

*JIOM Nepal, Volume 41, Number 2, August 2019, page 45-49*

## Comparison of Sevoflurane and Isoflurane for Myocardial Protection During Coronary Artery Bypass Surgery in a Tertiary Care Center in Nepal

Priska Bastola, Bishwas Pradhan, Madindra Basnet

Department of Cardiothoracic and Vascular Anaesthesia, Maharajgunj Medical Campus, Manmohan Cardiothoracic Vascular And Transplant Center, Maharajgunj, Kathmandu, Nepal

### Corresponding author:

Priska Bastola, MBBS, MD

Department of Cardiothoracic and Vascular Anaesthesia, Maharajgunj Medical Campus, Manmohan Cardiothoracic Vascular And Transplant Center, Maharajgunj, Kathmandu, Nepal

Email: [priskasb@gmail.com](mailto:priskasb@gmail.com)

Submitted : Jun 6, 2019

Accepted : Jul 23, 2019

### ABSTRACT

#### Introduction

Myocardial protection during Coronary Artery Bypass Graft (CABG) has always been an area of concern so we aimed to evaluate the level of release of Creatine Phosphokinase (CPK-MB) and Troponin I (cTnI) at various time intervals in the first 24 hours after on pump CABG in patients receiving either Sevoflurane or Isoflurane. Furthermore clinically relevant patient outcomes were also evaluated in patients undergoing on pump coronary artery bypass grafting.

#### Methods

This was a prospective randomized trial in patients undergoing on pump coronary artery bypass graft surgery, which was conducted from January 2016 till June 2017. A total of 105 patients were enrolled out of which there were 53 in Isoflurane and 52 in Sevoflurane group who received the respective volatile anesthetic agents throughout the surgery except during bypass at 1-1.5 MAC. The primary outcome was comparison of the CPK MB and cTnI levels at 0 hr, 6 hr, 12 hr and 24 hr after surgery from baseline, whereas the secondary outcomes were duration of intensive care unit stay, usage of vasopressors and inotropes, renal dysfunction, stroke.

#### Results

No significant difference in CPK MB and cTnI levels at all time intervals in both the groups, the other secondary outcome parameters were comparable.

#### Conclusion

The study found no difference in the cardiac markers between the two anesthetics. Based on the data, Sevoflurane and Isoflurane might be used equivalently in patients undergoing coronary artery bypass graft surgery with extracorporeal circulation without any difference in their myocardial protection function.

**Keywords:** *Coronary artery bypass graft, isoflurane, myocardial injury, myocardial protection, sevoflurane*

### INTRODUCTION

Every year, over one million patients undergo cardiac surgical procedures.<sup>1</sup> Despite the improvements in myocardial protection and perioperative management, morbidity and mortality are still relevant hence reducing myocardial necrosis could have strong implications in postoperative clinical outcomes.<sup>2</sup> Prevention and adequate treatment of perioperative myocardial ischemia and its consequences are the frequent challenges of current anesthetic practice.<sup>3</sup> It has been observed that, CABG with the use of cardiopulmonary bypass (CPB) is associated with intraoperative myocardial damage, resulting in postoperative cardiac morbidity and mortality.<sup>4</sup> Anesthetic or ischemic preconditioning is a phenomenon whereby a brief exposure to

volatile anesthetic agents or exposure to several episodes of brief myocardial ischemia followed by brief reperfusion periods, respectively, protect the heart from the potentially fatal consequences of the subsequent prolonged period of myocardial ischemia and reperfusion.<sup>5</sup>

The potential benefits gained by reducing cardiac damage have led to a renewed interest in cardiac protection strategies, including pharmacologic preconditioning.<sup>6-12</sup> Trials have been conducted using volatile anesthetic agents (Isoflurane, Sevoflurane, Desflurane) at different concentrations and timing during cardiopulmonary bypass but, the myocardial protection is variable. Serum troponin concentration is a widely used biomarker of myocardial injury. A reduction in postoperative troponin release has been

Table 1. Baseline demographic variables and clinical characteristics of patients

Patient characteristics	Isoflurane (n= 53)	Sevoflurane (n=52)	p-value
Age (Mean $\pm$ SD yrs)	59.70 $\pm$ (9.2)	59.70 $\pm$ (10.10)	0.99
Weight (Mean $\pm$ SD Kg)	62.70 $\pm$ (9.7)	62 $\pm$ (9.70)	0.32
Height (Mean $\pm$ SD cm)	159.10 $\pm$ (10)	158.10 $\pm$ (11.40)	0.36
Body Surface Area (Mean $\pm$ SD Kg/m <sup>2</sup> )	1.66 $\pm$ (0.1)	1.64 $\pm$ (0.10)	0.36
Diabetes Mellitus (%)	42.50	42.20	0.60
Hypertension (%)	68.80	59.60	0.14

associated with a lower degree of myocardial damage and a better outcome.<sup>13</sup>The aim of our study was to compare the effect of Isoflurane and Sevoflurane on myocardial protection in On-pump CABG patients, quantified for cTn I and CPK-MB release.

## METHODS

This was a prospective interventional study conducted at the Manmohan cardiothoracic vascular and transplant center, Institute of medicine Tribhuvan University. It was conducted from January 2015 till June 2016 after approval by the Institutional review board (Institute of Medicine, Maharajgunj medical campus). The primary outcome variable in the study was used as the main variable to calculate the sample size. A difference in the cardiac troponin I of 2ng/ml between the Sevoflurane and Isoflurane at the end of 24 hrs postoperatively was used to calculate the sample size, where a minimum sample size of 25 in each group was calculated (with a power of 80% and an alpha error of 5%) but, to improve the power of the study we conducted the study for a period of one and half years we included a minimum of 52 patients in each study arm, the power was increased to 98%. Patients undergoing elective cardiac surgery were screened if they fulfilled the inclusion criteria of Age  $\geq$ 30 years, Elective coronary bypass surgery, Normal left ventricular function (defined as a left ventricular ejection fraction  $\geq$  55% on preoperative transthoracic echocardiography). While we excluded patients with additional surgical procedures (e.g. valve replacement/reconstruction) with recent myocardial infarction (7 days before surgery), pregnant or lactating individuals. The patients were randomly divided by computer generated random number into two groups who would receive either Sevoflurane or Isoflurane and a total of 105 patients were enrolled. There were 53 patients in Isoflurane (I) group and 52 in Sevoflurane

group (S). Baseline CPK-MB and cTnI were measured in the morning of surgery. All preoperative patients received Tab. Diazepam 10mg on the night before surgery while the other medications were stopped on the day of the surgery except for beta-blockers, nitrates, low dose aspirin. Perioperative monitoring included a 5-lead electrocardiogram, peripheral saturation and noninvasive blood pressure monitoring followed by 1mg midazolam and 3 mg morphine intravenously with supplemental oxygen at 4lt/min, then an arterial line for continuous blood pressure monitoring was placed. Anesthesia was induced in both the groups with inj. Midazolam 100microgram/kg, Inj. Morphine 0.15 mg/kg (in addition to the dose given prior) and Inj. Propofol 0.5- 1mg/kg in titration. Once adequacy of ventilation was assessed patients received vecuronium 0.15 mg/kg which was followed by endotracheal intubation after which they were maintained on either Sevoflurane or Isoflurane with oxygen flow of 3l/min to achieve a MAC of 1.5. The oxygen flow was then reduced to 1.5l/min once MAC of 1.5 was achieved. Patients received either Sevoflurane or Isoflurane until application of cross clamp after which both the groups received Propofol infusion at 100microgram/kg/min till removal of cross clamp, inhalational anesthetic agent was then resumed as per the group until the end of surgery. On reaching the intensive care unit Post-operative CPK-MB, cTnI was sent at 0hr, 6hrs, 12 hrs and 24 hrs. Continuous data were presented as mean  $\pm$  standard deviation or as median (interquartilerange) where appropriate. Categorical data were presented as numbers and percentages. Data were compared using the Student t-test, Mann-Whitney U-test, or Fisher exact test as appropriate. P values  $\leq$  0.05 were considered significant. Statistical analyses were performed using IBM SPSS Statistics version 21 (IBM Corp, Armonk, NY ).

Table 2. Intraoperative variables

Duration	Time (min)		p-value
	Isoflurane (n= 53)	Sevoflurane (n=52)	
Duration of Anesthesia (Mean $\pm$ SD)	308.48 $\pm$ (52 )	305.10 $\pm$ (64.70)	0.83
Duration of Surgery (Mean $\pm$ SD)	271.80 $\pm$ (48 )	265.50 $\pm$ (64.70)	0.74
Duration of Aortic Clamp (Mean $\pm$ SD)	65.50 $\pm$ (14.80)	70.20 $\pm$ (47.40)	0.99
Duration of CardioPulmonary Bypass (Mean $\pm$ SD)	101.50 $\pm$ (23.40)	98.70 $\pm$ (25.40)	0.72

Table 3. Preoperative and postoperative cardiac and renal function

Patient variables	Isoflurane (n= 53)	Sevoflurane (n=52)	p-value
Pre-Operative EF (%)	55	54	0.33
RWMA Pre- Operative (%)	38	39	0.78
Post-Operative EF (%)	45	48	0.67
RWMA Post - Operative (%)	49	52	0.62
Serum Creatinine Baseline (Mean $\pm$ SD mg/dl)	1.02 $\pm$ (0.80)	0.98 $\pm$ (0.50)	0.72
Serum Creatinine (at 24hrs) (Mean $\pm$ SD mg/dl)	1.37 $\pm$ (0.80)	1.23 $\pm$ (0.50)	0.58

## RESULTS

During the study period from Jan 2016 to June 2017, 105 patients qualifying and consenting were randomly assigned to receive either Sevoflurane (52 patients) or Isoflurane (53 patients). The baseline demographic and clinical characteristics of the 2 groups are summarized in Table 1 and show no statistical differences. Age, weight, height, Body surface area, diabetes mellitus, hypertension were similar in both the groups. Both the groups were similar in terms of the duration of anesthesia, surgery, aortic cross clamp time and bypass time (Table 2). The two groups had no statistically significant difference in their pre and post-operative ejection fraction and creatinine levels as shown in (Table 3). There was no difference in the duration of mechanical ventilation, reexploration, reintubation, duration of ICU stay and deaths as shown in (Table 4). Duration of inotropes used were also similar in both the groups as seen in the figure 1. Comparison of the baseline cardiac biomarkers CPK-MB (figure 2) and cTnI (figure 3) at different time intervals (0 hr, 6 hr, 12 hr and 24 hr) were not statistically significant.

## DISCUSSION

In the present study, we report that exposure of CABG patients to either Sevoflurane or Isoflurane did not result in a difference in the postoperative cardiac biomarkers (CPK-MB and cTnI) at different time intervals.

Troponin I is a reliable marker of myocardial ischemia and studies have shown that elevated values are a predictor of in-hospital death after cardiac surgery,<sup>14</sup> with a peak occurring between 10 and 20 h after surgery.<sup>15</sup> All recent prospective studies in cardiac surgery have reported positive results in myocardial protection with Isoflurane<sup>16,17</sup>

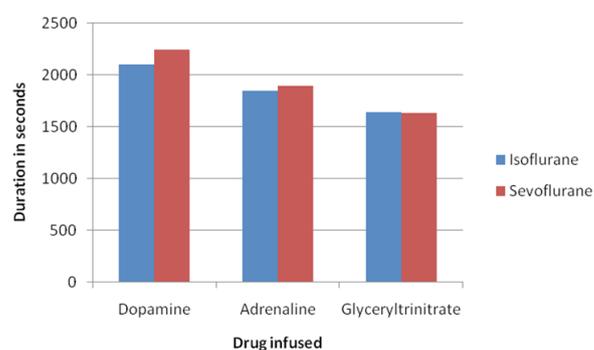


Figure 1. Duration of inotropes use

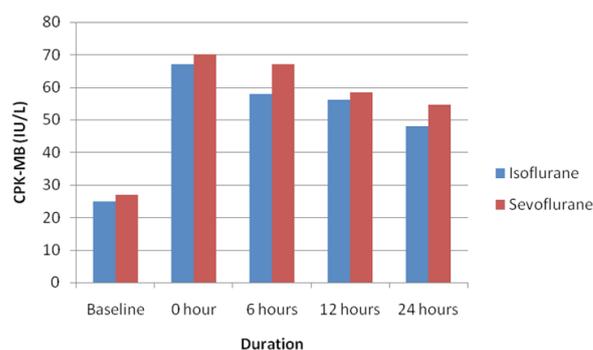


Figure 2. CPK-MB at various intervals

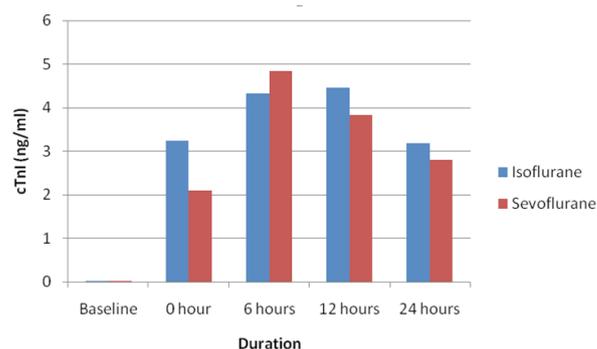


Figure 3. cTnI at various intervals

Table 4. Postoperative data in the intensive care unit

Post operative variables	Isoflurane (n= 53)	Sevoflurane (n=52)	p-value
Duration of Mechanical Ventilation (Mean $\pm$ SD min)	776 $\pm$ (75)	1160 $\pm$ (110)	0.28
Reexplored (%)	8	3	0.15
Reintubated (%)	2	3	0.57
Deaths (%)	2	4	0.33
Duration Of ICU stay (Mean $\pm$ SD Days)	3.50 $\pm$ (0.10)	3.90 $\pm$ (0.20)	0.15

or Sevoflurane preconditioning.<sup>18</sup> Either of the two agents have shown their myocardial protection ability to be superior over the other but our study showed equivalence in its ability to protect the myocardium which could be due to the difference in the study methodologies. The timing and duration of administration of volatile anesthetic agent seems to be governing the myocardial protective role which is also seen in a study by DeHert and colleagues<sup>19</sup> which showed in two groups of coronary patients where, Sevoflurane administered during all surgical procedure (before, during and after CPB) group produced a decrease in myocardial damage assessed by a decrease in postoperative troponin I levels and by an improvement of cardiac function after CPB. But, our study showed a rise in the value of the cardiac biomarkers (CPK-MB and cTnI) at 6hrs and 12 hrs postoperatively consistent to the rise seen in a study by Xia Z et al.<sup>20</sup> The rise could probably be explained by a longer aortic cross clamping of mean value of more than 65 mins in both the groups as protective effects of volatile anesthetic agents is maximal when the duration is within 35 mins.<sup>21</sup> But, we did not find any change in the regional wall motion abnormality or electrocardiography which would suggest myocardial infarction in the postoperative period.

In our study we have replaced volatile anesthetic agents during cardiopulmonary bypass by continuous propofol infusion as a part of the institutional practice. Though the role of propofol in myocardial protection has been studied due to its antioxidant<sup>22</sup> and its ability in attenuating myocardial ischemia reperfusion in animal models<sup>23-25</sup> but its effect on humans are still variable.<sup>19,26</sup> Whether propofol has contributed to myocardial protection in our patients is questionable due to its limited exposure during CPB, we consider it is an area for future studies.

One of the major strengths of this study is that it corresponds to the daily clinical practice, as we did not change the protocol of anesthetic management and surgical intervention for CABG patients. We also observed that the secondary outcomes (duration of mechanical ventilation, ICU stay) were not different in both the groups despite the discontinuation in the administration of either Sevoflurane or Isoflurane during CPB. This finding is similar to the study by Jones et al<sup>27</sup> who compared the above parameters in CABG patients receiving Sevoflurane or Isoflurane.

In summary, this prospective randomized trial, with administration of Sevoflurane and Isoflurane after induction till start of CPB, which is resumed after release of aortic cross clamp has not shown to have clinically significant difference in the major clinical outcome.

## CONCLUSION

In our study, Sevoflurane was found to be similar to Isoflurane in clinically important compatible primary

outcome of evidence of myocardial damage in terms of Troponin I and CPK-MB at different time intervals after CABG. Both of the groups were similar in terms of other clinically important secondary outcomes like duration of inotropes use, length of ICU stay. We could conclude that both of the volatile anesthetic agents could be used in patients undergoing CABG surgery.

## ACKNOWLEDGEMENT

This study was supported by the Society of Anaesthesiologist "John Sandison Research Grant."

## CONFLICT OF INTEREST

None declared.

## REFERENCES

1. Mozaffarian D, Benjamin EJ, Go AS. Heart disease and stroke statistics–2015 update: a report from the American Heart Association. *Circulation* 2015; 131:e29–322.
2. Bignami E, Guarnieri M, Pieri M. Volatile anaesthetics added to cardiopulmonary bypass are associated with reduced cardiac troponin. *Perfusion* 2017; 32 (7):547–53.
3. J. Fra<sup>o</sup>Bdorf, S. De Hert and W. Schlack. Anaesthesia and myocardial ischaemia/reperfusion. *British Journal of Anaesthesia* 2009; 103 (1): 89–98.
4. Shroyer AL, Coombs LP, Peterson ED. The Society of Thoracic Surgeons: 30-day operative mortality and morbidity risk models. *Ann Thorac Surg* 2003; 75: 1856–64.
5. Stadnicka A, Marinovic J, Ljubkovic M, Bienengraeber MW, Bosnjak ZJ. Volatile anesthetic-induced cardiac preconditioning. *J Anesth.* 2007; 21:212–19.
6. De Hert SG: The concept of anaesthetic-induced cardioprotection: Clinical relevance. *Best Pract Res Clin Anaesthesiol.* 2005; 19:445–59.
7. De Hert SG, Turani F, Mathur S, et al: Cardioprotection with volatile anesthetics: Mechanisms and clinical implications. *Anesth Analg* 2005; 100:1584–93.
8. Weber NC, Schlack W: The concept of anaesthetic-induced cardioprotection: Mechanisms of action. *Best Pract Res Clin Anaesthesiol* 2005; 19:429–43.
9. Zaugg M, Schaub MC, Foex P: Myocardial injury and its prevention in the perioperative setting. *Br J Anaesth* 2004; 93:21–33.
10. Kato R, Foex P: Myocardial protection by anaesthetic agents against ischemia-reperfusion injury: An update for anesthesiologists. *Can J Anaesth.* 2002; 49:777–91.
11. Riess ML, Stowe DF, Warltier DC: Cardiac pharmacological preconditioning with volatile anesthetics: From bench to bedside? *Am J Physiol Heart Circ Physiol.* 2004; 286:H:1603–07.
12. Piriou V, Chiari P: Con: Ischemic preconditioning is not necessary because volatile agents accomplish it. *J Cardiothorac Vasc Anesth.* 2004; 18:803–05.
13. Fellahi JL, Le Manach Y, Daccache G, et al. Combination of EuroSCORE and cardiac troponin I improves the prediction of adverse outcome after cardiac surgery. *Anesthesiology.* 2011; 114: 330–39.

14. Lasocki S, Provenche `re S, Be ´nessiano J. Cardiac troponin I is an independent predictor of in-hospital death after adult cardiac surgery. *Anesthesiology*. 2002; 97: 405–11.
15. Mongredien A, Provenche `re S, Berroeta C, Desmots JM, Philip I. Prognostic value of postoperative cTnI in cardiac surgery: comparison of Abbott and Dade assays. *Clin Chim Acta*. 2005; 354: 209–11.
16. 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: 418–21
17. 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: 841–7
18. Julier K, da Silva R, Garcia C. 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: 1315–27.
19. De Hert SG, ten Broecke PW, Mertens E. Sevoflurane but not propofol preserves myocardial function in coronary surgery patients. *Anesthesiology*. 2002; 97:42–9.
20. Xia Z, Huang Z, Ansley DM. Large-dose propofol during cardiopulmonary bypass decreases biochemical markers of myocardial injury in coronary surgery patients: a comparison with isoflurane. *Anesth Analg* 2006; 103: 527–32
21. De Hert SG, Van der Linden PJ, Cromheecke S, et al. Choice of primary anesthetic regimen can influence intensive care unit length of stay after coronary surgery with cardiopulmonary bypass. *Anesthesiology* 2004;101:9–20
22. Murphy PG, Myers DS, Davies MJ, et al. The antioxidant potential of propofol (2,6-diisopropylphenol). *Br J Anaesth* 1992; 68:613–8.
23. Xia Z, Godin DV, Ansley DM. Propofol enhances ischemic tolerance of middle-aged rat hearts: effects on 15-F(2t)-isoprostane formation and tissue antioxidant capacity. *Cardiovasc Res*. 2003; 59:113–21.
24. Ko SH, Yu CW, Lee SK, et al. Propofol attenuates ischemiareperfusion injury in the isolated rat heart. *Anesth Analg*. 1997; 85:719–24.
25. Kokita N, Hara A, Abiko Y, et al. Propofol improves functional and metabolic recovery in ischemic reperfused isolated rat hearts. *Anesth Analg*. 1998; 86:252–8.
26. Sayin MM, Ozatamer O, Tasoz R. Propofol attenuates myocardial lipid peroxidation during coronary artery bypass grafting surgery. *Br J Anaesth*. 2002; 89:242–6.
27. Jones PM, Bainbridge D, Chu M. Comparison of isoflurane and sevoflurane in cardiac surgery:a randomized non-inferiority comparative effectiveness trial. *Can J Anesth*. 2016; 63:1128–39.