in duration of tracheal intubation,ICU and hospital length of stay, or postoperativecomplications.*

***Conclusion:** Continuous intravenous infusions of fentanyl have been used to provide intraoperative analgesia also give good-to-excellent postoperative analgesia furthermore early extubation and the quality of postoperative recovery in cardiac surgical patients can be enhanced when fentanyl is used as part of a balanced anesthetic.*

(JBSA 2020; 33(1): 28-35)

Introduction:

High-dose opioid anesthesia during cardiac surgery has been the mainstay of cardiac anesthesia for decades due to its ability to preserve hemodynamic stability and attenuate hormonal and metabolic response to surgical stress.[1]

The inclusion of an opioid as a component of a balanced anesthetic technique provides hemodynamic stability, decreases volatile anesthetic requirements,and improves postoperative analgesia.[2,3] Large morphine doses were generally abandoned after the introduction of fentanyl because its use in high doses (50–100 μg/kg) was associated with less hypotension during induction of anesthesia.

Because major complications after cardiac surgery are relatively infrequent, investigators have increasingly sought methods to improve the quality of recovery[4]. A 40-item quality of recovery score (QoR-40) has been developed and validated in patients after anesthesia and surgery.[5-7] In cardiac surgical patients, a low QoR-40 score is predictive of postoperative complications, increased hospital length of stay, and poor quality-of-life.[7] It has been noted that theQoR-40 is a suitable tool to assess the effect of clinical interventions on postoperative recovery.[6,7]We further observed that these subjects had less pain, required fewer postoperative analgesics, and exhibited a more positive mood response in the intensive care unit (ICU) compared with those receiving morphine.

The hypothesis of this study is that the use of fentanyl as part of a balanced anesthetic would lead to improved patient health status and recovery during the first 3 days after cardiac surgery with CPB compared with morphine.

Methods:

This comparative randomized double blind study was conducted in the department of cardiothoracic vascular anaesthesia and critical care of Apollo Hospitals,Dhaka on 100 patients undergoing elective CABG.Study period was (January-July),2019. The study was approved by the institutional review board, and informed consent was obtained from all subjects. One hundred patients presenting for elective CABG surgery, between the ages of 18 and 79, were enrolled in the study. Exclusion criteria included (1) concurrent valvular surgery or the presence of valvular disease, (2) reoperative procedures, (3) unstable angina or elevated cardiac enzymes within 48 hours of surgery, (4) morphine or fentanyl allergy, (5) the need for an intra-aortic balloon pump or inotropic agents preoperatively, (6) psychiatric or central nervous system disturbances precluding completion of the QoR-40.

Patients were allocated to the morphine group or the fentanyl group .

The anesthetic technique was standardized. Anti-hypertensive and anti-anginal medications were continued until the morning of surgery. Pre-anaesthesia medication consisted of oral 1 mg of clonazepam at bed time on the night prior to surgery and midazolam 7.5mg approximately 2 hours prior to anaesthesia and surgery.

After arrival to the anaesthetic room.patients were administered oxygen (O2) by nasal canula and monitoring of ECG (5 lead) with automated ST segment analysis (Marquette Solar 5000, GE Medical System, Milwaukee, USA) and pulse oximetry was initiated. A 18-G intravenous cannula was inserted in the dorsum of right hand and an 20-G; 45 mm intra-arterial cannula was introduced into the right radial artery for monitoring of the arterial pressure and obtaining arterial blood for analysis.A trichannel 7fr central venous catheter was introduced into right internal jugular vein for measurement of central venous pressure and drug infusion. General anaesthesia was induced, while patients breathed 100% O2 by facemask, using a combination of fentanyl (4-5) μg/kg, midazolam 100 μg/kg . Endotracheal intubation was performed after administration of pancuronium bromide 0.15 mg/ kg and mechanical ventilation was initiated. Low-flow technique (fresh gas flow of 3 L/min) using anaesthesia machine (Aestiva/5,7900 Datex Ohmeda, Madison, MI, USA) to achieve end-tidal carbon-dioxide tensions of 32 ± 3 mm Hg was used. Haemodynamic parameters were maintained within 20% of the basal values with adrenaline,dopamine, phenylephrine, and glyceryltrinitrate, as required. Intraoperative hypothermia was prevented by the use of warm airflow at 400 (Bair Hugger warming unit, model

505, Augustine Medical Inc, Eden Prairie, MN, USA), warming blanket (Hemotherm, Cincinnati Sub Zero, Cincinnato, Ohio, USA), warm intravenous fluids. Filling pressures and fluid balance was maintained using normal saline 0.9% . Total amount of midazolam administered during entire procedure was restricted to 10mg . Inhalational anesthetic isoflurane given as required.

Patients were preoperatively randomized into 2 groups consisting of 50 patients in each group. Perioperative analgesia was supplemented with the use of fentanyl or morphine infusion after anaesthetic induction in the operating room. Patients in morphine group (1 mg/mL) with an infusion rate of 0.05 mg/kg/h .Another group patients were given fentanyl (10 µg/mL) with an infusion rate of 1 µg/kg/h .

Hemodynamic data were recorded immediately before and after induction of anesthesia, during internal mammary artery dissection, 15 minutes after separation from CPB, at chest closure, on arrival to the ICU, and 12 and 24 hours after baseline measurements (post-induction). Hemodynamic data included heart rate, mean arterial pressure, central venous pressure.

Result:

Table I. *Patient characteristics of the study patients*

	Fentanyl (n=50)	Morphine (n=50)	P value
Male	40 (80%)	42 (84%)	[a]0.603[ns]
Age (years)	64.9±9.9	61.1±10.1	[b]0.060[ns]
Weight (kg)	76.3±11.6	79.1±15.4	[b]0.307[ns]
Height (cm)	172.0±10.3	171.9±9.8	[b]0.960[ns]
Ejection fraction	0.51±0.11	0.53±0.12	[b]0.387[ns]
ASA physical status	2.8±0.6	2.9±0.5	[b]0.368[ns]
Smoker	5 (10%)	7 (14%)	[a]0.538[ns]
Myocardial infarction	10 (20%)	12 (24%)	[a]0.629[ns]
Congestive heart failure	4 (8%)	2 (4%)	[a]0.400[ns]
Atrial fibrillation	5 (10%)	3 (6%)	[a]0.461[ns]
Hypertension	40 (80%)	31 (62%)	[a]0.047[s]
COPD/emphysema/asthma	9 (18%)	10 (20%)	[a]0.799[ns]
Sleep apnea	3 (6%)	12 (24%)	[a]0.011[s]
Liver disease	1 (2%)	0 (0%)	[a]0.315[ns]
Renal insufficiency	1 (2%)	4 (8%)	[a]0.169[ns]
Thyroid disease	2 (4%)	3 (6%)	[a]0.646[ns]
Diabetes	30 (60%)	28 (56%)	[a]0.823[ns]
Cerebrovascular accident	0 (0%)	2 (4%)	[a]0.153[ns]
Transient ischemic attack	4 (8%)	3 (6%)	[a]0.695[ns]
Peripheral vascular disease	1 (2%)	2 (4%)	[a]0.558[ns]
Medications			
â-blockers	40 (80%)	38 (76%)	[a]0.629[ns]
ACE inhibitors	19 (38%)	23 (46%)	[a]0.418[ns]
Insulin	5 (10%)	12 (24%)	[a]0.062[ns]
Statins	35 (70%)	42 (84%)	[a]0.096[ns]

s= significant, ns= not significant

[a]P value reached from chi square test

[b]P value reached from unpaired t-test

Forty (80%) patients were hypertension in Fentanyl group and 31(62%) in Morphine group. Three (6%) patients were sleep apnea in Fentanyl group and 12(24%) in Morphine group. The difference were statistically significant ($p<0.05$) but other patient characteristics were not statistically significant ($p>0.05$) between two groups.

Table II *Hemodynamic data of the study patients*

	Fentanyl (n=50)	Morphine (n=50)	P value
Heart rate (bpm)			
Preinduction	70.4±11.2	73.8±14.3	0.189^{ns}
30-min postinduction	64.8±10.9	62.0±12.1	0.227^{ns}
15-min post-CPB	81.8±11.0	80.9±10.6	0.678^{ns}
30-min post-CPB	82.0±11.8	82.4±10.5	0.858^{ns}
ICU admission	83.2±13.9	83.0±10.2	0.935^{ns}
ICU 4 h	82.7±11.1	81.8±11.4	0.690^{ns}
ICU 8 h	81.2±11.3	83.0±12.2	0.446^{ns}
Mean arterial pressure (mmHg)			
Preinduction	91.2±12.1	93.7±12.8	0.318^{ns}
30-min postinduction	75.1±13.0	73.2±9.9	0.413^{ns}
15-min post-CPB	70.1±8.6	70.4±9.2	0.867^{ns}
30-min post-CPB	72.0±8.8	74.3±10.3	0.233^{ns}
ICU admission	71.2±10.9	74.0±11.1	0.206^{ns}
ICU 4 h	72.8±9.8	73.4±10.9	0.773^{ns}
ICU 8 h	74.1±9.9	75.5±9.7	0.477^{ns}
Central venous pressure (mmHg)			
30-min postinduction	11.4±4.3	11.5±4.1	0.906^{ns}
15-min post-CPB	11.7±5.0	11.9±4.4	0.832^{ns}
30-min post-CPB	10.6±4.2	12.6±4.6	0.025^{s}
ICU admission	9.3±4.1	9.8±4.4	0.558^{ns}
ICU 4 h	8.9±3.9	9.0±4.0	0.899^{ns}
ICU 8 h	8.4±4.1	8.6±3.9	0.803^{ns}

s= significant, ns= not significant

P value reached from unpaired t-test

At 30-min post-CPB, mean central venous pressure was found 10.6±4.2 mmHg in Fentanyl group and 12.6±4.6 mmHg in Morphine group which was statistically significant ($p<0.05$) but other hemodynamic data were not statistically significant ($p>0.05$) between two groups.

Table III. Pain, sedation, and postoperative opioid consumption of the study patients

		Fentanyl (n=50)	Morphine (n=50)	P value
VAS score	Preoperative	0.0±0.0	0.0±0.0	-
	Postoperative Day 1	1.9±0.6	3.2±1.1	0.001[s]
	Postoperative Day 2	2.0±0.5	3.8±0.9	0.001[s]
	Postoperative Day 3	2.2±0.8	3.5±0.8	0.001[s]
Sedation score	Preoperative	0.5±0.1	0.5±0.1	1.00[ns]
	Postoperative Day 1	0.6±0.2	0.6±0.1	1.00[ns]
	Postoperative Day 2	0.8±0.4	0.7±0.2	0.117[ns]
	Postoperative Day 3	0.9±0.3	0.8±0.2	0.053[ns]
Inj.Tramadolhydrochloride	Postoperative Day 1	144.1±27.3	157.0±37.1	0.051[ns]
(mg/24 hours)	Postoperative Day 2	154.6±28.3	207.9±30.4	0.001[s]
	Postoperative Day 3	172.4±22.6	238.1±39.0	0.001[s]
Inj. Paracetamol	Postoperative Day 1	1.7±0.5	1.9±0.6	0.073[ns]
(gm/24 hours)	Postoperative Day 2	2.0±0.6	2.8±0.8	0.001[s]
	Postoperative Day 3	2.9±1.0	3.6±1.1	0.001[s]

s= significant, ns= not significant. P value reached from unpaired t-test

VAS score on postoperative Days 1 (1.9 vs 3.2, *P*= 0.001), Day 2 (2.0 vs 3.8, *P* = 0.001) and Day 3 (2.2 vs 3.5, *P*= 0.001) were higher in morphine than fentanyl group. Tramadol hydrochloride on postoperative Day 2 (154.6 vs 207.9, *P*= 0.001) and postoperative Day 3 (172.4 vs 238.1, *P*= 0.001) were higher in morphine than fentanyl group. Paracetamol dose on postoperative Day 2 (2.0 vs 2.8, *P* = 0.001) and Day 3 (2.9 vs 3.6, *P*= 0.001) were higher in morphine than fentanyl group.

Table IV. *Quality of Recovery (QoR)-40 Dimensions and Global Score*

		Fentanyl (n=50)	Morphine (n=50)	P value
Emotional state	Preoperative	40.9±8.6	38.2±12.4	0.209[ns]
	Postoperative Day 1	42.2±10.9	35.9±13.1	0.010[s]
	Postoperative Day 2	40.8±9.2	36.6±12.6	0.059[ns]
	Postoperative Day 3	40.1±10.6	38.2±12.9	0.243[ns]
Physical comfort	Preoperative	58.6±8.7	55.2±9.3	0.062[ns]
	Postoperative Day 1	52.0±11.0	46.3±10.9	0.011[s]
	Postoperative Day 2	51.4±11.2	46.0±11.1	0.017[s]
	Postoperative Day 3	51.6±11.1	47.0±12.0	0.049[s]
Psychological support	Preoperative	35.2±5.1	34.9±5.4	0.776[ns]
	Postoperative Day 1	34.8±5.8	34.3±6.2	0.678[ns]
	Postoperative Day 2	35.3±5.0	32.4±7.0	0.019[s]
	Postoperative Day 3	35.2±5.3	32.5±6.8	0.029[s]
Physical independence	Preoperative	25.6±10.3	25.0±9.7	0.764[ns]
	Postoperative Day 1	18.4±11.0	14.7±10.1	0.082[ns]
	Postoperative Day 2	19.8±10.8	18.6±10.5	0.574[ns]
	Postoperative Day 3	20.7±11.1	19.0±10.8	0.440[ns]
Pain	Preoperative	28.7±3.1	28.9±2.4	0.369[ns]
	Postoperative Day 1	29.4±2.8	28.6±2.7	0.149[ns]
	Postoperative Day 2	29.6±2.5	27.5±3.0	0.001[s]
	Postoperative Day 3	29.7±2.2	27.3±2.9	0.001[s]
Global QoR-40	Preoperative	188.3±11.2	184.2±11.0	0.067[ns]
	Postoperative Day 1	174.8±11.9	162.5±11.2	0.001[s]
	Postoperative Day 2	175.0±11.3	166.1±12.5	0.001[s]
	Postoperative Day 3	178.1±11.1	167.3±12.3	0.001[s]

s= significant, ns= not significant. P value reached from unpaired t-test

Table V. *Intensive Care Unit and Final Recovery Variables*

	Fentanyl (n=50)	Morphine (n=50)	P value
Temperature >38°C	5 (10%)	14 (28.0%)	[a]0.022[s]
Duration of tracheal intubation (h)	9.8±3.3	10.6±3.2	[b]0.221[ns]
Tracheal intubation (>12 h)	10 (20.0%)	11 (22.0%)	[a]0.806[ns]
ICU length of stay (h)	46.7±6.4	50.8±7.1	[b]0.124[ns]
ICU length of stay (>72 h)	4 (8.0%)	5 (10.0%)	[a]0.727[ns]

s= significant, ns= not significant
[a]P value reached from chi square test
[b]P value reached from unpaired t-test

Temperature >38°C was found (10.0% vs 28.0%, *P*= 0.022) was higher in morphine than fentanyl group.

Emotional state on postoperative Days 1 (42.2 vs 35.9, *P*= 0.010) was higher in fentanyl than morphine. Physical comfort on postoperative Days 1 (52.0 vs 46.3, *P*= 0.011), Day 2 (51.4 vs 46.0, *P* = 0.017) and Day 3 (51.6 vs 47.0, *P*= 0.049) were higher in fentanyl than morphine. Psychological support on postoperative Day 2 (35.3 vs 32.4, *P* = 0.019) and Day 3 (35.2 vs 32.5, *P*= 0.029) were higher in fentanyl than morphine. Pain on postoperative Day 2 (29.6 vs 27.5, *P* = 0.001) and Day 3 (29.7 vs 27.3, *P*= 0.001) were higher in fentanyl than morphine. Global QoR-40 scores on postoperative Days 1 (174.8 vs 162.5, *P*= 0.001), Day 2 (175.0 vs 166.1 *P* = 0.001) and Day 3 (178.1 vs 167.3, *P*= 0.001) were higher in the subjects receiving fentanyl compared with patients given morphine.

Discussion:

Pain relief is an important priority for anaesthesiologist, particularly in post operative patients suffering from severe pain. Using analgesics such as narcotics is a routine measure to alleviate pain of such patients. In cardiac surgical patients, routine and standard administration of morphine may not lead to significant pain relief. Yet, higher doses may lead to adverse events. Therefore, it seems a good idea to consider other analgesics like fentanyl in such patients.

In this study observed that forty (80%) patients were hypertension in Fentanyl group and 31(62%) in Morphine group. Three (6%) patients were sleep apnea in Fentanyl group and 12(24%) in Morphine group. The difference were statistically significant (p<0.05) but other patient characteristics were not statistically significant (p>0.05) between two groups. Murphy et al.[8] study reported patient characteristics were similar between the groups, except for a higher incidence of sleep apnea in the fentanyl group.

In this study showed at 30-min post-CPB, mean central venous pressure was found 10.6±4.2 mmHg in Fentanyl group and 12.6±4.6 mmHg in Morphine group. Which was statistically significant (p<0.05) but other hemodynamic data were not statistically significant (p>0.05) between two groups.

In this study observed VAS score on postoperative Days 1 (1.9 vs 3.2, *P*= 0.001), Day 2 (2.0 vs 3.8, *P* = 0.001) and Day 3 (2.2 vs 3.5, *P*= 0.001) were higher in morphine than fentanyl group. Tramadol hydrochloride on postoperative Day 2 (154.6 vs 207.9, *P*= 0.001) and postoperative Day 3 (172.4 vs 238.1, *P*= 0.001) were higher in morphine than fentanyl group. Paracetamol injectable dose on postoperative Day 2 (2.0 vs 2.8, *P* = 0.001) and Day 3 (2.9 vs 3.6, *P*= 0.001) were higher in morphine than fentanyl group. Furyk et al.[9] compared inhalational fentanyl versus IV morphine in pediatric patients suspected of having broken limbs in emergency department in Australia. They revealed that there were no significant differences between the two groups regarding decrease in pain scores, vital signs or side effects. Galinski et al. [10] compared the analgesic effectiveness of fentanyl versus morphine, In their study about 62% patients in

the morphine group and 76% in the fentanyl group reported satisfactory pain management. Side effects showed no significant difference between the two groups. The authors concluded that fentanyl had comparable effects to morphine and they suggested to use fentanyl in acute severe pain in pre-hospital setting.

In this study observed emotional state on postoperative Days 1 (42.2 vs 35.9, *P*= 0.010) was higher in fentanyl than morphine. Physical comfort on postoperative Days 1 (52.0 vs 46.3, *P*= 0.011), Day 2 (51.4 vs 46.0, *P* = 0.017) and Day 3 (51.6 vs 47.0, *P*= 0.049) were higher in fentanyl than morphine. Psychological support on postoperative Day 2 (35.3 vs 32.4, *P* = 0.019) and Day 3 (35.2 vs 32.5, *P*= 0.029) were higher in fentanyl than morphine. Pain on postoperative Day 2 (29.6 vs 27.5, *P* = 0.001) and Day 3 (29.7 vs 27.3, *P*= 0.001) were higher in fentanyl than morphine. Global QoR-40 scores on postoperative Days 1 (174.8 vs 162.5, *P*= 0.001), Day 2 (175.0 vs 166.1 *P* = 0.001) and Day 3 (178.1 vs 167.3, *P*= 0.001) were higher in the subjects receiving fentanyl compared with patients given morphine. Murphy et al.[8] reported QoR-40 scores in both groups decreased maximally on Day 1 and improved gradually during postoperative days 2 and 3. However, global QoR-40 scores on postoperative days 1 (173 vs 160, *P*= 0.0001), 2 (174 vs 164, *P*= 0.0001), and 3 (177 vs 167, *P* = 0.001) were higher in the subjects receiving morphine compared with patients given fentanyl. QoR-40 scores in the dimensions of emotional state (*P* = 0.01– 0.0001), physical comfort (*P* < 0.001-0.0001), and pain (*P* < 0.001– 0.0001) were higher in the morphine group on postoperative days 1 through 3. No differences between the groups were noted in the dimensions of psychological support and physical independence.

In this study observed that temperature >38°C was found (10.0% vs 28.0%, *P*= 0.022) was higher in morphine than fentanyl group.

Kanowitz et al.[11] performed a retrospective analysis of over 2,000 patients who had been given fentanyl for analgesia by out-of-hospital personnel.16 They reported a rate of post-fentanyl vital sign abnormalities of only 0.6%, with no deaths or hospitalizations. While this study lacked a control group, it did show a statistically significant reduction in pain score after fentanyl administration, reducing the reported pain level from severe to mild. A study by Nielsen et al[12]. of fentanyl administered by Danish advanced emergency medical technicians showed an overall adverse event rate of 5%, of which only two cases (0.4%) were serious and only one required naloxone.

Conclusion:

Continuous intravenous infusions of fentanyl have been used to provide intraoperative analgesia also give good-to-excellent postoperative analgesia, neutralizes the effects of ambulation or coughing on the quality of analgesia in patients after sternotomy, and improves postoperative pulmonary function compared with morphine. Early extubation and the quality of postoperative recovery in cardiac surgical patients can be enhanced when fentanyl is used as part of a balanced anesthetic.

References:

1. Ronga LQ, Kamelb MK, Rahoumab M, Naikb A, Mehtab K and Abouarabb AA et al. High-dose versus low-dose opioid anesthesia in adult cardiac surgery: A meta-analysis, Journal of Clinical Anesthesia, 2019; 57 : 57–62.
2. Bovill JG, Sebel PS, Stanley TH. Opioid analgesics in anesthesia: with special reference to their use in cardiovascular anesthesia.Anesthesiology 1984;61:731–55.
3. Bennett GM, Stanley TH. Cardiovascular effects of fentanyl during enflurane anesthesia in man. Anesth Analg 1979;58: 179–82.
4. Herrera FJ, Wong J, Chung F. A systematic review of postoperative recovery outcomes measurements after ambulatory surgery. Anesth Analg 2007;105:63–9
5. Myles PS, Weitkamp B, Jones K, Melick J, Hensen S. Validity and reliability of postoperative quality of recovery score: the QoR-40. Br J Anaesth 2000;84:11–5.
6. Myles PS, Hunt JO, Fletcher H, Solly R, Woodward D, Kelly S. Relation between quality of recovery in hospital and quality of life at 3 months after cardiac surgery. Anesthesiology 2001;95:862–7.

7. Leslie K, Troedel S, Irwin K, Pearce F, Ugoni A, Gillies R, Pemberton E, Dharmage S.Quality of recovery from anesthesia in neurosurgical patients. Anesthesiology 2003;99:1158 – 65.

8. Murphy GS, Szokol JW, Marymont JH, Gerrnberg SB, Avram MJ, Vender JS, et al. Morphine-Based Cardiac Anesthesia Provides Superior Early Recovery Compared with Fentanyl in Elective Cardiac Surgery Patients. Anesth Analg 2009; 109: 311–319.

9. Furyk JS, Grabowski WJ, Black LH. Nebulized fentanyl versus intravenous morphine in children with suspected limb fractures in the emergency department: a randomized controlled trial. Emerg Med Australas, 2009;21(3):203-9.

10. Galinski M, Dolveck F, Borron SW, Tual L, Van Laer V, Lardeur JY, et al. A randomized, double-blind study comparing morphine with fentanyl in prehospital analgesia. Am J Emerg Med. 2005;23(2):114-9.

11. Kanowitz A, Dunn TM, Kanowitz EM, Dunn WW, Vanbuskirk K. Safety and effectiveness of fentanyl administration for prehospital pain management. Prehosp Emerg Care. 2006; 10:1–7.

12. Nielsen ND, Dahl MK, Hansen PA, Brogaard K. Safety and efficiency of prehospital pain management with fentanyl administration by emergency medical technicians. J Emerg Med. 2007; 33(3):335.