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# Serum troponin I concentrations assessed 18-24 hours after coronary artery bypass grafting are significant predictors of early patient prognosis

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**Abstract. – OBJECTIVE: Coronary heart disease (CHD) is a frequent medical condition in developed countries and is one of the most serious diseases threatening patients' lives. Perioperative myocardial infarction is the major cause of perioperative cardiac death and cardiac arrest, but is difficult to be precisely identified by observing clinical symptoms or assessing cardiac enzyme levels or by ECG examination. Therefore, assessment of patient prognosis requires reliable predictors. In this regard, we tested the prognostic value of serum troponin I (TnI) concentrations.**

**PATIENTS AND METHODS: 98 patients undergoing elective simple off-pump coronary artery bypass grafting were recruited. Venous blood samples were collected within 3-5 hours, 18-24 hours, and 36-48 hours post-operation, and associations of TnI concentrations with early outcomes measures (duration of assisted ventilation, length of stay in the ICU, length of postoperative stay, administration of antihypotensive medications, use of intra-aortic balloon pump, and ECG abnormalities) were evaluated. Correlations of postoperative TnI concentrations with the outcomes measures were analyzed by using median TnI concentrations as the cut-off value.**

**RESULTS: TnI concentrations assessed within 18-24 hours post-operation showed significant associations with most tested outcome measures ($p < 0.05$ for four out of five comparisons). Furthermore, after building ROC curves, the highest AUC values (> 0.9) were also observed for TnI1 concentrations assessed within this time frame. The optimal cutoff value for TnI concentration was 1.78 ng/ml.**

**CONCLUSIONS: TnI concentrations assessed within 18-24 hours after elective off-pump coronary artery bypass grafting can effectively predict early patient prognosis.**

*Key Words:*
Off-pump, Coronary artery bypass grafting, Cardiac troponin I, Early prognosis.

## Introduction

Coronary heart disease (CHD) is a common cardiovascular disorder threatening patients' lives. The morbidity and mortality of CHD have been gradually rising in China and elsewhere, and there is a trend toward the disease onset at a younger age. Also, the number of patients requiring coronary artery bypass grafting (CABG) is increasing. A major short-term complication of CABG is perioperative myocardial infarction (MI). It is the major cause of perioperative cardiac death and cardiac arrest in these patients[1].

The surgery is accompanied by manual manipulation of the heart, including displacement of the heart, application of mechanical pressure, fixation of the heart by stabilizers, and suturing. These cause mechanical damages to the heart. As a result of myocardial injury, concentrations of troponin I (TnI), the protein specific to the myocardium, start rising as early as 3-5 hours after the surgery[2]. These concentrations further peak at 12-24 hours post-surgery and remain elevated for another 6-14 hours[3]. As TnI concentrations fluctuate after the operation, it is not clear whether these concentrations have prognostic values and if yes, in which time frame after the surgery should these concentrations be assessed. The goal of the present study was to assess the prognostic value of serum TnI concentrations measured at different times post-operation.

## Patients and Methods

### Patients

Between December 2013 and December 2014, 98 patients who underwent elective simple off-pump CABG at the Department of Cardiac

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Surgery of the Second Hospital of Hebei Medical University were enrolled in this study. All patients agreed to participate in this study. Study patients comprised 56 male and 42 female patients whose age ranged from 43 to 78 years ([mean ± SD] age of 60.19 ± 6.84 years). Of these patients, 26 had a prior history of MI, 54 presented with hypertension, 41 had hyperlipidemia, 33 had diabetes mellitus, 10 had neurological disorders, and 33 presented with other diseases (Table I).

### Quantification of TnI

Venous blood samples were collected at 3-5, 18-24, and 36-48 hour post coronary artery bypass grafting. TnI concentrations in these blood samples were respectively defined as TnI0, TnI1, and TnI2 throughout the manuscript. TnI was assessed by ELISA (Jianglaibio Company, Shang Hai, China).

### Preoperative Preparation and Postoperative Management

All patients underwent routine examinations before surgery, including routine blood tests and imaging. Patients presenting with severe incision pain postoperatively were immediately treated with analgesics. Patients who experienced nausea and vomiting were treated with antispasmodics.

### Outcome Measures for Early Prognosis

The following parameters were selected as outcome measures for early prognosis: (1) duration of assisted ventilation, (2) length of stay in the ICU, (3) length of postoperative stay, (4) administration of antihypotensive medications (dopamine, epinephrine, norepinephrine, levosimendan, all delivered by a micro-infusion pump), (5) use of intra-aortic balloon pump, and (6) ECG abnormalities (pathological Q wave, ST-segment elevation or depression, left bundle branch block, T-wave inversion, etc.).

### Statistical Analysis

Data were expressed as absolute numbers and percent, or as mean ± SD. Data analyses were performed by using the SPSS (SPSS Inc., Chicago, IL, USA), version 17.0. To test for association between TnI concentrations and early prognosis, data with a bivariate normal distribution were analyzed using the Pearson correlation analysis, and non-normally distributed data with the Spearman rank correlation test. A Receiver Operating Characteristic (ROC) curve was built to evaluate the predictive value of postoperative serum TnI concentrations for early prognosis. The area under the curve (AUC) of > 0.7 was considered as having predictive value. The $p < 0.05$ was considered statistically significant.

**Table I.** Clinical characteristics of study patients.

| Gender, M/F | 56/42 |
|---|---|
| Age, years | 60.19 ± 6.84 |
| Number of bypass grafts | 3.93 ± 0.701 |
| Comorbidities and risk factors, absolute number (%) | |
| Hypertension | 54 (55.1%) |
| Hyperlipidemia | 41 (41.8%) |
| Diabetes | 33 (33.6%) |
| Neurological disorders | 10 (10.2%) |
| Prior MI history | 26 (26.5%) |
| Others | 33 (33.6%) |

Data are either mean ± SD or absolute values (%). MI, myocardial infarction

## Results

### TnI Concentrations and Prognosis

Preoperative serum TnI concentrations were within the normal range in all patients (Table II). Comparisons of TnI concentrations at 3-5, 18-24, and 36-48 hours post-operation (defined as TnI0, TnI1 and TnI2) with preoperative TnI revealed statistical differences ($p < 0.05$ for all comparisons; Table II). Postoperative duration of assisted ventilation comprised 15.0 ± 20.02 hours, the length of the ICU stay was 72.02 ± 33.71 hours, and postoperative hospital stay was 11.67 ± 4.37 days. Furthermore, postoperative antihypotensive medication was administered in 26 (26.53%) patients, an intra-aortic balloon pump was applied in 3 (3.06%) patients, and ECG abnormalities

**Table II.** Clinical characteristics of study patients.

| Time point | Troponin concentrations |
|---|---|
| Before surgery | 0.00 (0.00, 0.01) |
| 3-5 hours after | 0.60 (0.30, 1.51)* |
| 12-18 hours after | 2.59 (1.27, 8.53)* |
| 36-48 after | 0.92 (0.47, 2.50)* |

Data are median (range). *$p < 0.05$ compared with before surgery.

were observed in 27 (27.55%) patients. Of these 27 patients, 2 presented with the new onset of pathological Q waves, 2 with simple left bundle branch block, 12 with ST segment abnormalities, 5 with simple T-wave inversion, 1 with the newly onset of Q wave accompanied with left bundle branch block, and 5 with ST segment abnormality complicated with T-wave inversion. Echocardiography showed segmental ventricular wall motion dysfunction in eight of these patients.

### Association of TnI0, TnI1 and TnI2 Concentrations with Early Prognosis

Correlations of postoperative TnI concentrations with the outcomes measures for early prognosis were analyzed by using median TnI concentrations as the cut-off value. We observed that TnI1 concentrations (i.e., those assessed at 18-24 hours postoperatively) showed significant associations with most tested outcome measures, ($p < 0.05$; Table III).

### Sensitivity and Specificity of Prognostic Value of TnI1 Concentrations

ROC curves were built to evaluate the sensitivity and specificity of serum TnI0, TnI1, and TnI2 concentrations as predictors of early prognosis (Figures 1A-1F). The highest AUC values were observed with TnI1 concentrations: 0.991 *vs*. administration of antihypotensive medications (Figure 1A), 0.966 *vs*. the use of intra-aortic balloon pump (Figure 1B), 0.791 *vs*. ICU stay (Figure 1C), 0.959 *vs*. the length of postoperative hospital stay (Figure 1D), 0.937 *vs*. duration of assisted ventilation (Figure 1E), and 0.980 *vs*. ECG abnormalities (Figure 1F).

### The Optimal Cut-off Value of cTnI to Predict Early Prognosis

By using 5, 10, 50, and 100 times of the upper limit of normal TnI concentrations (respectively, 0.20, 0.40, 2.0, 4.0 ng/ml) and 25%, 50%, 75%, 90% of TnI distribution (respectively, 0.29 ng/ml, 0.63 ng/ml, 1.78 ng/ml, 6.99 ng/ml) as cut-off values, TnI1 concentrations (assessed within 18-24 hours post-operation) were tested for predicting the aforementioned early prognosis outcomes (Table IV). We documented that the Tn concentration of > 1.78 ng/ml assessed post-operatively within 18-24 hours was most powerful for predicting the outcomes.

**Table III.** Correlation between TnI concentrations and early prognosis outcomes.

| Variables | r | p |
|---|---|---|
| | **TnI0** | |
| Length of ICU stay | 0.114 | 0.236 |
| Duration of assisted ventilation | 0.177 | 0.081 |
| Length of postoperative hospital stay | 0.174 | 0.087 |
| Administration of antihypotensive medications | 0.195 | 0.055 |
| IABP | 0.052 | 0.611 |
| ECG abnormalities | 0.181 | 0.075 |
| | **TnI1** | |
| Length of ICU stay | 0.434 | < 0.001 |
| Duration of assisted ventilation | 0.670 | < 0.001 |
| Length of postoperative hospital stay | 0.830 | < 0.001 |
| Administration of antihypotensive medications | 0.601 | < 0.001 |
| IABP | 0.178 | 0.080 |
| ECG abnormalities | 0.571 | < 0.001 |
| | **TnI2** | |
| Length of ICU stay | 0.206 | 0.042 |
| Duration of assisted ventilation | 0.168 | 0.099 |
| Length of postoperative hospital stay | 0.332 | 0.001 |
| Administration of antihypotensive medications | 0.231 | 0.022 |
| IABP | 0.178 | 0.080 |
| ECG abnormalities | 0.206 | 0.042 |

IABP, intra-aortic balloon pump.

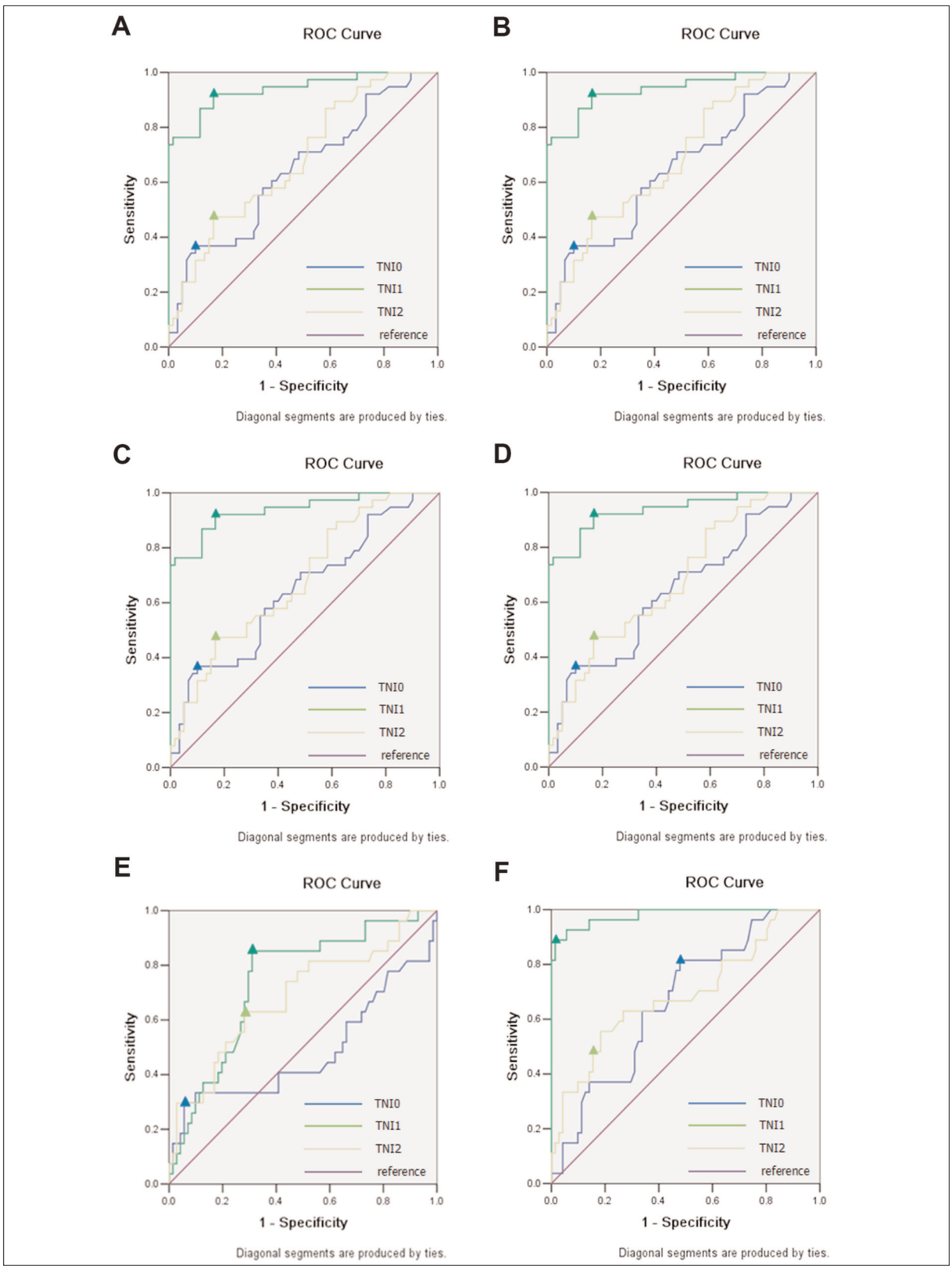


**Figure 1.** ROC curve with AUC indicating the value of TnI1 in predicting early prognosis. The prediction was based on ***(A)*** administration of antiphypotensive medications, ***(B)*** use of intra-aortic balloon pump, ***(C)*** length of ICU stay, ***(D)*** length of postoperative hospital stay, ***(E)*** duration of assisted ventilation, ***(F)*** ECG abnormalities.

**Table IV.** Sensitivity and specificity of TnI1 concentrations to predict early prognosis outcomes.

| A. | Administration of antihypotensive agents | | IABP | | Length of postoperative hospital stay | |
|---|---|---|---|---|---|---|
| TnI1 concentration, ng/ml | Sensitivity | Specificity | Sensitivity | Specificity | Sensitivity | Specificity |
| 0.20 | 100.0 | 18.5 | 100.0 | 19.2 | 100.0 | 18.8 |
| 0.29 | 100.0 | 25.8 | 100.0 | 25.6 | 100.0 | 24.4 |
| 0.40 | 100.0 | 40.5 | 100.0 | 40.7 | 100.0 | 41.1 |
| 0.63 | 100.0 | 54.2 | 100.0 | 52.3 | 100.0 | 50.3 |
| 1.78 | 100.0 | 78.6 | 80.0 | 75.4 | 67.1 | 76.2 |
| 2.00 | 100.0 | 83.1 | 80.0 | 81.2 | 67.1 | 79.6 |
| 4.00 | 100.0 | 89.2 | 80.0 | 87.2 | 67.1 | 85.1 |
| 6.99 | 90.0 | 93.4 | 80.0 | 90.4 | 67.1 | 90.3 |
| **B.** | **Duration of assisted ventilation** | | **ECG abnormalities** | | **Length of ICU stay** | |
| TnI1 concentration, ng/ml | Sensitivity | Specificity | Sensitivity | Specificity | Sensitivity | Specificity |
| 0.20 | 100.0 | 18.8 | 100.0 | 19.4 | 100.0 | 17.8 |
| 0.29 | 100.0 | 25.5 | 100.0 | 25.3 | 100.0 | 23.6 |
| 0.40 | 100.0 | 41.3 | 100.0 | 40.4 | 100.0 | 40.5 |
| 0.63 | 100.0 | 53.5 | 100.0 | 52.9 | 100.0 | 52.7 |
| 1.78 | 100.0 | 77.5 | 100.0 | 76.4 | 100.0 | 75.4 |
| 2.00 | 90.0 | 82.2 | 88.0 | 82.5 | 78.0 | 83.1 |
| 4.00 | 90.0 | 88.5 | 88.0 | 88.3 | 78.0 | 87.6 |
| 6.99 | 90.0 | 92.6 | 88.0 | 90.4 | 78.0 | 91.7 |

TnI1 concentrations were assessed 18-24 hours post-operation. IABP, intra-aortic balloon pump.

## Discussion

Coronary Heart Disease (CHD) is a frequent medical condition in developed countries and is one of the most serious diseases threatening patients' lives. Perioperative Myocardial Infarction (PMI) is the major cause of perioperative cardiac death and cardiac arrest[1]. MI is difficult to diagnose by observing clinical symptoms or by ECG examination. Therefore, patient prognosis requires reliable predictors, and in this regard we tested the prognostic value of serum TnI concentrations in this study. We recruited 98 patients undergoing elective simple off-pump coronary artery bypass grafting. Serum TnI concentrations were measured within 3-5, 18-24, and 36-48 hours post-operation. The rationale for using TnI as the predictor of early patient prognosis came from the fact that serum TnI concentrations increase after all types of cardiac surgery and are closely associated with intraoperative ischemic duration[4].

We demonstrate that TnI concentrations begin to rise within 3-5 hours, peak within 18-24 hours, and gradually decrease within 36-48 hours post-operation. Patients with higher postoperative TnI concentrations required a longer postoperative hospital stay, longer ICU stay, and longer duration of assisted ventilation. Furthermore, antihypotensive medications were administered more frequently in these patients, and there was a higher rate of intra-aortic balloon pump use and more common ECG abnormalities. It should be noted, though, that not all patients presenting with higher TnI concentrations exhibited worse prognosis. Some patients whose TnI concentrations reached more than 50 times of normal value still had a good prognosis. It is possible that other conditions can contribute TnI elevation.

The ESC/ACC/AHA and WHF definition of myocardial infarction released in October 2007 indicated that abnormal ECG changes similar to those in spontaneous MI might occur during or after coronary artery bypass grafting[5]. In addition, elevation of cardiac biochemical markers several times over the normal values (e.g., 10 × 99$^{th}$ percentile of the upper reference limit of the assay) accompanied by pathological Q wave, new onset of with left bundle branch block, new onset of occlusion of bridging vessels or coronary arteries confirmed by coronary angiography, and imaging evidence indicating new loss of viable myocardium, is considered the evidence supporting the diagnosis of MI. It has been reported[6] that serum cTnI concentrations assessed during late procedures of CABG is the key indicator to predict adverse outcomes, allowing for prediction of adverse events and timely interventions to reduce complications. Also, the following three conditions can be highly suggestive of perioperative MI: peak concentration of serum TnI of > 3.7 μg/L after elective CABG, serum TnI of > 3.1 μg/L 12 hours after aortic revascularization, or > 2.5 μg/L 24 hours after aortic revascularization[7]. Here we showed that TnI concentrations are significantly elevated in these patients. Together with abnormal changes in ECG and echocardiography, this suggests the high possibility of perioperative MI, which was treated by timely symptomatic therapy.

## Conclusions

TnI concentrations assessed within 18-24 hours after elective off-pump CABG can effectively predict early patient prognosis.

### Conflict of Interest

The Authors declare that there are no conflicts of interest.

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