# Comparison of the myocardial protective effect of sevoflurane and isoflurane in high-risk cardiac patients undergoing coronary artery bypass grafting surgery: a randomized study

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**Objective**
The aim of this study was to assess the effect of sevoflurane and isoflurane in high-risk cardiac patients undergoing coronary artery bypass grafting surgery.
**Patients and methods**
This study included 228 patients undergoing coronary artery bypass grafting surgery. This was a randomized study. This study was carried out at cardiac centers. The patients in this study were divided into two groups. In the sevoflurane group, the patients received sevoflurane (end-tidal concentration of 1–4%) as an inhalational agent during the entire procedure (before, during, and after cardiopulmonary bypass). In the isoflurane group, the patients received isoflurane (end-tidal concentration of 0.5–2%) as an inhalational agent during the entire procedure (before, during, and after cardiopulmonary bypass). The monitors measured the heart rate, mean arterial blood pressure, a continuous ECG with an automatic ST-segment analysis (leads II and V), central venous pressure, mean arterial pulmonary pressure, pulmonary capillary wedge pressure, pulmonary and systemic vascular resistances, cardiac index, urine output, troponin I level, creatine kinase-MB level, required pharmacological, and mechanical support.
**Results**
The administration of sevoflurane decreased the heart rate, mean arterial blood pressure, cardiac index, mean arterial pulmonary pressure, and pulmonary and systemic vascular resistances compared with the administration of isoflurane ($P<0.05$). Also, it decreased the incidence of myocardial infarction, reflected in the troponin I level, creatine kinase-MB, ECG changes, and the development of new regional wall motion abnormalities ($P<0.05$). Sevoflurane decreased the requirement for pharmacological and mechanical support compared with isoflurane ($P<0.05$).
**Conclusion**
Sevoflurane is more cardioprotective than isoflurane. It decreases the incidence of myocardial infarction and the requirement for pharmacological and mechanical support, and duration of stay in the ICU and hospital.

**Keywords:**
coronary artery bypass grafting surgery, creatine kinase-MB isoenzyme, isoflurane, myocardial protection, sevoflurane, troponin I

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## Introduction

Volatile anesthetics improve protection, postischemic recovery, cardiac function, and reduce arrhythmias on reperfusion against myocardial ischemia by pharmacological preconditioning [1–6].

All volatile anesthetics induce a dose-dependent decrease in myocardial contractility, mediate the formation of nitric oxide, maintain the intracellular and/or mitochondrial calcium homeostasis, and moderate the opening of ATP-sensitive potassium channels [7,8]. These effects decrease the myocardial oxygen demand; therefore, they play a beneficial role in the myocardial oxygen balance during myocardial ischemia [7].

In humans, administration of volatile anesthetics at doses of 0.5–2.0 minimum alveolar concentration throughout cardiac surgery results in less myocardial injury, less inotropic support, and reduced mortality [3,9–13].

Sevoflurane and isoflurane are the most common volatile anesthetics used during cardiac surgery and we hypothesized that sevoflurane and isoflurane provide equal myocardial protection in patients undergoing coronary artery surgery.

The aim of the present study was to evaluate the perioperative myocardial protective effects of sevoflurane and isoflurane in high-risk cardiac patients undergoing coronary artery bypass grafting (CABG).

## Outcomes

The primary outcome was the myocardial protective effect assessed by the stability of the hemodynamic status of the patients and the postoperative cardiac markers [troponin I and creatine kinase-MB (CK-MB)]. The secondary outcomes were the requirement for pharmacological and mechanical support in addition to the safety of the study medications, which was assessed by the occurrence of any adverse events.

## Sample size calculation

Power analysis was carried out using the $\chi^2$-test for independent samples on the number of patients with elevated postoperative troponin I levels because this was the main outcome variable in the present study. A pilot study was carried out before starting this study because there are no available data in the literature for the comparison of the myocardial protective effect in high-risk cardiac patients undergoing coronary artery surgery. The results of the pilot study showed that the postoperative troponin I level increased in 30% of the patients in the sevoflurane group and 60% of patients in the isoflurane group. On the basis of a power of 0.8, $\alpha$ error of 0.05, and $\beta$ error of 0.2, a minimum sample size of 114 patients was calculated for each group.

## Patients and methods

After obtaining informed consent and approval from the local ethics and research committee in two cardiac centers, a prospective randomized study of 228 high-risk cardiac patients undergoing CABG surgery using cardiopulmonary bypass (CPB) was carried out. The inclusion criteria were patients with coronary artery disease (patients with ischemic heart disease or percutaneous transluminal coronary angioplasty, pervious CABG, hypertension, and patients with poor ventricular function (ejection fraction of 20–40%), or pulmonary hypertension. Exclusion criteria included patients with congestive heart failure, acute myocardial infarction, emergency, redo cases, combined CABG and valvular surgery or aortic artery surgery, malfunctioning artificial heart valve, obstructive cardiomyopathy, pericardial disease, and renal or hepatic impairment. The patients were assessed using New York Heart Association [14], American Society of Anesthesiologists Physical Status Score [15], and Euroscore [16]. The patients were allocated randomly (using simple randomization through a process of coin-tossing) into two equal groups ($n$=114 each).

### Sevoflurane group

The patients received sevoflurane (end-tidal concentration of 1–4%) as an inhalational agent during the entire procedure (before, during, and after CPB).

### Isoflurane group

The patients received isoflurane (end-tidal concentration of 0.5–2%) as an inhalational agent during the entire procedure (before, during, and after CPB).

End-tidal concentrations of sevoflurane and isoflurane were recorded every 5 min during the procedure using Fabius GS Premium (Dräger, Lübeck, Germany).

### Anesthetic technique

For all patients and under local anesthesia, a radial arterial cannula, a central venous line, and a pulmonary artery catheter were inserted before operation to enable continuous hemodynamic monitoring. Induction was performed by intravenous fentanyl (3–5 μg/kg), etomidate (0.3 mg/kg), and rocuronium (0.8 mg/kg). Anesthesia was maintained with oxygen/air (50%), sevoflurane, or isoflurane according to the study medication protocol in addition to an infusion of fentanyl (1–3 μg/kg/h) and cisatracurium (1–2 μg/kg/min). CPB was established with cannulation of the ascending aorta and the right atrium. At the end of the surgical intervention, the patients were prepared for weaning from CPB. If there was difficulty in weaning from CPB, pharmacological support (dopamine or epinephrine or norepinephrine, milrinone, or nitroglycerine) or mechanical support (intra-aortic balloon pump) was started. At the end of surgery, the patients were transferred to cardiac surgery ICU under full monitoring.

### Monitoring of patients

Hemodynamic monitoring included measurement of the heart rate, mean arterial blood pressure (MAP), a continuous ECG with automatic ST-segment analysis (leads II and V), central venous pressure, mean arterial pulmonary pressure, pulmonary capillary wedge pressure, pulmonary and systemic vascular resistances, cardiac index, urine output, troponin I level, CK-MB level, and the required pharmacological and mechanical support. The cardiovascular variables derived, namely, the cardiac index, and pulmonary and systemic vascular resistances, were calculated using standard formulae and the measurements were based on the bolus thermodilution technique using the mean of three

consecutive 10 ml injectates of 5% glucose through the Swan Ganz catheter (Edwards Lifesciences, California, USA). Postoperatively, transthoracic echocardiography was performed for patients with ischemic changes in the ECG and elevated cardiac biomarkers to diagnose the development of new regional wall motion abnormalities. Postoperative coronary angiography was performed for patients with elevated cardiac biomarkers to assess the patency of the coronary grafts.

Hemodynamic values were determined serially at the following time-points. T0: baseline reading; T1: reading 15 min after induction; T2: reading before CPB; T3: reading 30 min after CPB; T4: reading at ICU admission; T5: reading at the sixth hour after ICU admission; T6: reading at the 12th hour after ICU admission; and T7: reading at the 24th hour after ICU admission. The troponin level was checked before surgery, before CPB, at the time of ICU admission, and at the sixth, 12th, 24th, 48th, and 72nd postoperative hours.

### Statistical analysis

Data were described statistically as mean±SD or frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between the study groups was performed using the Student *t*-test for independent samples. Repeated measures analysis of variance was carried out to determine the effect of sevoflurane and isoflurane on hemodynamics and cardiac biomarkers at different follow-up intervals. For comparison of categorical data, the $\chi^2$-test was performed. The exact test was used when the expected frequency was less than 5. *P* values less than 0.05 were considered statistically significant. All statistical calculations were carried out using the computer program SPSS (statistical package for the social sciences; SPSS Inc., Chicago, Illinois, USA) version 15 for Microsoft Windows.

## Results

Table 1 shows no significant differences in the demographic data, co-morbidities, preoperative medications, New York Heart Association class, Euroscore, and the American Society of Anesthesiologists Physical Status Score physical status score ($P>0.05$).

Table 2 shows the changes in the heart rate, MAP, and central venous pressure of patients. There was no significant difference in the preoperative heart rate, MAP, and central venous pressure of the patients of the two groups ($P>0.05$). After induction, the heart rate decreased in the sevoflurane group and increased in the patients of the isoflurane group during the procedure and through the first 24 h in the ICU and the difference in the heart rate between the two groups was significant ($P<0.05$). After induction, there were minimal changes in the MAP in patients of the sevoflurane group and an increase in the MAP in patients of the isoflurane group and the difference between the two groups was significant ($P<0.05$). There was no change in the central venous pressure of patients during the procedure and through the first 24 h in the ICU between the two groups ($P>0.05$).

Table 3 shows the changes in the cardiac index, mean pulmonary arterial blood pressure, and the pulmonary capillary wedge pressure. There was no significant difference in the preoperative cardiac index, the mean pulmonary arterial blood pressure, and the pulmonary capillary wedge pressure between the two groups ($P>0.05$). After induction, the cardiac index and the mean pulmonary arterial blood pressure decreased in patients of the sevoflurane group and increased in patients of the isoflurane group during the procedure and through the first 24 h in the ICU and the difference in the cardiac index and the mean pulmonary arterial blood pressure between the two groups was significant ($P<0.05$). There was no significant change in the pulmonary capillary wedge pressure of patients during the procedure and through the first 24 hours in the ICU between the two groups ($P>0.05$).

Table 4 shows the changes in the systemic and pulmonary vascular resistances of patients. There were no significant differences in the preoperative systemic and pulmonary vascular resistances of the patients between the two groups ($P>0.05$). After induction, the systemic and pulmonary vascular resistances decreased in patients of the sevoflurane group and increased in the patients of the isoflurane group during the procedure and through the first 24 h in the ICU and the difference in the systemic and pulmonary vascular resistances between the two groups was significant ($P<0.05$).

Table 5 shows the changes in the blood levels of troponin I and CK-MB, ECG changes, myocardial infarction, and postoperative coronary angiography. There was no significant difference in the blood levels of troponin I and CK-MB preoperatively and before CPB between the two groups ($P>0.05$). After CPB, the troponin I and CK-MB increased in the patients of the two groups. The increase was markedly higher in the patients of the isoflurane group than in the patients of the

**Table 1 Preoperative data of patients**

| Variables | Sevoflurane group (*n*=114) | Isoflurane group (*n*=114) | *P* value |
|---|---|---|---|
| Age (years) | 54.50±11.25 | 53.69±10.73 | 0.578 |
| Weight (kg) | 86.46±11.65 | 87.18±11.58 | 0.640 |
| Sex | | | |
| Male : female | 63 (55.26) : 51 (44.74) | 59 (51.75) : 55 (48.25) | 0.595 |
| Diabetes mellitus | 98 (85.96) | 95 (83.33) | 0.581 |
| Hypertension | 88 (77.19) | 90 (78.94) | 0.748 |
| Ischemic heart diseases | 114 (100) | 114 (100) | 1.000 |
| Atrial fibrillation | 37 (32.45) | 33 (28.94) | 0.565 |
| Pulmonary hypertension | 46 (40.35) | 41 (35.96) | 0.495 |
| Ejection fraction (%) | 30.70±9.14 | 32.53±7.44 | 0.098 |
| Angiotensin-converting enzyme inhibitors | 83 (72.80) | 79 (69.29) | 0.412 |
| β-blockers | 88 (77.19) | 84 (73.68) | 0.452 |
| Calcium channels-blockers | 36 (31.57) | 42 (36.84) | 0.326 |
| Aspirin | 114 (100) | 114 (100) | 0.545 |
| Statins | 87 (76.31) | 84 (73.68) | 0.190 |
| Stroke | 3 (2.63) | 2 (1.75) | 0.404 |
| Carotid stenosis | | | |
| <50% | 21 (18.42) | 18 (15.78) | 0.597 |
| Unilateral | 9 (7.89) | 7 (6.14) | 0.604 |
| Bilateral | 12 (10.52) | 11 (9.64) | 0.825 |
| Renal function | | | |
| Impairment | 15 (15.15) | 12 (10.52) | 0.538 |
| Dialysis | 6 (5.26) | 4 (3.50) | 0.517 |
| Smoking | | | |
| Current smokers | 49 (42.98) | 45 (39.47) | 0.590 |
| Ex-smokers | 35 (30.70) | 26 (24.56) | 0.178 |
| NYHA | | | |
| II | 27 (23.68) | 30 (26.31) | 0.759 |
| III | 80 (70.17) | 78 (68.42) | 0.885 |
| IV | 7 (6.14) | 6 (5.26) | 1.000 |
| ASA | | | |
| III | 89 (78.07) | 82 (71.92) | 0.358 |
| IV | 25 (21.92) | 32 (28.07) | 0.358 |
| Euroscore (%) | 14.26±4.15 | 13.80±4.43 | 0.419 |
| Body surface area ($m^2$) | 1.77±0.17 | 1.76±0.15 | 0.638 |
| Coronary artery bypasses grafting | 114 (100) | 114 (100) | 1,000 |

Data are presented as mean±SD and *n* (%); ASA, American Society of Anesthesiologists Physical Status Score; NYHA, New York Heart Association.

sevoflurane group through the first 24 postoperative hours, then the levels decreased through the second 24 postoperative hours, and continued to decrease through the third 24 postoperative hours. The difference between the two groups was significant ($P<0.05$) (Fig. 1a and b). A total of 26 patients showed ECG changes (ST-segment changes) in the sevoflurane group and 39 patients showed ECG changes in the isoflurane group ($P=0.039$). A total of 13 patients showed postoperative myocardial infarction in the sevoflurane group compared with 24 patients in the isoflurane group ($P=0.048$). A total of 13 patients showed postoperative new regional wall motion abnormalities in the sevoflurane group compared with 24 patients in the isoflurane group ($P=0.048$). A total of four patients showed postoperative myocardial infarction and associated occluded coronary grafts in the sevoflurane group compared with nine patients in the isoflurane group ($P=0.153$).

Table 6 shows the intraoperative data and the outcomes of the patients of the two groups. There was no difference in the number of coronary grafts, CPB time, cross clamping time, blood loss, transfused packed red blood cells, hematocrit value, transfused fluids, intraoperative urine output, and neurological and renal complications between the two groups ($P>0.05$). Weaning from CPB was easier in patients in the sevoflurane group than the patients in the isoflurane group. Patients in the sevoflurane group needed smaller doses of pharmacological support (dopamine, epinephrine, norepinephrine, nitroglycerine, and milrinone) than the patients in the isoflurane group ($P<0.05$), and the requirement for mechanical support (intra-aortic

**Table 2 Heart rate, mean arterial blood pressure, and central venous pressure of patients**

| Variables | Sevoflurane group (*n*=114) | Isoflurane group (*n*=114) | *P* value |
|---|---|---|---|
| Heart rate (bpm) | | | |
| T0 | 78.52±10.75 | 76.80±9.81 | 0.208 |
| T1 | 74.80±10.24 | 78.13±9.55 | 0.011* |
| T2 | 74.10±8.62 | 77.00±8.40 | 0.011* |
| T3 | 73.98±9.15 | 78.00±10.34 | 0.002* |
| T4 | 74.90±9.30 | 78.18±10.27 | 0.012* |
| T5 | 73.79±10.30 | 77.50±13.13 | 0.018* |
| T6 | 74.66±10.70 | 78.14±13.52 | 0.032* |
| T7 | 74.97±11.35 | 79.22±13.79 | 0.011* |
| Mean arterial blood pressure (mmHg) | | | |
| T0 | 104.95±16.00 | 105.30±15.61 | 0.867 |
| T1 | 103.95±14.35 | 108.78±16.50 | 0.019* |
| T2 | 102.76±13.75 | 109.10±16.30 | 0.002* |
| T3 | 106.70±14.64 | 111.58±17.42 | 0.023* |
| T4 | 107.94±14.20 | 113.51±18.68 | 0.012* |
| T5 | 108.60±13.95 | 113.79±18.14 | 0.016* |
| T6 | 107.91±14.10 | 112.76±18.25 | 0.025* |
| T7 | 107.86±13.36 | 113.28±18.96 | 0.013* |
| Central venous pressure (mmHg) | | | |
| T0 | 10.87±1.68 | 11.15±1.24 | 0.153 |
| T1 | 12.25±1.20 | 12.53±1.35 | 0.099 |
| T2 | 12.77±1.36 | 12.95±1.58 | 0.357 |
| T3 | 13.35±1.44 | 13.10±1.52 | 0.203 |
| T4 | 13.41±1.16 | 13.59±1.23 | 0.256 |
| T5 | 13.30±1.37 | 13.45±1.14 | 0.369 |
| T6 | 12.86±1.46 | 13.16±1.33 | 0.106 |
| T7 | 12.75±1.62 | 12.84±1.17 | 0.631 |

Data are presented as mean±SD; T0, baseline reading; T1, reading 15 min after induction; T2, reading before cardiopulmonary bypass; T3, reading 30 min after cardiopulmonary bypass; T4, reading at ICU admission; T5, reading at the sixth hour after ICU admission; T6, reading at the 12th hour after ICU admission; T7, reading at the 24th hour after ICU admission; *$P<0.05$, significant comparison between the two groups.

balloon pump) and pacing was lower in patients of the sevoflurane group than those in the isoflurane group ($P<0.05$). A total of 10 patients showed postoperative atrial fibrillation in the sevoflurane group compared with 21 patients in the isoflurane group ($P=0.033$). The ICU and hospital lengths of stay were shorter in patients of group M than group C ($P<0.05$). The incidence of mortality was lower in patients in the sevoflurane group than those in the isoflurane group, but the difference was insignificant ($P>0.05$).

## Discussion

There was an increase in the heart rate, MAP, cardiac index, and systemic and pulmonary vascular resistances with isoflurane. This may increase the work performed by the heart, increasing the oxygen demand and disturbing the oxygen supply/demand ratio, therefore the myocardial becomes liable to more ischemia, which is already suffering from ischemia. However, in the sevoflurane group, there was a decrease in the heart rate, MAP, cardiac index, and systemic and pulmonary vascular resistances, and this decrease resulted in a decrease in the work performed by the heart, decreasing the oxygen demand and maintaining or improving the oxygen supply/demand ratio, therefore protecting the myocardium from ischemia. The myocardial protective effect was documented by the ECG changes and an increase in the troponin I and CK-MB isoenzyme with isoflurane than with sevoflurane.

The findings of the present study are in agreement with the results of other studies. Ceyhan *et al.* [17] found that the levels of CK-MB and troponin-T were significantly lower in the sevoflurane group compared with the isoflurane group through the 24th postoperative hour and they concluded that sevoflurane provides better myocardial protection than isoflurane. Searle *et al.* [18] showed that the incidence of postoperative myocardial infarction was 2.2% in the sevoflurane group and 4.5% in the isoflurane group, but this was insignificant. Ebert *et al.* [19] reported that the increase in the heart rate produced by the surgery was less with sevoflurane than that with isoflurane and the heart rate of patients with coronary artery disease patients undergoing cardiac or noncardiac surgery was more

**Table 3 Cardiac index, mean pulmonary arterial blood pressure, and pulmonary artery wedge pressure**

| Variables | Sevoflurane group (*n*=114) | Isoflurane group (*n*=114) | *P* value |
|---|---|---|---|
| Cardiac index (l/min/m$^2$) | | | |
| T0 | 2.53±0.27 | 2.47±0.30 | 0.113 |
| T1 | 2.45±0.23 | 2.54±0.35 | 0.022* |
| T2 | 2.43±0.25 | 2.53±0.36 | 0.015* |
| T3 | 2.42±0.28 | 2.52±0.36 | 0.020* |
| T4 | 2.43±0.36 | 2.55±0.35 | 0.011* |
| T5 | 2.43±0.32 | 2.54±0.35 | 0.014* |
| T6 | 2.42±0.30 | 2.53±0.37 | 0.014* |
| T7 | 2.44±0.34 | 2.55±0.38 | 0.022* |
| Mean pulmonary arterial blood pressure (mmHg) | | | |
| T0 | 25.19±4.64 | 24.76±3.82 | 0.445 |
| T1 | 23.35±4.56 | 25.16±4.48 | 0.002* |
| T2 | 23.37±5.25 | 25.44±6.80 | 0.010* |
| T3 | 22.90±4.25 | 24.46±5.51 | 0.017* |
| T4 | 22.63±4.60 | 24.54±5.15 | 0.003* |
| T5 | 22.89±4.67 | 24.47±5.10 | 0.015* |
| T6 | 22.58±5.25 | 24.45±5.68 | 0.010* |
| T7 | 22.14±4.71 | 24.31±5.98 | 0.003* |
| Pulmonary capillary wedge pressure (mmHg) | | | |
| T0 | 14.46±2.45 | 13.98±2.60 | 0.152 |
| T1 | 15.25±3.36 | 14.90±3.54 | 0.444 |
| T2 | 15.57±3.25 | 15.16±3.70 | 0.375 |
| T3 | 15.40±3.13 | 15.29±3.30 | 0.796 |
| T4 | 14.72±2.96 | 15.20±3.17 | 0.238 |
| T5 | 15.10±3.00 | 15.43±3.31 | 0.431 |
| T6 | 15.28±3.08 | 14.75±2.80 | 0.175 |
| T7 | 14.69±2.84 | 14.82±2.53 | 0.715 |

Data are presented as mean±SD; T0, baseline reading; T1, reading 15 min after induction; T2, reading before cardiopulmonary bypass; T3, reading 30 min after cardiopulmonary bypass; T4, reading at ICU admission; T5, reading at the sixth hour after ICU admission; T6, reading at the 12th hour after ICU admission; T7, reading at the 24th hour after ICU admission; *$P<0.05$, significant comparison between the two groups.

**Table 4 Systemic and pulmonary vascular resistances of patients**

| Variables | Sevoflurane group (*n*=114) | Isoflurane group (*n*=114) | *P* value |
|---|---|---|---|
| Systemic vascular resistance (dyne/s/cm$^5$) | | | |
| T0 | 1311.65±125.38 | 1303.89±136.20 | 0.654 |
| T1 | 1276.75±122.00 | 1316.16±130.45 | 0.019* |
| T2 | 1265.42±128.68 | 1310.73±135.94 | 0.010* |
| T3 | 1260.60±125.46 | 1305.24±137.13 | 0.011* |
| T4 | 1255.48±127.19 | 1300.85±142.61 | 0.012* |
| T5 | 1266.54±132.90 | 1314.37±147.20 | 0.011* |
| T6 | 1258.73±130.47 | 1305.30±145.56 | 0.011* |
| T7 | 1268.36±133.18 | 1312.42±144.80 | 0.017* |
| Pulmonary vascular resistance (dyne/s/cm$^5$) | | | |
| T0 | 436.40±89.26 | 428.53±93.15 | 0.515 |
| T1 | 413.69±91.86 | 439.98±95.65 | 0.035* |
| T2 | 408.17±93.26 | 440.38±98.50 | 0.012* |
| T3 | 406.75±94.90 | 439.63±99.44 | 0.011* |
| T4 | 411.46±92.39 | 438.70±97.58 | 0.031* |
| T5 | 407.40±90.85 | 439.00±95.22 | 0.011* |
| T6 | 412.67±87.73 | 438.30±93.69 | 0.034* |
| T7 | 410.84±88.23 | 437.90±91.65 | 0.024* |

Data are presented as mean±SD; T0, baseline reading; T1, reading 15 min after induction; T2, reading before cardiopulmonary bypass; T3, reading 30 min after cardiopulmonary bypass; T4, reading at ICU admission; T5, reading at the sixth hour after ICU admission; T6, reading at the 12th hour after ICU admission; T7, reading at the 24th hour after ICU admission; *$P<0.05$, significant comparison between the two groups.

stable with sevoflurane than isoflurane. Lee *et al.* [20] documented that the cardiac index and stroke volume index were significantly higher in the isoflurane group than in the control group and the same findings were

**Table 5 Blood levels of troponin I, creatine kinase-MB, ECG changes, myocardial infarction, and postoperative coronary angiography**

| Variables | Sevoflurane group (*n*=114) | Isoflurane group (*n*=114) | *P* value |
|---|---|---|---|
| Troponin I (ng/ml) | | | |
| Baseline | 0.72±0.13 | 0.71±0.10 | 0.515 |
| Before CPB | 0.74±0.11 | 0.72±0.12 | 0.190 |
| ICU admission | 1.44±0.32 | 1.58±0.54 | 0.018* |
| Sixth hour | 1.73±0.53 | 1.91±0.70 | 0.029* |
| 12th hour | 2.75±1.60 | 3.28±1.75 | 0.017* |
| 24th hour | 2.89±1.67 | 3.46±1.84 | 0.015* |
| 48th hour | 2.13±1.25 | 2.59±1.47 | 0.011* |
| 72nd hour | 1.39±0.30 | 1.52±0.48 | 0.015* |
| Creatine kinase-MB (ng/ml) | | | |
| Baseline | 5.31±1.19 | 5.27±1.22 | 0.802 |
| Before CPB | 5.43±1.24 | 5.35±1.20 | 0.621 |
| ICU admission | 5.47±1.44 | 5.60±1.52 | 0.508 |
| Sixth hour | 8.43±2.30 | 9.17±2.40 | 0.018* |
| 12th hour | 9.32±2.53 | 10.02±2.65 | 0.042* |
| 24th hour | 9.86±2.59 | 10.63±2.75 | 0.031* |
| 48th hour | 7.46±2.24 | 8.15±2.30 | 0.022* |
| 72nd hour | 5.56±1.45 | 5.68±1.60 | 0.553 |
| ECG changes | 26 | 39 | 0.039* |
| Myocardial infarction | 13 | 24 | 0.048* |
| Regional wall motion abnormalities | 13 | 24 | 0.048* |
| Coronary angiography (occluded grafts) | 4 | 9 | 0.153 |

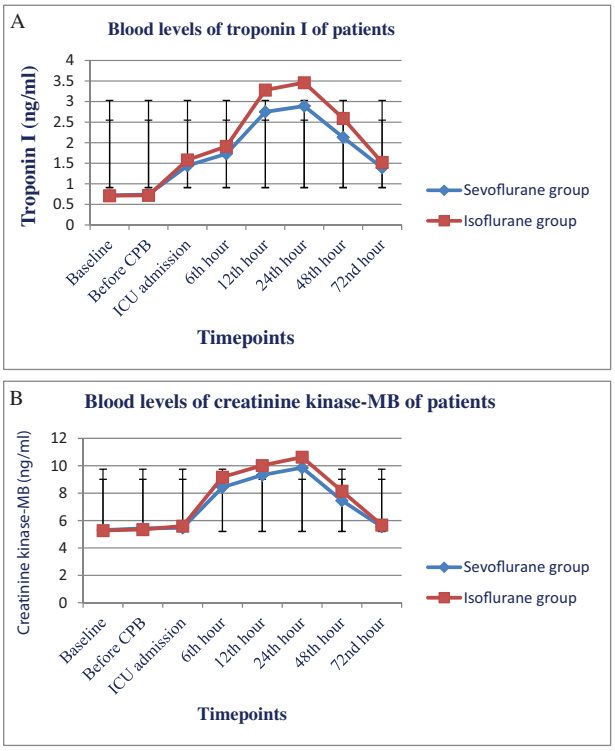
Data are presented as mean±SD and number; 12th hour, reading at the 12th postoperative hour; 24th hour, reading at the 24th postoperative hour; 48th hour, reading at the 48th postoperative hour; sixth hour, reading at the sixth hour after ICU admission; 72nd hour, reading at the 72nd post operative hour; CPB, cardiopulmonary bypass; ICU admission, reading at ICU admission; *$P<0.05$, significant comparison between the two groups.

reported by Wang *et al.* [21], who also reported no difference in the postoperative levels of troponin I and CK-MB isoenzyme in patients preconditioned by isoflurane compared with the control group.

In a meta-analysis study, Li *et al.* [22] showed that the use of sevoflurane is associated with a lower troponin I level and a better cardioprotective effect compared with propofol and similar results were reported by Yang *et al.* [23] Liu *et al.* [24] found that the cardiac output and stroke volume improved significantly in the sevoflurane group compared with the propofol, but there was no difference in the cardiac troponin I, creatine kinase-MB, and lactate dehydrogenase levels between the two groups.

The myocardial protective effect of sevoflurane is superior to isoflurane and this may be related to many factors: (a) isoflurane has been associated with the phenomena of coronary steal that leads to the redistribution of blood from a poorly perfused region of the myocardium to an area that is perfused adequately [25,26], and this may suggest that isoflurane is associated with a higher incidence of myocardial ischemia as a result of coronary steal phenomena [27], while the sevoflurane is not associated with coronary steal phenomena [19]; (b) isoflurane increases the heart rate [28–30], which

**Figure 1**




(a) Blood levels of troponin I of patients; (b) blood levels of creatine kinase-MB of patients. ICU admission: reading at ICU admission; sixth hour: reading at the sixth hour after ICU admission; 12th hour: reading at the 12th postoperative hour; 24th hour: reading at the 24th postoperative hour; 48th hour: reading at the 48th postoperative hour; 72nd hour: reading at the 72nd postoperative hour.

**Table 6 Intraoperative data and outcome of patients (data are presented as mean±SD, number, %)**

| Variables | Sevoflurane group (*n*=114) | Isoflurane group (*n*=114) | *P* value |
|---|---|---|---|
| Number of coronary grafts | | | |
| 3 | 25 | 32 | 0.638 |
| 4 | 66 | 61 | 0.505 |
| 5 | 16 | 13 | 0.551 |
| 6 | 7 | 8 | 0.789 |
| CPB time (min) | 118.36±25.10 | 116.83±24.54 | 0.642 |
| Cross clamping time (min) | 94.71±17.54 | 92.45±16.15 | 0.312 |
| Epinephrine(μg/kg/min) | 0.07±0.02 | 0.08±0.05 | 0.049* |
| Norepinephrine (μg/kg/min) | 0.04±0.02 | 0.05±0.04 | 0.018* |
| Nitroglycerine (μg/kg/min) | 0.75±0.52 | 0.92±0.64 | 0.028* |
| Milrinone (μg/kg/min) | 0.33±0.24 | 0.40±0.19 | 0.015* |
| Intra-aortic balloon pump | 28 | 42 | 0.044* |
| Pacing | 31 | 45 | 0.049* |
| Transfused P-RBC (unit) | 3.56±0.46 | 3.64±0.55 | 0.234 |
| Hematocrit (%) | 38.16±3.76 | 38.64±3.54 | 0.322 |
| Blood loss (ml) | | | |
| Intraoperative (ml) | 2275.63±235.15 | 2248.42±227.85 | 0.375 |
| Postoperative (ml/24 h) | 683.41±132.26 | 691.95±138.55 | 0.634 |
| Intraoperative fluids | | | |
| Crystalloids (ml) | 3363.85±644.31 | 3390.24±672.68 | 0.762 |
| Hesteril 6% | 635.69±135.47 | 663.46±147.20 | 0.139 |
| Postoperative fluids 24 h | | | |
| Crystalloids (ml) | 4360.23±838.76 | 4315.64±866.96 | 0.693 |
| Hesteril 6% | 970.48±293.65 | 967.15±286.36 | 0.931 |
| Intraoperative urine output (ml) | 2135.61±265.14 | 2096.74±247.80 | 0.254 |
| Atrial fibrillation | 10 | 21 | 0.033 |
| Neurological complication (stroke) | 2 | 2 | 1.000 |
| New acute renal impairment | 9 | 13 | 0.369 |
| New renal failure | 4 | 3 | 0.701 |
| Postoperative dialysis | | | |
| Temporarily | 3 | 2 | 0.651 |
| Permanent | 1 | 1 | 1.000 |
| ICU length of stay (days) | 4.72±1.43 | 5.20±1.40 | 0.011* |
| Hospital length of stay (days) | 8.87±2.83 | 9.76±3.44 | 0.034* |
| Mortality | 4 | 9 | 0.153 |

CPB, cardiopulmonary bypass; P-RBC, packed red blood cells; *$P<0.05$, significant comparison between the two groups.

can increase the myocardial oxygen demand and can be detrimental to ischemic patients undergoing cardiac surgery [31]; (c) sevoflurane shows more depressant activity on the myocardium more than isoflurane [32,33], and this may minimize the work performed and oxygen requirement associated with surgical stress [34]; (d) sevoflurane has been shown to exert a better ischemic preconditioning effect than other volatile agents [35]; (d) sevoflurane preserves the cardiac functions after coronary surgery using CPB [6]; and (e) sevoflurane is responsible for the increase in the myocardial ATP during reperfusion [36]. Sevoflurane induces anti-inflammatory effects in different types of CABG surgeries under CPB [37,38].

In contrast to the findings of the present study, Kiani *et al*. [39] compared the protective effect of isoflurane-induced preconditioning (2.5 minimum alveolar concentrations) in patients undergoing elective CABG surgery and they found a significant decrease in the CK-MB isoenzyme levels at 24 h postoperatively. Belhomme *et al*. [4] reported a decrease in the postoperative release of troponin I and CK-MB isoenzyme following the administration of isoflurane in comparison with the control group and the same findings were documented by Lee *et al*. [20].

Hemmerling *et al*. [40] showed that sevoflurane and isoflurane exerted the same ischemic cardioprotective effects in off-pump cardiac bypass surgery. Tomai *et al*. [41] found that isoflurane could reduce myocardial injury only in patients with impaired left ventricular function [ejection fraction (EF)<50%] undergoing CABG.

Searle *et al*. [18] found no difference in the heart rate, blood pressure, and cardiac index between sevoflurane

and isoflurane. Also, no difference was found in the postoperative morbidities between the two groups.

Bennett *et al.* [42] evaluated myocardial injury using transesphageal echocardiography and ECG during anesthesia with sevoflurane and isoflurane and they found no difference between sevoflurane and isoflurane. Wang *et al.* [21] showed no difference in the blood pressure, mean pulmonary artery pressure, pulmonary capillary wedge pressure, central venous pressure, systemic vascular resistance, and pulmonary vascular resistance between the isoflurane and the control group.

Sarkar *et al.* [43] evaluated the hemodynamics of isoflurane, sevoflurane, and desflurane by echo cardiography and they found that the left ventricular relaxation function improved with isoflurane, sevoflurane, and desflurane, but there was no significant difference in the heart rate, blood pressure, central venous pressure, pulmonary capillary wedge pressure, systemic vascular resistance index, and cardiac index between the three groups; the same finding was reported by Venkatesh *et al.* [34]. In a study carried out by Jones *et al.* [44], the outcome of sevoflurane and isoflurane was evaluated in cardiac surgical patients with different ejection fractions (LVEF >54%, LVEF 40–54%, LVEF 20–39%, LVEF <20%); they concluded that sevoflurane was not superior or inferior to isoflurane and the outcomes were the same in the two groups. Diana *et al.* [45] evaluated myocardial ischemia using transesphageal echocardiography and coronary sinus lactate metabolism and they found no difference in the incidence of myocardial ischemia between the sevoflurane and isoflurane groups.

In the present study, the awakening and extubation times were significantly earlier with sevoflurane than isoflurane and these findings are similar with the results of other studies [33,46].

### Study limitations

There are limitations in the present study. First, the study was not a blinded study and second, the present study had small study samples.

## Conclusion

Sevoflurane induces a better cardioprotective effect than isoflurane during CABG surgery. It decreases the incidence of myocardial infarction and the requirement for pharmacological and mechanical support, and duration of stay in the ICU and hospital.

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### Conflicts of interest

There are no conflicts of interest.

## References

1 Cope DK, Impastato WK, Cohen MV, Downey JM. Volatile anesthetics protect the ischemic rabbit myocardium from infarction. Anesthesiology 1997; 86:699–709.

2 Chiari P, Bouvet F, Piriou V. Anaesthetic induced myocardial preconditioning: fundamental basis and clinical implications. Ann Fr Anesth Reanim 2005; 24:383–396.

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; 99:826–833.

4 Belhomme D, Peynet J, Louzy M, Launay JM, Kitakaze M, Menasche P. Evidence for preconditioning by isoflurane in coronary artery bypass graft surgery. Circulation 1999; 100:II340–II344.

5 Kato R, Foëx P. Myocardial protection by anesthetic agents against ischemia-reperfusion injury: an update for anesthesiologists. Can J Anaesth 2002; 49: 777–791.

6 De Hert SG. Anaesthetic preconditioning: how important is it in today's cardiac anesthesia? J Cardiothorac Vasc Anesth 2006; 20:473–476.

7 Landoni G, Fochi O, Bignami E, Calabrò MG, D'Arpa MC, Moizo E, *et al.* Cardiac protection by volatile anesthetics in non-cardiac surgery? A meta-analysis of randomized controlled studies on clinically relevant endpoints. HSR Proc Intensive Care Cardiovasc Anesth 2009; 1:34–43.

8 Hu ZY, Liu J. Mechanism of cardiac preconditioning with volatile anaesthetics. Anaesth Intensive Care 2009; 37:532–538.

9 Redel A, Stumpner J, Tischer-Zeitz T, Lange M, Smul TM, Lotz C, *et al.* Comparison of isoflurane-, sevoflurane-, and desflurane-induced pre- and postconditioning against myocardial infarction in mice in vivo. Exp Biol Med (Maywood) 2009; 234:1186–1191.

10 Landoni G, Greco T, Biondi-Zoccai G, Nigro Neto C, Febres D, Pintaudi M, *et al.* Anaesthetic drugs and survival: a Bayesian network meta-analysis of randomized trials in cardiac surgery. Br J Anaesth 2013; 111:886–896.

11 Guarracino F, Landoni G, Tritapepe L, Pompei F, Leoni A, Aletti G, *et al.* Myocardial damage prevented by volatile anesthetics: a multicenter randomized controlled study. J Cardiothorac Vasc Anesth 2006; 20: 477–483.

12 Bignami E, Biondi-Zoccai G, Landoni G, Fochi O, Testa V, Sheiban I, *et al.* Volatile anesthetics reduce mortality in cardiac surgery. J Cardiothorac Vasc Anesth 2009; 2:594–599.

13 De Hert S, Vlasselaers D, Barbe R, Ory JP, Dekegel D, Donnadonni R, *et al.* A comparison of volatile and non volatile agents for cardioprotection during on pump coronary surgery. Anaesthesia 2009; 64:953–960.

14 The Criteria Committee of the New York Heart Association. Nomenclature and criteria for diagnosis of diseases of the heart and blood vessels. 9th ed. Boston, Massachusetts: Little, Brown & Co.; 1994. 253–256.

15 Wolters U, Wolf T, Stützer H, Schröder T. ASA classification and perioperative variables as predictors of postoperative outcome. Br J Anaesth 1996; 77:217–222.

16 Nashef SA, Roques F, Sharples LD, Nilsson J, Smith C, Goldstone AR, *et al.* EuroSCORE II. Eur J Cardiothorac Surg 2012; 41:734–744.

17 Ceyhan D, Tanrıverdi B, Bilir A. Comparison of the effects of sevoflurane and isoflurane on myocardial protection in coronary bypass surgery. Anadolu Kardiyol Derg 2011; 11:257–262.

18 Searle NR, Martineau RJ, Conzen P, al-Hasani A, Mark L, Ebert T, *et al.* Comparison of sevoflurane/fentanyl and isoflurane/fentanyl during elective coronary artery bypass surgery. Sevoflurane Venture Group. Can J Anaesth 1996; 43:890–899.

19 Ebert TJ, Harkin CP, Muzi M. Cardiovascular responses to sevoflurane: a review. Anesth Analg 1995; 81:S11–S22.

20 Lee MC, Chen CH, Kuo MC, Kang PL, Lo A, Liu K. Isoflurane preconditioning-induced cardio-protection in patients undergoing coronary artery bypass grafting. Eur J Anaesthesiol 2006; 23:841–847.

21 Wang X, Jarvinen O, Kuukasjarvi P, Laurikka J, Wei M, Rinne T, *et al.* Isoflurane produces only minor preconditioning in coronary artery bypass grafting. Scand Cardiovasc J 2004; 38:287–292.

**22** Li F, Yuan Y. Meta-analysis of the cardioprotective effect of sevoflurane versus propofol during cardiac surgery. BMC Anesthesiol 2015; 15:128.

**23** Yang XL, Wang D, Zhang GY, Guo XL. Comparison of the myocardial protective effect of sevoflurane versus propofol in patients undergoing heart valve replacement surgery with cardiopulmonary bypass. BMC Anesthesiol 2017; 17: 37.

**24** Liu X, Wang R, Luo H, Qin G, Wang LU, Ye Z, *et al.* Circulating microRNAs indicate cardioprotection by sevoflurane inhalation in patients undergoing off-pump coronary artery bypass surgery. Exp Ther Med 2016; 11: 2270–2276.

**25** Buffington CW, Davis KB, Gillispie S, Pettinger M. The prevalence of steal-prone coronary anatomy in patients with coronary artery disease: an analysis of the coronary artery surgery study registry. Anesthesiology 1988; 69:721–727.

**26** Leung JM, Hollenberg M, O'Kelley BF, Kao A, Mangano DT. Effects of steal-prone anatomy on intraoperative myocardial ischaemia. J Am Coll Cardiol 1992; 20:1205–1212.

**27** Priebe H-J. Isoflurane and coronary hemodynamics. Anesthesiology 1989; 71:960–976.

**28** Hess W, Arnold B, Schulte-Sasse U, Tarnow J. Comparison of isoflurane and halothane when used to control intraoperative hypertension in patients undergoing coronary artery bypass surgery. Anesth Analg 1983; 62:15–20.

**29** Moffitt EA, Barker RA, Glenn JJ, Imrie DD, DelCampo C, Landymore RW, *et al.* Myocardial metabolism and hemodynamic responses with isoflurane anesthesia for coronary artery surgery. Anesth Analg 1986; 65:53–61.

**30** Eger E III, Eisenkraft JB, Weiskopf RB. The pharmacology of inhaled anesthetics. 2nd ed. Chicago IL: Healthcare Press; 2002.

**31** Nishiyama T. Haemodynamic and catecholamine response to a rapid increase of isoflurane or sevoflurane concentration during a maintenance phase of anaesthesia in humans. J Anesth 2005; 19:213–217.

**32** Gentry-Smetana S, Redford D, Moore D, Larson DF. Direct effects of volatile anesthetics on cardiac function. Perfusion 2008; 23:43–47.

**33** Bennet SR, Griffins C. Sevoflurane versus isoflurane in patients undergoing valvular cardiac surgery. J Cardiothorac Vasc Anesth 2001; 15:175–178.

**34** Venkatesh BG, Mehta Y, Kumar A, Trehan N. Comparison of sevoflurane and isoflurane in OPCAB surgery. Ann Card Anaesth 2007; 10:46–50.

**35** Kalikiri P, Sachan R, Sachan G. Ischemic preconditioning of the heart. An insight into the concepts and mechanisms. J Ind Acad Clin Med 2005; 6:45–47.

**36** Cook TL, Beppu WJ, Hitt BA, Kosek JC, Mazze RI. A comparison of renal effects and metabolism of sevoflurane and methoxyflurane in enzyme-induced rats. Anesth Analg 1975; 54:829–835.

**37** De Hert SG, van der Linden PJ, Cromheecke S, Meeus R, Nelis A, van Reeth V, *et al.* Cardioprotective properties of sevoflurane in patients undergoing coronary surgery with cardiopulmonary bypass are related to the modalities of its administration. Anesthesiology 2004; 101: 299–310.

**38** Garcia C, Julier K, Bestmann L, Zollinger A, von Segesser LK, Pasch T, *et al.* Preconditioning with sevoflurane decreases PECAM-1 expression and improves one-year cardiovascular outcome in coronary artery bypass graft surgery. Br J Anaesth 2005; 94:159–165.

**39** Kiani A, Mirmohammad Sadeghi M, Gharipour M, Farahmand N, Hoveida L. Preconditioning by isoflurane as a volatile anesthetic in elective coronary artery bypass surgery. ARYA Atheroscler 2013; 9:192–197.

**40** 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; 25:230–236.

**41** Tomai F, De PR, Penta de PA, Colagrande L, Caprara E, Polisca P, *et al.* Beneficial impact of isoflurane during coronary bypass surgery on troponin I release. G Ital Cardiol 1999; 29:1007–1014.

**42** Bennett SR, Griffin SC. Sevoflurane versus isoflurane in patients undergoing coronary artery bypass grafting: a hemodynamic and recovery study. J Cardiothorac Vasc Anesth 1999; 13:666–672.

**43** Sarkar S, GuhaBiswas R, Rupert E. Echocardiographic evaluation and comparison of the effects of isoflurane, sevoflurane and desflurane on left ventricular relaxation indices in patients with diastolic dysfunction. Ann Card Anaesth 2010; 13:130–137.

**44** Jones PM, Bainbridge D, Chu MW, Fernandes PS, Fox SA, Iglesias I, *et al.* Comparison of isoflurane and sevoflurane in cardiac surgery: a randomized non-inferiority comparative effectiveness trial. Can J Anaesth 2016; 63: 1128–1139.

**45** Diana P, Tullock WC, Gorcsan J 3rd, Ferson PF, Arvan S. Myocardial ischemia: a comparison between isoflurane and enflurane in coronary artery bypass patients. Anesth Analg 1993; 77:221–226.

**46** Mourad MA, Hofmeister J, Behl R. Sevoflurane supplementation of three induction doses of fentanyl for anaesthesia of adult patients undergoing cardiac surgery. J Anesth 2003; 19:109–114.