

Original Research Article

Short-term outcome of patients with elevated serum cardiac troponin I following off-pump coronary artery bypass grafting

Pranab Bhattacharjee^{1*}, Istiaq Ahmed¹, A. S. M. Hossain Kabir², Tonusree Chakrabarty³, Amit Sen Gupta⁴, M. Sumaia Bin-te Shawkat⁵, Susmita Saha⁶, Mashfiq Anwar⁷

¹Department of Cardiovascular Surgery, Dhaka Medical College Hospital, Dhaka, Bangladesh

²Department of Cardiac Surgery, Sir Salimullah Medical College Mitford Hospital, Dhaka, Bangladesh

³Department of Blood Transfusion, Dhaka Medical College Hospital, Dhaka, Bangladesh

⁴Department of Surgery, Shaheed Suhrawardy Medical College Hospital, Dhaka, Bangladesh

⁵Department of Surgery, Shahid M. Monsur Ali Medical College, Sirajgonj, Bangladesh

⁶Resident Medical Officer, Asgar Ali Hospital, Dhaka, Bangladesh

⁷Clinical Attache, Glangwili General Hospital, Wales, United Kingdom

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*Correspondence:

Dr. Pranab Bhattacharjee,

E-mail: pranabarnab007@gmail.com

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ABSTRACT

Background: Coronary artery disease (CAD) is a global issue at present. It is one of the leading causes of death and disability in men and women in the USA, Western Europe and many other countries. Coronary artery bypass grafting (CABG) is the gold standard for revascularization in coronary artery disease. This study aimed to observe the short-term outcome of patients with elevated serum cardiac troponin I (cTnI) following off-pump coronary artery bypass grafting.

Methods: This was a prospective observational study and was carried out at the Department of Cardiac Surgery of the National Heart Foundation Hospital and Research Institute, Dhaka, Bangladesh during the period from July 2020 to October 2021. In this study, we included 80 patients admitted for elective CABG at National Heart Foundation Hospital and Research Institute.

Results: Among all patients, 11.3% patients had acute MI, followed by respiratory complication (11.3%), arrhythmia (10%), wound infection (6.3%), neurological complication (5%), renal complication (1.3%) and only 2.5% patients died. The mean±SD troponin I in 1st, 2nd and 3rd post operative days of the patients was 10.80±13.39, 7.99±10.39 and 4.73±6.98 respectively. The area under the recipient operational characteristic (ROC) curve was 0.931 with 95% CI were between 0.863 and 0.999, which was statistically highly significant (<0.001). There is no significant association of cTnI with respiratory, renal, neurological complications and wound infection.

Conclusions: Our findings showed that there was a significant association between raised cTnI concentrations after OPCAB surgery and adverse events in the early postoperative period.

Keywords: CAD, CABG, OPCAB, Short-term outcome, Troponin I

INTRODUCTION

Coronary artery disease (CAD) is a global issue at present. It is one of the leading causes of death and disability in men and women in the USA, Western

Europe and many other countries. CAD is not only a disease of the elderly in wealthy countries, but also it has a major global impact on working-age adults and is a growing problem in low- and middle-income countries.¹ In Bangladesh, data related to different aspects of CAD

are inadequate.² Only a limited number of small-scale epidemiological studies are available. The prevalence of CAD was 4.5%. Compared with the female 3.5%, the male participants had significantly higher prevalence of CAD 6.0%, in rural and 19.6% in an urban sample of working professionals.³ Despite marked disparity in values, there seems to be a rising prevalence of CAD throughout the world.⁴

Coronary artery bypass grafting (CABG) is the gold standard for revascularization in coronary artery disease. CABG is a technique that involves using an artery or vein from elsewhere in the body to bypass the blocked vessels, restoring adequate blood flow to the heart. The artery or vein is attached around the blockage, so that there is a new pathway for oxygenated blood to reach the heart muscle.⁵ Patients with left main disease, multivessel disease and left ventricular (LV) dysfunction benefit from CABG rather than percutaneous coronary intervention (PCI) or medical therapy.

CABG may be performed in one of three ways. CABG is commonly performed with the use of cardiopulmonary bypass (CPB) and cardioplegic arrest.⁶ Off-pump CABG is similar to traditional CABG because the sternum is opened to access the heart. However, the heart isn't stopped, and a heart-lung bypass machine isn't used. Off-pump CABG is sometimes called beating heart bypass grafting or Off-pump coronary artery bypass (OPCAB) grafting. It has gained wide acceptance due to the development of the stabilizer and associated operative techniques.⁷ It aims to relieve symptoms caused by coronary artery disease (CAD), protect the ischemic myocyte, improve ventricular function, prevent acute myocardial infarction (AMI) and prolong life as well as its quality. In the last three decades, a better understanding of the pathophysiology of atherosclerotic disease and advances in technology and surgical technique, promoted the reduction of the consequent complications to CABG.⁸

Perioperative and postoperative myocardial ischemia, leading to myocardial damage and necrosis, can occur to varying degrees after cardiac surgery. It is not always easy to identify and classify with standard ECG techniques or biochemical markers.⁹ Elevation of creatine kinase (CK) and its myocardial isoenzyme (CK-MB), as well as electrocardiographic changes, are frequent findings in the postoperative period of coronary artery bypass graft (CABG) surgery in the absence of myocardial damage. This confusion makes the diagnosis of this pathology difficult and has led to the coining of terms like 'possible' or 'probable' PMI to classify patients with post-CABG infarction.¹⁰ Cardiac troponin I (cTnI) and T (cTnT) are highly sensitive and specific markers of myocardial damage and have evolved as the "gold standard" for the diagnosis of myocardial infarction in patients presenting with an acute coronary syndrome.

Substantial biomarker elevations have been shown to be prognostically significant and usually represent coronary artery bypass grafting (CABG)-related MI. Identifying CABG-related MI using conventional electrocardiogram (ECG) and biochemical methods is difficult. Cardiac troponin I (cTnI) is a particularly sensitive biomarker introduced predominantly for risk stratification in patients with acute coronary syndrome and is the gold standard for identifying myocardial necrosis or infarction.¹¹

The diagnosis of CABG-related MI requires biomarker values more than five times the 99th percentile during the first 72 hours after CABG, together with the appearance of new pathologic Q-waves or new left bundle branch block, or angiographically documented new graft or native coronary artery occlusion, or imaging evidence of new loss of viable myocardium. Early biochemical identification of MI may enable strategies designed to limit injury, because ECG changes are commonly nonspecific. We hypothesized that certain biomarkers of injury and inflammation might provide a useful diagnostic tool for early detection of postoperative MI after CABG.

The 2012 Third Universal Definition defined postoperative myocardial infarction (PMI) after CABG as requiring two criteria: (1) cardiac biomarkers (with troponins preferred) rise >10-times 99% upper reference limit (URL) from a normal preoperative level; and (2) new pathological Q-waves or new left bundle branch block (LBBB) and/or imaging or angiographic evidence of new occlusion of native vessels or grafts, new regional wall motion abnormality, or loss of viable myocardium.¹²

Preoperative comorbidities and cardiovascular risk factors are the major determinants of postoperative complications that follow CABG. Preoperative ischemia is particularly associated with higher postoperative incidence of MI. This is compounded by postoperative tachycardia, hypotension and anemia. Indeed 71% of postoperative complications appeared in patients where the perioperative acute coronary syndrome was not resolved prior to surgical intervention.

PMI following CABG has an adverse outcome on postoperative mortality, morbidity, hospital stay as well as has negative impact on long term prognosis. It has puzzled clinicians a lot as there is lack of data from the "modern era" of cardiac surgery.¹³ Prompt diagnosis and early measure is essential for PMI management that can reduce the level of cardiac injury as well as postoperative mortality and morbidity.

In this study, we aimed to observe the short-term outcome of patients with elevated serum cardiac troponin I (cTnI) following off-pump coronary artery bypass grafting.

METHODS

This was a prospective observational study and was carried out at the Department of Cardiac Surgery of the National Heart Foundation Hospital and Research Institute, Mirpur, Dhaka, Bangladesh during the period from July 2020 to October 2021. In our study, we included 80 patients admitted for elective CABG at National Heart Foundation Hospital and Research Institute.

Inclusion criteria

Patients aged more than 18 years, patients for isolated OPCAB surgery, patients who were willing to participate in the study were included.

Exclusion criteria

Patients with acute myocardial infarction, patients with concomitant cardiac surgery, patients with emergency cardiac surgery, patients on pump CABG, patients with any history of acute illness (e.g., renal or pancreatic diseases, ischemic heart disease, asthma, COPD etc.) were excluded.

Statistical analysis

All data were recorded systematically in preformed data collection form. Quantitative data was expressed as mean and standard deviation and qualitative data was expressed as frequency distribution and percentage. Comparisons between groups were made with descriptive statistics like mean, frequency, range etc. The differences between groups were analyzed by inferential statistics like Student's t-test, and chi-square (X^2) test. When observations were recorded, a p-value of <0.05 was considered as significant. Statistical analysis was performed by using SPSS 23 (Statistical Package for Social Sciences) for Windows version 10. The study was approved by the Ethical Review Committee of National Heart Foundation Hospital and Research Institute, Mirpur, Dhaka., Bangladesh.

RESULTS

Table 1 shows the age distribution of the patients. Among 80 patients, maximum patients 37 (46.3%) were within the 55-64 years age group followed by 23 (28.7%) patients within the 45-54 years age group. The patients' mean ($\pm$ SD) age was 54.62 ($\pm$ 8.57) years with minimum and maximum ages of 34 and 71 years respectively. Maximum patients were male 77 (96.3%) and the remaining 3 (3.7) were female. The male-to-female ratio was 25.7:1.

Figure 1 shows the distribution of the patients according to risk factor profile and angiographic variables. Most (95.0%) of the patients had TVD. 58.8% patients had

HTN, 52.5% patients had DM and 21.3% patients had LMD.

Table 1: Demographic characteristics of the study patients.

Characteristics	Number of patients	Percentage
Age (years)		
<45	11	13.8
45-54	23	28.7
55-64	37	46.3
≥65	9	11.3
Mean±SD (years)	54.62 ±8.57	
Gender		
Male	77	96.3
Female	3	3.7

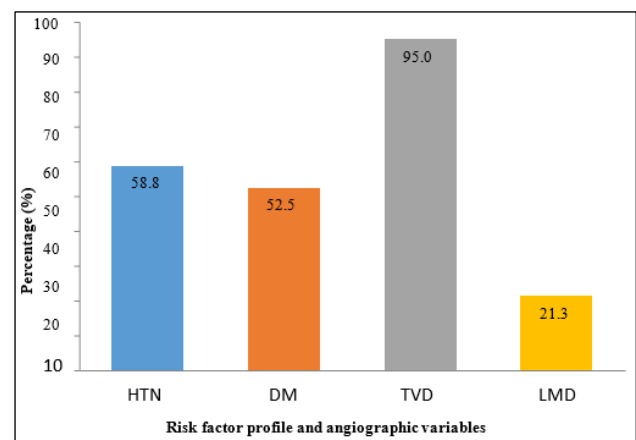


Figure 1: Bar diagram of the patients according to risk factor profile and angiographic variables (n=80).

Table 2 shows that the mean ($\pm$ SD) procedural time of the patients was 5.18 ($\pm$ 0.79) hours with minimum and maximum procedural time being 4 and 8 hours respectively. The mean ($\pm$ SD) number of grafts of the patients was 3.26 ($\pm$ 0.63) with minimum and maximum numbers of grafts being 2 and 5 respectively. The mean ($\pm$ SD) troponin I on 1st post-operative day of the patients was 10.80 ($\pm$ 13.39) and the median troponin I was 4.85 with minimum and maximum troponin I being 0.18 and 63.07 respectively. The mean ($\pm$ SD) troponin I on the patients' 2nd and 3rd post-operative days of the patients was 7.99 ($\pm$ 10.39) and 4.73 ($\pm$ 6.98) respectively. The median troponin I on the 2nd and 3rd postoperative days was 5.34 and 4.73 respectively.

Table 3 shows that MI patients having new ST change was 3.8% with Mean $\pm$ SD of troponin I on 1st POD 51.59 $\pm$ 10.47 ng/ml, having a new pathological Q wave was 6.3% with Mean $\pm$ SD of 44.34 $\pm$ 19.00 ng/ml, and having new LBBB was 3.8% with Mean $\pm$ SD of 16.00 $\pm$ 2.95 ng/ml on electrocardiogram. MI patients having new reduced ejection fraction was 8.8% with Mean $\pm$ SD of 29.52 $\pm$ 18.17 ng/ml, having new wall

motion abnormality was 11.3% with Mean±SD of 35.53±20.02 ng/ml on echocardiogram.

Table 2: Descriptive statistics of the patients according to intraoperative variables and troponin I on different days (n=80).

Intraoperative variables	Mean±SD	Min-Max
Procedural time (hrs)	5.18±0.79	4-8
Number of grafts	3.26±0.63	2-5
Troponin I		
1 st POD (ng/ml)	10.80 ± 13.39	0.18-63.07
2 nd POD (ng/ml)	7.99 ± 10.39	0.01-55.12
3 rd POD (ng/ml)	4.73 ± 6.98	0.01-45.66

Table 3: Distribution of the patients according to electrocardiogram findings and echocardiographic findings and descriptive statistics of troponin I at 1st POD (n=80).

Variables	Frequency	Percentage	Troponin I (Mean±SD)
Electrocardiogram findings			
New ST change	3	3.8	51.59±10.47
New path q	5	6.3	44.34±19.00
New LBBB	3	3.8	16.00±2.95
Echocardiograph finding			
EF reduction	7	8.8	29.52±18.17
New wall motion abnormality	9	11.3	35.53±20.02

Table 4: Distribution of the patients according to duration of mechanical ventilation, ICU stay, and hospital stay.

Duration of mechanical ventilation	Number of patients	Percentage
≤ 24 hours	59	73.8
>24 hours	21	26.3
Mean±SD (hours)	11.85±11.13	
ICU stay (days)		
≤2 days	53	66.3
>2 days	27	33.7
Mean±SD (days)	2.68±1.91	
Hospital stays (days)		
≤8 days	55	68.8
>8 days	25	31.2
Mean±SD (days)	9.04±2.23	

Table 4 shows that maximum 59 (73.8%) patients needed mechanical ventilation less than or equal to 24 hours and rest (26.3%) of patients needed mechanical ventilation more than 24 hours. Maximum 53 (66.3%) patients needed ICU support less than or equal to 2 days and remaining 27 (33.7%) patients needed ICU support more

than 2 days. Majority 55 (68.8%) of patients stayed in hospital after operation less than or equal to 8 days and rest 25 (31.2%) patients stayed in hospital after operation more than 8 days.

Table 5 shows that 11.3% of patients developed acute MI, respiratory complication involved 11.3% patients, followed by 10.0% patients had arrhythmia, 6.3% patients developed wound infection, 1.3% and 5.0% patients developed neurological complication and renal complication respectively. On the other hand, only 2.5% patients died in this study.

Table 5: Distribution of the patients according to morbidity and mortality and descriptive statistics of troponin I at 1st POD (n=80).

Morbidity and mortality			Troponin I (Mean±SD)
	Freq- uency	Percent	
Morbidity			
MI	9	11.3	35.53±20.12
Arrythmia	8	10.0	14.47±20.50
Renal complication	4	5.0	3.04±1.39
Neurological complication	1	1.3	2.72
Respiratory complication	9	11.3	8.14±7.38
Wound infection	5	6.3	8.30±8.69
Mortality	2	2.5	56.60±9.16

Table 6: Descriptive statistics of troponin I showing performance of diagnostic test.

Troponin I (ng/ml)	Disease positive	Disease negative	P value
Test positive (>6ng/ml)	8	2	10
Test negative (<6ng/ml)	1	69	70
Total	9	71	80

Chi-square test (χ^2 -test)

Table 6 showed performance of diagnostic test for Troponin I that revealed p value <0.001 which was statistically highly significant.

Figure 2 shows the receiver operator characteristics curve of increased troponin I for the prediction of developed acute MI. From the ROC curve analysis increased troponin, I cut off value was found where both sensitivity and specificity were higher than other cut off value i.e. if troponin I increased 15.11 times, then more chance to develop acute MI.

Table 7 shows that the receiver operative characteristics curve of increased troponin I for the prediction of developed acute MI. The area under the ROC curve was

0.931 with 95% CI that lay between 0.863 and 0.999, which was statistically highly significant.

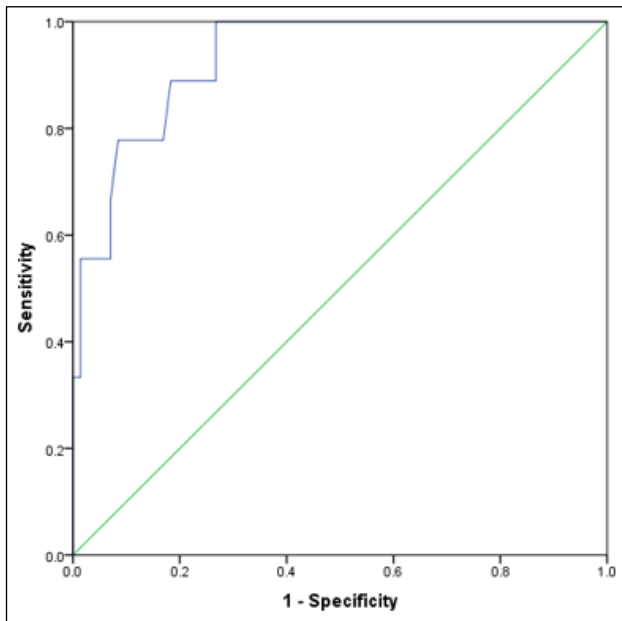


Figure 2: Receiver operating characteristics (ROC) curve of increased troponin I for the prediction of developed MI (n=80).

Table 7: Area under the curve (AUC) of receiver operative characteristics curve of increased troponin I for the prediction of developed acute MI (n=80).

Variable	AUC	95% CI	P value
Troponin I	0.931	0.863-0.999	<0.001

DISCUSSION

This study was conducted in the department of cardiac surgery of National Heart Foundation Hospital and Research Institute and this study aimed to find the impact of postoperative raised serum cardiac troponin I level on post-operative outcome following OPCAB. OPCAB was performed maintaining standard operative protocol and postoperative care was given as per standard protocol.

The study showed that the cut off value of troponin I for PMI was 15.11 ng/ml with 95% CI along with echocardiogram and/ or electrocardiographic evidence. According to the Forth Universal definition (2018), type V MI or MI following CABG is associated with an elevation of cTnI greater than ten times the upper range (0.6ng/mi) along with new changes in ECG or echocardiogram. Legare and his associates, in their study suggested that cTnI could confirm the diagnosis of postoperative myocardial infarction with a cutoff value of 10 to 15 ng /ml.¹⁴

The demographic variables of the participating patients were recorded and analyzed. Mean±SD age of study

population was 54.62 (±8.57) years with minimum and maximum age were 34 and 71 years respectively. Maximum (46.3%) patients age between 55 to 64 years, followed by 28.7% patients age between 45 to 54 years. A study carried out by Khalifa and his associates showed the mean age of study participants was 55.82±9.5years.¹⁵

Gender distribution of study population showed male predominance (96.3%). The male to female ratio were 25.7:1. This study signifies that; ischemic heart disease is more common in male. Sadony V. and his associates in their study showed that also showed male predominance (74.8%).¹⁶

Among the risk factors, 58.8% patients of study population had hypertension and 52.5% patients of study population had diabetes mellitus. A study carried out by Li and his associates showed 66.7% patients of study population had hypertension and 37.3% patients of study population had diabetes mellitus.¹⁷

Findings of coronary angiography before surgical procedure showed that most (95.0%) of the patients had triple vessel disease and 21.3% patients had left main disease. A study carried out by Mostafa and his associates showed three vessel disease was in 42% of patients and left main disease was in 20% of patients.¹²

Analysis of intraoperative variables showed the mean (±SD) procedural time of the patients were 518 (±0.79) minutes with minimum and maximum procedural time were 4 hours and 8 hours respectively. The mean (±SD) number of grafts of the patients were 3.26 (±0.63) with minimum and maximum number of grafts were 2 and 5 respectively. A study carried out by De Castro Martinez and his associates showed the mean (±SD) number of grafts of the patients were 2.3 (±0.8).¹⁰

On biochemical analysis the mean (±SD) troponin I on 1st post-operative day of the patients was 10.80 (±13.39) and the median troponin I was 4.85 with minimum and maximum troponin I being 0.18 and 63.07 respectively. The mean (±SD) troponin I on the patients' 2nd and 3rd post-operative days of the patients was 7.99 (±10.39) and 4.73 (±6.98) respectively. The median troponin I on the 2nd and 3rd postoperative days was 5.34 and 4.73 respectively.

A study carried out by Li and his associates showed the median cTnI concentrations were markedly elevated at first and second sampling times (0.140 µg/l, IQR 0.067-0.260 µg/l and 0.130 µg/l, IQR 0.063-0.340 µg/l, respectively). cTnI levels changed within 24 hours after the procedure.¹⁷

On electrocardiogram findings, the onset of new pathological Q was in 6.3% of patients and 3.8% patients had new ST change and new LBBB both. A study carried out by D. Paparella and his associates showed the number

of patients who experienced the onset of a new q-wave was 14.9%.¹⁸

On echocardiographic findings, 8.8% patients developed reduced ejection fraction compared with baseline status and 11.3% patients developed new wall motion abnormality. A study carried out by Mostafa and his associates showed mean baseline LVEF was 56±9% and mean of postoperative LVEF was 49±9% of patients.¹²

Maximum (73.8%) patients need mechanical ventilation less than or equal to 24 hours and rest (26.3%) patients need mechanical ventilation more than 24 hours. The mean (±SD) duration of mechanical ventilation of the patients were 1.185 (±1.113) days. A study carried out by Khalifa and his associates showed 10% of study participants needed mechanical ventilation more than 24 hours.¹⁵

Maximum (66.3%) patients needed ICU support less than or equal to 2 days and remaining 33.8% patients needed ICU support more than 2 days. The mean (±SD) duration of ICU stay of the patients was 2.68 (±1.91) days. Most of the patients (68.8%) stayed in hospital after operation less than or equal to 8 days and rest (31.3%) patients stayed in hospital after operation more than 8 days. The mean (±SD) duration of post operative hospital stay of the patients was 9.04 (±2.23) days. Patra and his associates in their study showed that the ICU length of stay (LOS) was for > 2days in 23.2% of study population and the hospital LOS was for >7 days in almost 60% of the study population.¹⁹

Out of all patients, 11.3% of patients developed acute MI, respiratory complication involved 11.3% patients, followed by 10.0% patients had arrhythmia, 6.3% patients developed wound infection, 1.3% and 5.0% patients developed neurological complication and renal complication respectively. On the other hand, only 2.5% patients died in this study.

Similar study carried out by Patra and his associates showed acute MI in 5.5%, atrial fibrillation in 14.6%, neurological complication in 1.7% and wound infection in 2.5% of study population.¹⁹

The area under the ROC curve was 0.931 with 95% CI were between 0.863 and 0.999, which was statistically highly significant. From the ROC curve analysis increased troponin I cut off value found where both sensitivity and specificity were higher than other cut off value; i.e. if troponin I increased 15.11 times, then more chance to develop acute MI. A study carried out by De Castro Martinez and his associates showed in the 12 patients who met criteria for PMI, the most sensitive and specific cTnI values appeared from 6 h to 10 h after aortic unclamping. At this point (10 h), cTnI>12 ng/ml resulted in a sensitivity of 90.9% (95% CI, 57.1-99.5) and a specificity of 88.5% (95% CI, 75.9-95.2), with a positive likelihood ratio of 7.88(95% CI, 3.73-17.11), negative

likelihood ratio of 0.10 (95% CI, 0.02-0.43), and an area under the curve of 0.91 (95% CI, 0.82-0.97).¹⁰

The findings of this study will greatly help cardiac surgeons to predict postoperative myocardial infarction and associated morbidities and therefore optimize management to prevent further aggravation.

This study has few limitations. This study was a single-center study. We took a small sample size due to COVID-19 pandemic. Our study only reflected the general difficulty in performing clinical studies on cardiac surgery patients while excluding patients with confounding variables. After evaluating those patients, we did not follow up with them for the long term and did not know other possible interference that may happen in the long term with these patients.

CONCLUSION

Our findings showed that there was a significant association between raised cTnI concentrations after OPCAB surgery and adverse events in the early postoperative period. Elevation of the cTnI level during early postoperative period after OPCAB surgery is associated with the development of adverse events and such data will be useful in identifying patients at an increased risk.

So further study with a prospective and longitudinal study design including a larger sample size needs to be done for early diagnosis and prompt management of postoperative myocardial infarction to reduce the adverse event to a greater extent.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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