# Hemodynamic, Hepatorenal, and Postoperative Effects of Desflurane-Fentanyl and Midazolam-Fentanyl Anesthesia in Coronary Artery Bypass Surgery

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**Objective:** The purpose of this study was to compare the hemodynamic, hepatorenal, and postoperative effects of desflurane-fentanyl and midazolam-fentanyl anesthesia during coronary artery bypass surgery.

**Design:** Prospective study.

**Setting:** University hospital.

**Participants:** Sixty patients undergoing elective coronary artery bypass grafting surgery with ejection fraction more than 45%.

**Interventions:** Anesthesia was induced with etomidate, 0.2 mg/kg, and fentanyl, 5 μg/kg, in group D (n = 30) and with midazolam, 0.1 to 0.3 mg/kg, and fentanyl, 5 μg/kg, in group M (n = 30). Anesthesia was maintained with desflurane, 2% to 6%, and fentanyl, 15 to 25 μg/kg, in group D and midazolam infusion, 0.1 to 0.5 mg/kg/h, and fentanyl, 15 to 25 μg/kg, in group M.

**Measurements and Main Results:** Hemodynamic monitoring included a 5-lead electrocardiogram, a radial artery catheter, and a pulmonary artery catheter. Data were obtained before induction of anesthesia ($t_0$), after induction of anesthesia ($t_1$), after intubation ($t_2$), after surgical incision ($t_3$), after sternotomy ($t_4$), before cardiopulmonary bypass ($t_5$), after protamine infusion ($t_6$), and at the end of the surgery ($t_7$). Blood samples were obtained to measure total bilirubin, aspartate aminotransferase, gamma glutamyl transferase, lactate dehydrogenase, alkaline phosphatase, creatinine, and blood urea nitrogen just before induction of anesthesia and at the first, fourth, and 14th days postoperatively.

**Conclusions:** Intraoperative hemodynamic responses were similar in both groups, and transient hepatic and renal dysfunctions were observed in the postoperative period in both groups. The extubation and intensive care unit discharge times were found to be shorter in the desflurane-fentanyl group.


***KEY WORDS: coronary artery bypass grafting, desflurane, midazolam, kidney, liver, postoperative effects***

IT HAS BEEN SUGGESTED that the temporary and mild-to-moderate disruption in hepatic and renal functions after cardiac surgery is more frequent than expected and has a direct influence on morbidity.[1] Factors thought to be responsible are the preoperative cardiac state, presence of an accompanying systemic illness, perioperative hemodynamic state, surgical procedure, hypothermia, and cardiopulmonary bypass (CPB).[2] In addition, influences of the anesthetic technique on hepatic and renal functions are debated.

Desflurane and midazolam are frequently used anesthetic agents during cardiac surgery. Their pharmacokinetic and pharmacodynamic properties allow earlier tracheal extubation without compromising intraoperative hemodynamic stability.[3,4] Although several hemodynamic studies including comparison of different anesthetic agents exist in the literature, the studies regarding the effects of desflurane and midazolam on cardiac and hepatorenal functions after cardiac surgery are not adequate. In this study, the authors aimed to compare the hemodynamic, hepatorenal, and postoperative effects of desflurane-fentanyl and midazolam-fentanyl anesthesia during cardiac surgery.

## METHODS

After obtaining informed consent from the patients and approval from the ethics committee, 60 patients undergoing elective coronary artery bypass grafting (CABG) surgery were included in the study. Patients with diabetes mellitus, bleeding disorders, ejection fractions <45%, and renal or hepatic failure were excluded. Patients were classified into desflurane (group D, n = 30) and midazolam (group M, n = 30) groups. The patients continued their medications including the morning of surgery. All patients were premedicated orally with 5 mg of diazepam 2 hours before the induction of anesthesia. In the operating room, veins on both arms were cannulated with 16-G catheters after a 5-lead electrocardiogram and $SpO_2$ monitoring (Dräger PM 8040-Cato, Lübeck, Germany). All patients were given 8 mL/kg of normal saline for prehydration. Radial artery cannulation (20-G catheter) and pulmonary artery cannulation (4-lumen thermodilution catheter, 7.5F, 110 cm, Abbott Labs, Zwolle, the Netherlands) were placed by way of the left radial artery and right internal jugular vein, respectively, under local anesthesia. The saline infusion rate was standardized for every patient as 5 mL/kg during the operation. Anesthesia was induced with 2% lidocaine, 1 mg/kg, etomidate, 0.2 mg/kg, and fentanyl, 5 μg/kg, in group D and 2% lidocaine, 1 mg/kg, midazolam, 0.1 to 0.3 mg/kg, and fentanyl, 5 μg/kg, in group M. Tracheal intubation was facilitated with vecuronium, 0.1 mg/kg, in both groups. The patients were ventilated manually with 100% $O_2$ until intubation and mechanically thereafter with Dräger, Cato (Lübeck, Germany) edition, (end-tidal $CO_2$ partial pressure 35-40 mmHg). $N_2O$ was not administered in either group, and anesthesia was maintained with desflurane, 2% to 6%, and fentanyl, 15 to 25 μg/kg, in group D and midazolam, 0.1 to 0.5 mg/kg/h, and fentanyl, 15 to 25 μg/kg, in group M. In both groups, doses of the anesthetics used were adapted to maintain optimal anesthetic and surgical conditions, while maintaining hemodynamic stability. The total fentanyl dose administered was recorded, and the administration times of fentanyl were standardized as during induction, before incision, before sternotomy, and before and during CPB in either group.

A roller pump (Cobe Cardiovascular Inc, Arvada, CO), a hollow-fiber membrane oxygenator (Dideco D 708 Simplex, Mirandola, Italy), a polyvinylchloride tubing set, a 2-stage venous cannula, a venous reservoir (Dideco D 740, Simplex), and an arterial filter (Dideco D 734 Micro 40, Simplex) were used for CPB. The circuit was primed with 1,600 mL of Ringer's lactate, 150 mL of mannitol, 1 g of ceftizoxime, and 2,500 IU of heparin. Mild systemic hypothermia (33°C) was achieved using the nonpulsatile pump flow of 2.0 to 2.4 L/min/m$^2$. During CPB, hematocrit was maintained between 20% to 25%, and the mean arterial pressure was maintained between 50 to 70 mmHg (with sodium nitroprusside or phenylephrine hydrochloride administration as required). Anticoagulation was obtained by the administration of bo-

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**Table 1. Demographic Data and Surgical Characteristics**

| | Desflurane (n = 30) | Midazolam (n = 30) |
|---|---|---|
| Age (y) | 54.3 ± 10.2 | 55.0 ± 8.2 |
| BSA ($m^2$) | 1.82 ± 0.20 | 1.83 ± 0.16 |
| Sex (M/F) | 24/6 | 25/5 |
| Smoker (Y/N) | 7/23 | 10/20 |
| Ejection fraction (%) | 49.6 ± 6.8 | 50.2 ± 5.1 |
| Number of grafts (n) | 2.8 ± 1.0 | 2.9 ± 1.0 |
| Medical history | | |
| Previous MI (n, %) | 10 (%33) | 9 (%30) |
| Hypertension (n, %) | 9 (%30) | 8 (%27) |
| Beta-blockers (n, %) | 15 (%50) | 12 (%40) |
| Calcium antagonists (n, %) | 11 (%37) | 13 (%43) |
| Nitrates (n, %) | 23 (%76) | 25 (%83) |
| Duration of surgery (min) | 237.8 ± 21.7 | 240.2 ± 22.3 |
| Duration of CPB (min) | 95.7 ± 28.0 | 97.6 ± 24.5 |
| Aorta cross-clamp (min) | 63.3 ± 20.3 | 65.7 ± 19.8 |
| Total amount of cardioplegia (mL) | | |
| Anterograde | 613 ± 101 | 616 ± 126 |
| Retrograde | 1498 ± 545 | 1,503 ± 468 |
| Fentanyl induction (μg) | 389.1 ± 101.8 | 407.6 ± 107.8 |
| Fentanyl maintenance (μg) | 1408.3 ± 307.6 | 1,340.8 ± 317.4 |
| Midazolam induction (mg) | — | 15.73 ± 3.18 |
| Midazolam maintenance (mg) | — | 33.06 ± 13.46 |

NOTE. Values are mean ± SD or absolute number.

Abbreviations: BSA, body surface area; CPB, cardiopulmonary bypass.

vine lung heparin (300 IU/kg) just before the institution of CPB and supplemented as required to maintain an activated coagulation time >480 seconds.

The myocardium was protected via combined anterograde and retrograde cold blood cardioplegia with a blood-crystalloid ratio of 4:1 after aortic cross-clamping. Warm blood cardioplegia was given a few minutes before the aortic clamp was removed. All distal anastomoses were performed during cross-clamping, and all proximal anastomoses were performed after the removal of cross-clamps in the warming period. When the rectal temperature reached 36°C, the CPB was terminated. At the termination of CPB, 1.3 mg of protamine for every 100 U of total heparin dose was administered and confirmed by the return of activated coagulation time to baseline values. Shed mediastinal blood was not reinfused in any patient. The indication for transfusion was defined as a hematocrit level less than 20% during CPB and less than 25% in the postoperative period. The same surgical team performed all operations with the standard surgery and perfusion techniques. For anesthetic requirements during CPB, 0.1 mg/kg of midazolam + 200 μg of fentanyl (100 μg at the beginning of the CPB and 100 μg during the heating period) + 6 mg of vecuronium were administered. Complications during the study such as tachycardia (heart rate >100 beats/min), bradycardia (HR <50 beats/min), hypertension (systolic arterial pressure >160 mmHg) and hypotension (mean arterial pressure [MAP] <60 mmHg), and the inotropic and vasodilator agents used were recorded.

The HR, MAP, central venous pressure, mean pulmonary arterial pressure, and pulmonary capillary wedge pressure values before induction ($t_0$), after induction ($t_1$), after intubation ($t_2$), after incision ($t_3$), after sternotomy ($t_4$), before cardiopulmonary bypass ($t_5$), after protamine administration ($t_6$), and at the end of surgery ($t_7$) were recorded. At the same time, the cardiac index, systemic vascular resistance index, pulmonary vascular resistance index, left ventricular stroke work index, and the right ventricle stroke work index values were recorded, which are the mean of 3 measurements using the thermodilution method (Marquette Solar 8000, D6015TM, Beaverton, OR).

Blood samples were taken just before the induction of anesthesia (preoperative) and on the first, fourth, and 14th postoperative days for total bilirubin, aspartate aminotransferase, alanine aminotransferase, γ-glutamyl transpeptidase, lactate dehydrogenase (LDH), alkaline phosphatase, creatinine (Crt), and blood urea nitrogen levels. At the same times, the creatinine clearance (CClr) was calculated using the Cockcroft-Gault formula (CClr = [140 − age] × body weight/serum creatinine × 72). The calculated CClr value was multiplied with 0.85 for women.[5] Also, qualitative protein and glucose were analyzed in the urine samples at the same times. The results were evaluated as positive or negative and recorded accordingly. Although abnormal values in the hepatic function tests were defined as values exceeding the higher limits of normal, abnormal values of the CClr were defined and expressed as values below the lower limit of normal.

After the operation, all patients were given morphine, 2 to 3 mg, intravenously in the intensive care unit (ICU). This dose was repeated soon after extubation. Tracheal extubation was performed when the patient met the following criteria: patient awake, oriented, and cooperative; chest tube output <100 mL/h; no arrhythmias; urine output >0.5 mL/kg/h; absence of residual muscle paralysis; and adequate ventilatory parameters (vital capacity >12 mL/kg, respiratory rate <25 breaths/min, minute ventilation >90 mL/kg/min, $F_IO_2$ <0.6, positive end-expiratory pressure <7.5 $cmH_2O$, $PO_2$ >90 mmHg). The ICU discharge criteria required that the patient be oriented with minimal sedation, hemodynamically stable without the use of intravenous inotropes, oxygen saturation >90% on an $F_IO_2$ of <0.6, absent carbon dioxide retention, urine output >0.5 mL/kg/h, and a chest tube output <50 mL/h.[6] In the postoperative period, time to extubation, duration of the ICU stay, and requirement of inotropic agents and the number of patients with arrhythmias and myocardial ischemia were evaluated and recorded.

Statistical analyses were performed with software package SPSS V 11.0 (SPSS Inc, Chicago, IL). Because all measurements and calculated data were distributed abnormally (tested by the Kolmogorov-Smirnov test), the Wilcoxon signed-rank sum test was used for intragroup comparisons, whereas the Mann-Whitney *U* test was used for the comparisons between the 2 groups. The nonparametric data were evaluated with the chi-square test or Fisher exact test, when appropriate. The results were expressed as mean ± standard deviation, and in every evaluation, $p < 0.05$ was taken to indicate statistical significance.

## RESULTS

The patients' demographic characteristics, the fentanyl doses used during the operations, and the anesthetic and surgical data were similar in the 2 groups (Table 1). The intraoperative hemodynamic data of both groups are presented in Table 2. Evaluation between the 2 groups revealed that the mean pulmonary arterial pressure at $t_4$, $t_5$ and $t_6$; pulmonary capillary wedge pressure at $t_4$ and $t_l$ and the right ventricle stroke work index at $t_5$ and $t_6$ were lower in group M than in group D and the LVSWI was lower at $t_4$ in group D than in group M.

Intraoperative complications and inotropic agents used are shown in Table 3. There was no statistically significant difference between the 2 groups. The preoperative and postoperative serum level of liver enzymes and renal function tests of both groups are shown in Table 4. There were no significant differences between the 2 groups compared with the number of