Comparison of the cardioprotective effect of isoflurane versus sevoflurane during cardiopulmonary bypass in congenital heart surgery

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Aims
This study aimed to detect the difference in the preconditioning effect between isoflurane and sevoflurane when they are used just before aortic cross-clamp and continued throughout the bypass period by measuring cardiac troponin I (cTnI) in the postbypass period.
Settings and design
This individual closed-envelope randomization study was carried out in the Abou Ell-Resh Pediatric Hospital, Cairo University Unit of congenital heart surgery in collaboration with the anesthesia department. The study was approved by the local ethical committee and a written informed consent was obtained from the guardians of the patient. This study was carried out from March 2011 to September 2012 (18 months). Patients were allocated randomly to two equal groups of 30 patients each.
Participants and methods
Acyanotic and cyanotic patients were allocated randomly to two equal groups of 30 patients each using individual closed-envelope randomization. Patients were allocated randomly to two equal groups as follows: group I, isoflurane group ($n = 30$) (received isoflurane) and group S, sevoflurane group ($n = 30$) (received sevoflurane). cTnI, a baseline sample was obtained before cardiopulmonary bypass (T0), 8 h after bypass (T8), and 24 h after bypass (T24). Parametric data were described as mean, SD, median, and SEM. The two groups studied were compared using Student's *t*-test. Repeated measures of the same group were compared using two-way analysis of variance, followed by post-hoc Tukey's comparison tests. For nonparametric data, nonparametric tests were used for comparison such as the Mann–Whitney *U*-test, median, or quartiles. *P* value less than 0.05 was considered significant (size estimation with two means is 28).
Results
Comparison of sevoflurane and isoflurane acyanotic cases showed that the cTnI ($P = 0.02$ and 0.01, respectively). Comparison of isoflurane and sevoflurane cyanotic cases showed that the cTnI values 8 and 24 h after bypass were higher in cyanotic cases of the isoflurane group than those of the sevoflurane group, but the difference was statistically insignificant. In terms of the difference between cyanotic and acyanotic cTnI results in the isoflurane group, cTnI values 8 h after cardiopulmonary bypass were higher in cyanotic cases compared with acyanotic cases, but this difference was insignificant, with a *P* value of 0.42. At 24 h after CPB, cTnI values were significantly higher in cyanotic cases with a *P* value of 0.015. In terms of the difference between cyanotic and acyanotic cTnI results in the sevoflurane group, the cTnI level 8 h after CPB was significantly higher in cyanotic cases compared with acyanotic cases with a *P* value of 0.001; it was also significantly higher in cyanotic cases 24 h after CPB with a *P* value of 0.005.
Conclusion
The present study showed that sevoflurane is superior to isoflurane in myocardial protection in surgical correction of congenital heart diseases only in acyanotic cases, with no difference in cyanotic cases.

Keywords:
congenital heart disease, isoflurane, preconditioning, sevoflurane

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Introduction

During repair of congenital heart defects, the child's heart is exposed to impaired myocardial function during the entire procedure.

A significant number of experimental studies have indicated that volatile anesthetics protect against ischemic myocardial dysfunction. This is known as pharmacological preconditioning [1].

Anesthetic preconditioning refers to the phenomenon in which exposure of the heart to a volatile anesthetic before myocardial ischemia results in protection during myocardial ischemia, improved cardiac function, and reduced arrhythmias on reperfusion. This type of protection strongly resembles ischemic preconditioning [2,3].

In recent years, there has been increased interest in the mechanisms involved in anesthetic-induced cardioprotection. Ischemic preconditioning and anesthetic preconditioning share similar molecular mechanisms, including activation of guanine nucleotide-binding proteins, activation of multiple kinases, mediation of nitric oxide formation and reactive oxygen species release, maintenance of intracellular and/or mitochondrial Ca^{2+} homeostasis, and moderation of the opening of ATP-sensitive potassium channels [4].

The aim of this work was to detect the difference in the preconditioning effect between isoflurane and sevoflurane when they are used just before aortic cross-clamp and continued throughout the bypass period by measuring cardiac troponin I (cTnI) in the postbypass period.

Participants and methods

Patient population

This individual prospective closed-envelope randomization study was carried out in the Abou Ell-Resh Pediatric Hospital, Cairo University Unit of congenital heart surgery in collaboration with the anesthesia department. The study was approved by the local ethical committee and a written informed consent was obtained from the guardians of the patient. This study was carried out from March 2011 to September 2012 (18 months). Patients were allocated randomly to two equal groups of 30 patients in each group. The study included cyanotic and acyanotic patients. The patients were between 2 and 6 years old and weighed between 8 and 20 kg.

Excluded patients had pre-existing heart failure, pre-existing thrombocytopenia, pre-existing renal failure, preoperative use of inotropes or vasopressors, and procedure needs ischemic time more than 1 h.

Study procedure

Patients were allocated randomly to two equal groups as follows:

Group I: Isoflurane group (n = 30) (received isoflurane as an inhalational agent before, during, and after cardiopulmonary bypass).

Group S: Sevoflurane group (n = 30) (received sevoflurane as an inhalational agent before, during, and after cardiopulmonary bypass).

The anesthesiologist interviewed the guardians, examined the patients, and assessed all routine investigations including complete blood count, coagulation profile, liver function tests, renal function tests, blood grouping, chest radiography, recent echocardiography, and angiography if available.

Anesthetic technique

Patients were premedicated with ketamine (5 mg/kg), midazolam (0.1 mg/kg), and atropine (0.02 mg/kg) intramuscularly 20 min before induction. ECG, pulse oximeter, and a noninvasive blood pressure monitor were connected to the patients.

Fentanyl (2 μg/kg) and midazolam (0.1 mg/kg) intravenously were used for induction, pancuronium (0.15 mg/kg) was used to facilitate endotracheal intubation, and 0.08 mg/kg was repeated intraoperatively to maintain muscle relaxation; the patients received an anesthetic agent according to the group to which they were allocated. Group I received isoflurane 1–1.5 by dial and group S received sevoflurane 1.5–2 by dial for maintenance throughout the procedure, with the bispectral index maintained between 40 and 60%. Fentanyl (15–20 μg/kg) was administered at divided doses to maintain analgesia during the procedure (3–5 μg/kg before skin incision, 3–5 μg/kg before sternotomy, 5 μg/kg during bypass, and 3–5 μg/kg in the postbypass period).

A three-channel central venous line (internal jugular or femoral vein) for inotrope and vasodilator infusion and central venous pressure monitoring were performed. An arterial line (radial or femoral) was inserted for invasive blood pressure monitoring. A urinary catheter was inserted to monitor urine output. The body temperature was monitored using two probes, one in the nasopharynx for core body temperature monitoring and the other on the big toe for peripheral temperature monitoring. Arterial blood gases were assessed after induction and repeated as required. A 7.5-MHz multiplaneTEE probe and system (NC, USA) was used for echo cardiographic monitoring.

In all patients, median sternotomy was performed. Heparin (300–400 IU/kg) was administered for anticoagulation and confirmed at an activated cloting time (ACT) level not less than three times the baseline level or greater than 450 s. CPB was initiated after a standard aorto-bicaval cannulation, and a membrane oxygenator and a nonpulsatile roller pump were used.

Priming solution contained lactated Ringer's solution supplemented with heparin. Fresh blood was included to achieve a hematocrit between 20 and 22% during CPB.

Preconditioning was performed just before aortic cross-clamp using isoflurane 2.5% for 10 min, followed by a 10 min washout in the isoflurane group (group I); in the sevoflurane group, sevoflurane 4% was used for 10 min, followed by a 10 min washout. Anesthesia was maintained during CPB by isoflurane 2–2.5% in group I and sevoflurane 2–4% in group S. Both groups received fentanyl (5 μg/kg) during CPB.

Moderate hypothermia between 26 and 28° was maintained during CPB.

Cold blood cardioplegia (blood : crystalloid was 1 : 3 containing K^+ 30 mEq/l and $NaHCO_3$ 26 mmol/l) was administered at a dose of 20 ml/kg and top-up doses of 10 ml/kg were administered every 25–35 min to arrest the heart and maintain cardioprotection during aortic cross-clamp.

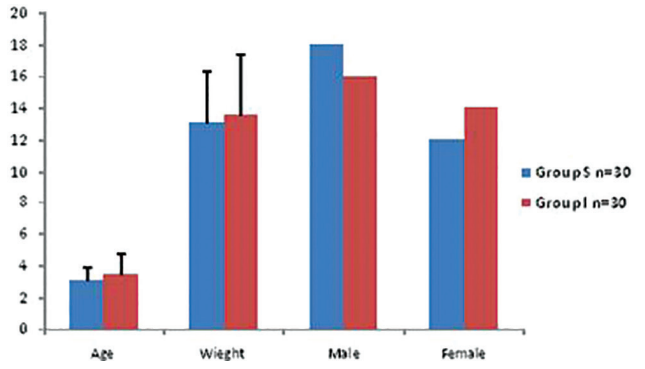
Sample size and estimation

On the basis of different levels of cTnI serum levels (measured three times), a baseline sample was obtained before cardiopulmonary bypass (T0), 8 h after bypass (T8), and 24 h after bypass (T24). Sevoflurane or isoflurane was used in 30 cases in each group. Data are described as mean ± SD; *P* values less than 0.05 were considered significant.

Statistical analysis

The data were analyzed and presented as mean, SD, median, and SEM. The two groups studied were compared using Student's *t*-test. Repeated measures of the same group were compared using two-way analysis of variance, followed by post-hoc Tukey's comparison tests. *P* value less than 0.05 were considered significant.

Figure 1



Demographic sevoflurane group. Group I, isoflurane group.

Results

Demographic data

All 60 patients were enrolled in the study. All demographic and operative data were comparable between both groups (Figs. 1 and 2, Tables 1 and 2).

Effect on cardiac troponin I values

The cTnI values showed a significant increase 8 h after CPB in both groups compared with the baseline values; there was a significant difference between the two groups.

cTnI values decreased significantly 24 h after CPB in both groups compared with the values at 8 h. In the sevoflurane group, cTnI values decreased close to the baseline values and were lower than those in the isoflurane group; however, cTnI values did not reach the baseline values and there were also no significant differences between the two groups (Table 3, Fig. 3).

Difference between acyanotic cases of sevoflurane and isoflurane groups in cardiac troponin I values

cTnI values increased in acyanotic cases of both sevoflurane and isoflurane groups at 8 h after CPB compared with the baseline values; at 24 h after CPB, cTnI values decreased in both groups, but did not reach baseline values.

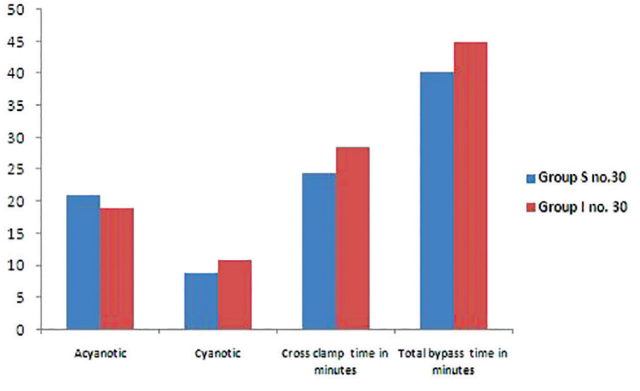
Comparison of sevoflurane and isoflurane acyanotic cases showed that cTnI values at 8 and 24 h after CPB were significantly higher in the isoflurane group (*P* = 0.02 and 0.01, respectively) (Table 4).

Table 1 Demographic data

Demographic data	Group S (*n* = 30)	Group I (*n* = 30)	*P* value
Age (years)	3.07 ± 0.83	3.47 ± 1.3	0.16
Weight	13.1 ± 3.2	13.6 ± 3.8	0.64
Sex (male/female)	18/12	16/14	0.60

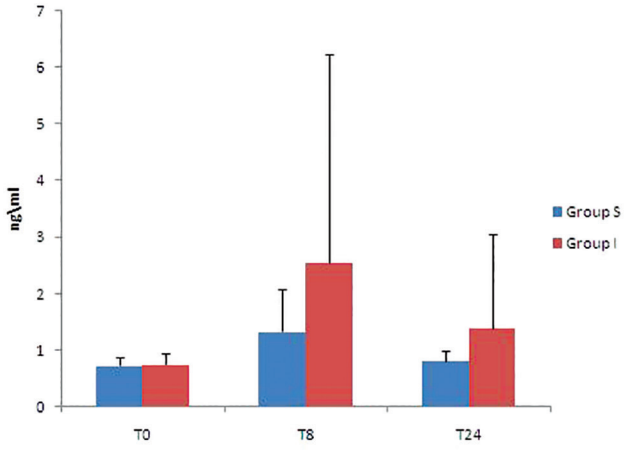
Data are described as mean ± SD; Group S, sevoflurane group; group I, isoflurane group; *P* < 0.05 is considered significant.

Figure 2



Operative date. Group S, sevoflurane group; group I, isoflurane group.

Figure 3



Cardiac troponin I (cTnI) T0, T8, and T24 in ng/ml measured in the sevoflurane and isoflurane groups.

Table 2 Operative data

Operative data	Group S (n = 30)	Group I (n = 30)	P value
Acyanotic	21 (70)	19 (63.5)	0.08
Cyanotic	9 (30)	11 (36.5)	0.079
Cross-clamp time (min)	24.5 ± 8.7	28.5 ± 7.6	0.06
Total CPB time (min)	40.2 ± 9.3	45.2 ± 11.3	0.07

Data are described as mean ± SD, ratio, or n (%);
Group S, sevoflurane group; group I, isoflurane group; $P < 0.05$ is considered significant.

Difference between cyanotic cases of sevoflurane and isoflurane groups in cardiac troponin I values

cTnI values increased in cyanotic cases of both sevoflurane and isoflurane groups at 8 h after CPB compared with the baseline values; at 24 h after CPB, cTnI values decreased in both groups compared with their values at 8 h after CPB, but did not reach baseline values.

Comparison of isoflurane and sevoflurane cyanotic cases showed that cTnI values 8 and 24 h after bypass were higher in cyanotic cases of the isoflurane group than those of the sevoflurane group, but the difference was statistically insignificant (Table 5).

Difference between cyanotic and acyanotic cardiac troponin I results in the sevoflurane group

The cTnI level 8 h after CPB was significantly higher in cyanotic cases compared with acyanotic cases (P = 0.001); it was also significantly higher in cyanotic cases 24 h after CPB (P = 0.005) (Table 6).

Difference between cyanotic and acyanotic cardiac troponin I results in the isoflurane group

cTnI values 8 h after cardiopulmonary bypass were higher in cyanotic cases compared with acyanotic cases, but this difference was insignificant (P = 0.42). At 24 h after CPB, cTnI values was significantly higher in cyanotic cases (P = 0.015) (Table 7).

Table 3 Troponin I values (ng/ml)

Troponin	Group S (n = 30)	Group I (n = 30)	P value
T0	0.73 ± 0.14	0.75 ± 0.19	0.63
T8	1.33 ± 0.76*	2.57 ± 3.7*	0.08
T24	0.87 ± 0.19**	1.38 ± 1.67**	0.1

Data are described as mean ± SD; cTnI, cardiac troponin I;
T0, cTnI baseline value; T8, cTnI value 8 h after CPB;
T24, cTnI value 24 h after CPB; group S, sevoflurane group;
group I, isoflurane group; $P < 0.05$ is considered significant;
*Statistically significant difference ($P < 0.05$) between this variable at this time and baseline value in the same group; **Statistically significant difference ($P < 0.05$) between this variable at this time and T8 in the same group.

Table 4 Results of cTnI (ng/ml) in acyanotic cases of sevoflurane and isoflurane groups

Troponin	Group S (n = 21)	Group I (n = 19)	P value
T0	0.75 ± 0.12	0.7 ± 0.18	0.2
T8	1.1 ± 0.24	2.1 ± 2.1*	0.02
T24	0.8 ± 0.17	0.94 ± 0.2*	0.01

Data are described as mean ± SD; cTnI, cardiac troponin I;
T0, cTnI baseline value; T8, cTnI value 8 h after CPB;
T24, cTnI value 24 h after CPB; group S, sevoflurane group;
group I, isoflurane group; $P < 0.05$ is considered significant;
*Statistically significant difference ($P < 0.05$) comparing the two groups at the same time.

Table 5 cTnI (ng/ml) in cyanotic cases of sevoflurane and isoflurane groups

Troponin	Group S (n = 9)	Group I (n = 11)	P value
T0	0.84 ± 0.15	0.76 ± 0.2	0.3
T8	1.86 ± 1.23	3.5 ± 5.8	0.6
T24	10.0 ± 0.18	2.2 ± 2.7	0.07

Data are described as mean ± SD; cTnI, cardiac troponin I;
T0, cTnI baseline value; T8, cTnI value 8 h after cardiopulmonary bypass; T24, cTnI value 24 h after cardiopulmonary bypass;
group S, sevoflurane group; group I, isoflurane group; $P < 0.05$ is considered significant.

Table 6 Difference between cyanotic and acyanotic results of cTnI (ng/ml) in the sevoflurane group

Troponin	Acyanotic (n = 40)	Cyanotic (n = 20)	P value
T0	0.75 ± 0.12	0.84 ± 0.15	0.08
T8	1.1 ± 0.24	1.86 ± 1.23*	0.001
T24	0.8 ± 0.17	1 ± 0.18*	0.005

Data are described as mean ± SD; cTnI, cardiac troponin I;
T0, cTnI baseline value; T8, cTnI value 8 h after CPB; T24, cTnI value 24 h after CPB; $P < 0.05$ is considered significant;
*Statistically significant difference ($P < 0.05$) comparing the two groups at the same time.

Table 7 Difference between cyanotic and acyanotic results of cTnI (ng/ml) in the isoflurane group

Troponin	Acyanotic (n = 40)	Cyanotic (n = 20)	P value
T0	0.7 ± 0.18	0.76 ± 0.2	0.5
T8	2.1 ± 2.1	3.5 ± 5.8	0.4
T24	0.94 ± 0.2	2.2 ± 2.7*	0.015

Data are described as mean ± SD; cTnI, cardiac troponin I; T0, cTnI baseline value; T8, cTnI value 8 h after CPB; T24, cTnI value 24 h after CPB; $P < 0.05$ is considered significant; *Statistically significant difference ($P < 0.05$) comparing the two groups at the same time.

Discussion

The main findings in the present study were as follows: comparison of sevoflurane and isoflurane acyanotic cases indicated that the cTnI values were significantly higher in the isoflurane group. Comparison of isoflurane and sevoflurane cyanotic cases showed that cTnI values were higher in cyanotic cases of the isoflurane group than those of the sevoflurane group, but the difference was statistically insignificant. In the isoflurane group, cTnI values were higher in cyanotic cases compared with acyanotic cases, but this difference was insignificant. In the sevoflurane group, the cTnI level was significantly higher in cyanotic cases compared with acyanotic cases.

Similar results were found by Malagon and colleagues. They compared three different anesthesia techniques with respect to their effects on myocardial protection in 90 pediatric patients scheduled for open heart surgery. Anesthesia was induced with sevoflurane, followed by a bolus of sufentanil (1 mg/kg) and pancuronium (0.2 mg/kg). For maintenance of anesthesia, patients were divided into three groups (30 patients in each group), and they received either a continuous infusion of midazolam (0.2 mg/kg/h), a continuous infusion of propofol (6–8 mg/kg/h), or sevoflurane with an end-tidal concentration of 2–3% throughout the operation. Each patient in the three groups received a continuous infusion of sufentanil (2 mg/kg/h) throughout the operation. Cardiac troponin T (cTnT) was measured at 8, 15, and 24 h after admission to ICU. Although patients in the sevoflurane group tended to have lower cTnT (mean value = 1.7) than the midazolam (mean value = 2.7) and propofol (mean value = 2.6) groups, the difference was not statistically significant [3]. cTnT concentrations were consistently higher in cyanotic patients after bypass in all three groups; however, the differences were statistically insignificant [5].

In the present study, cTnI was used as a marker of myocardial injury. Its values were significantly higher in cyanotic patients after bypass compared with acyanotic patients in both groups; however, the difference in cTnI values between sevoflurane and isoflurane cyanotic patients was insignificant.

In a trial conducted to determine why cTnI may be higher in cyanotic patients, Allen and colleagues described a phenomenon similar to reperfusion injury that occurs at the start of CPB in cyanotic patients. Their study showed that increased amounts of oxygen free radicals are generated in cyanotic infants with the initiation of CPB and this production is reduced by initiating CPB at an FiO_2 of 0.21 or by effectively filtering white blood cells. They studied 21 cyanotic patients allocated to three groups; the first group received 100% oxygen at the beginning of CPB, the second group received 21% oxygen, and the third group received 100% oxygen and underwent CPB using a leukocyte filter. Biopsies from the right atrium were taken to detect the depletion of tissue antioxidants secondary to oxygen free radical formation during reoxygenation [6].

In another study by Modi and colleagues on the effect of cyanosis on the basal metabolic state of hearts of patients with congenital heart disease, the study included 181 pediatric patients undergoing open heart surgeries (37 cyanotic and 144 acyanotic), where myocardial biopsies were taken before aortic cross-clamp and analyzed for lactate, adenine nucleotide, and purines. The study showed that cyanosis was associated with higher myocardial lactate concentrations, but with no differences in adenine nucleotide or purine content. The higher myocardial lactate content in cyanotic patients indicates a greater dependence on anaerobic metabolism for ATP production in keeping with the reduction in oxygen availability. This suggests that these hearts are more metabolically stressed and may develop tissue acidosis that leads to irreversible myocardial injury sooner during ischemia than do acyanotic hearts [7].

In the present study, cTnI values showed a significant increase at 8 h after bypass compared with the baseline values in both groups; at 24 h after bypass, the cTnI values decreased in both groups but did not reach baseline values. However, in the sevoflurane group, the T24 values were very close to the baseline values. On comparing both groups, cTnI values were lower in the sevoflurane group than the isoflurane group at both 8 and 24 h after bypass, but the difference did not reach statistical significance. However, on comparing only acyanotic cases, cTnI was significantly lower in the sevoflurane group at both 8 and 24 h after CPB, with P values of 0.02 and 0.01, respectively.

Postoperative cTnI concentration in the sevoflurane group was significantly lower than that in the isoflurane group, especially in acyanotic patients; also, inotropic use, duration of ventilation, and ICU stay were decreased.

Similar to the results of the present study, but in adult patients, Ceyhan and colleagues showed that sevoflurane is better than isoflurane in producing myocardial protection in adult patients undergoing coronary artery bypass graft surgery. The study included 40 patients undergoing CABG surgery allocated to two groups: in the first group (n = 20), patients received volatile anesthesia with sevoflurane at 2–4% and in the second group (n = 20), patients received isoflurane

at 1–2%. Following intubation, the patients in both groups received an infusion of remifentanil at a rate of 0.1–0.4 mg/kg/min intravenously. cTnT and creatine kinase MB (CK-MB) (markers of myocardial injury) were significantly lower in the sevoflurane group ($P < 0.001$) [8].

The cardioprotective effects of sevoflurane may depend on the concentration used. A recent laboratory investigation reported beneficial effects with 1.0 minimum alveolar concentration (MAC). Lower concentrations often showed no effect [8].

Several studies have reported the cardioprotective effect of sevoflurane. In a study carried out by Julier and colleagues, 72 patients undergoing CABG surgery were allocated to two groups. In the first group, sevoflurane 4% was administered during the first 10 min of CPB just before aortic cross-clamping without washout. The other group received an oxygen/air mixture without sevoflurane; in both groups, anesthesia was maintained with propofol infusion during the rest of the procedure. A significantly lower postoperative release of brain natriuretic peptide – a sensitive biochemical marker of myocardial contractile dysfunction – was observed in the sevoflurane group [9].

In another study on sevoflurane, Pouzet and colleagues could associate the administration of a volatile anesthetic to activation of protein kinase C. During the first 10 min of CPB, 10 patients were treated with sevoflurane 2.5 MAC through the gas mixture delivered to the oxygenator. In the control group, patients received 10 min of sevoflurane-free CPB. In this protocol, no washout period was present, and the aorta was cross-clamped at the completion of the 10-min treatment (or after a time-matched period of sevoflurane-free CPB in the control patients). The primary endpoint variables in this study were the myocardial tissue levels of protein kinase C, tyrosine kinase, and p38 mitogen-activated protein kinase, all of which have been linked to the signal transduction of both ischemic and anesthetic preconditioning. These kinases were obtained from right atrial biopsies that were taken before and 10 min after CPB. Sevoflurane induced a significant increase in tyrosine kinase activity, which was not observed in the control patients. Although the postoperative troponin I levels tended to be lower in the sevoflurane group, there was no statistical difference between the two groups [10].

Cromheecke and colleagues also studied the cardioprotective effect of sevoflurane on patients undergoing aortic valve surgeries. They studied 30 patients allocated to two groups: the first group received a continuous intravenous infusion of propofol and the second group received sevoflurane. Both groups received an infusion of remifentanil throughout the procedure. Postbypass cTnI was significantly lower in the sevoflurane group, and the sevoflurane group also had significantly higher stroke volume [11].

Tomai and colleagues studied the effects of an isoflurane preconditioning protocol in coronary surgery patients. Forty consecutive patients were assigned randomly to receive either no pretreatment (control group) or a pretreatment with isoflurane for about 15 min until an end-tidal concentration of 1.5% was achieved. This was followed by a 10-min washout period, after which CPB was started. Compared with before CPB, the hemodynamic variables (cardiac index, left ventricular stroke work index, ejection fraction) remained unchanged after CPB in both groups. Troponin I and CK-MB values increased transiently in the postoperative period, but this increase was similar in both groups. However, when the comparisons were restricted to those patients with a preoperative ejection fraction less than 50%, 24 h postoperative release of CK-MB and troponin I were lower in the isoflurane-treated group ($n = 9$) than in the control group ($n = 11$) [12].

In another study by Lee and colleagues on 40 patients scheduled for elective coronary artery bypass graft operations, a similar preconditioning protocol was used in the form of isoflurane 2.5 MAC administered for 15 min, followed by a 5-min washout period before aortic cross-clamping. The control group received a time-matched period of isoflurane-free cardiopulmonary bypass. Hemodynamic data, troponin I release, and inotropic support were assessed and recorded perioperatively. In the isoflurane group, the mean cardiac index after cardiopulmonary bypass was significantly higher than the prebypass value ($P < 0.05$), whereas no difference was found in the control group. At 15 min after cardiopulmonary bypass and 6 h after surgery, the changes in the cardiac index and stroke volume index were significantly higher in the isoflurane group than in the control group ($P < 0.05$). Compared with the controls, the mean troponin I level was significantly reduced in the isoflurane group at 24 h after surgery ($P = 0.042$) [13].

Haroun-Bizri and colleagues also studied the effect of isoflurane on the cardiac index. They assigned 49 patients to two groups. In the study group, anesthesia was supplemented during the pre-CPB period with isoflurane, which was titrated to a concentration of 0.5–2%; in the control group, no inhalational anesthetic was administered. After CPB, the cardiac index was higher in the isoflurane treatment group [14].

Recently, anesthetic preconditioning paralleled that of ischemic preconditioning. The use of volatile anesthetics as preconditioning agents in high-risk patients undergoing cardiac and noncardiac surgeries can potentially reduce morbidities and mortalities [15].

However, the cellular mechanism of anesthetic preconditioning has not been fully investigated in terms of the possible protective mechanism. Involves adenosine, adenosine receptors protein kinase C play the central role in detecting anesthetic preconditioning [16].

The results showed that sevoflurane is superior to isoflurane in producing better preservation and protection against myocardial injury only in acyanotic cases, with no difference in cyanotic cases.

This study reported only one parameter of measurement; another method of measurement and detection, for example transesophageal echocardiography, may be used for better accuracy of gross cardiac function and cellular level investigations.

To apply it on complex congenital heart disease cases which take prolonged by pass time.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

References

1 De Hert SG. Cardioprotection with volatile anesthetics: clinical relevance. Curr Opin Anaesthesiol 2004; 17:57–62.

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

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

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

5 Malagon I, Hogenbirk K, van Pelt J, Hazekamp MG, Bovill JG. Effect of three different anaesthetic agents on the postoperative production of cardiac troponin T in paediatric cardiac surgery. Br J Anaesth 2005; 94:805–809.

6 Allen BS, Rahman S, Ilbawi MN, Kronon M, Bolling KS, Halldorsson AO, Feinberg H. Detrimental effects of cardiopulmonary bypass in cyanotic infants: preventing the reoxygenation injury. Ann Thorac Surg 1997; 64:1381–1387.discussion 1387–1388

7 Modi P, Suleiman MS, Reeves BC, Pawade A, Parry AJ, Angelini GD, Caputo M. Basal metabolic state of hearts of patients with congenital heart disease: the effects of cyanosis, age, and pathology. Ann Thorac Surg 2004; 78:1710–1716.

8 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.

9 Julier K, da Silva R, Garcia C, Bestmann L, Frascarolo P, Zollinger A, *et al.* Preconditioning by sevoflurane decreases biochemical markers for myocardial and renal dysfunction in coronary artery bypass graft surgery: a double-blinded, placebo-controlled, multicenter study. Anesthesiology 2003; 98:1315–1327.

10 Pouzet B, Lecharny JB, Dehoux M, Paquin S, Kitakaze M, Mantz J, Menasché P. Is there a place for preconditioning during cardiac operations in humans? Ann Thorac Surg 2002; 73:843–848.

11 Cromheecke S, Pepermans V, Hendrickx E, Lorsomradee S, Ten Broecke PW, Stockman BA, *et al.* Cardioprotective properties of sevoflurane in patients undergoing aortic valve replacement with cardiopulmonary bypass. Anesth Analg 2006; 103:289–296.table of contents

12 Tomai F, De Paulis R, Penta de Peppo A, 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.

13 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.

14 Haroun-Bizri S, Khoury SS, Chehab IR, Kassas CM, Baraka A. Does isoflurane optimize myocardial protection during cardiopulmonary bypass? J Cardiothorac Vasc Anesth 2001; 15:418–421.

15 Kwok WM, Aizawa K. Preconditioning of the myocardium by volatile anesthetics. Curr Med Chem Cardiovasc Hematol Agents 2004; 2:249–255.

16 Hara T, Masui K, *et al.* Cardioprotection, protein kinase C translocation and Src-protein tyrosine kinase activation mediate isoflurane-induced preconditioning in vivo: potential downstream targets of mitochondrial adenosine triphosphate-sensitive potassium channels and reactive oxygen species by anaesthetics. 2006; 55:552–559.