Troponin-I Level After Major Noncardiac Surgery and Its Association With Long-Term Mortality

A Retrospective Cohort With a 7-Year Follow-Up Period

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SUMMARY

Individuals with intermediate to high cardiac risk for major noncardiac surgery suffer from perioperative myocardial ischemic injury. The purpose of this study was to evaluate the long-term impact of postoperative cardiac troponin elevation on clinical outcome after major noncardiac surgery.

Patients ($n = 750$) aged ≥ 50 years who underwent major noncardiac surgery were eligible for the study. Postoperative cardiac troponin-I data were collected retrospectively and consecutively. The primary outcome measure was all-cause mortality. The median follow-up period was 1727 days in all patients.

Among 750 patients, 92 (12.2%) showed elevated postoperative troponin-I above 0.10 ng/mL. Operative mortality was 4.1% (31 subjects), and patients with troponin-I elevation showed a higher operative mortality rate (RR: 4.23, 95% CI: 2.67–11.31, $P < 0.001$). In multivariate Cox regression analysis, a troponin-I concentration above 0.10 ng/mL was associated with all-cause mortality (RR: 1.73, 95% CI: 1.27–2.36, $P < 0.001$). It should be noted that there was a significant difference between patients with elevated and non-elevated troponin-I in the rate of mortality until 6 months. However, these differences disappeared after 6 months.

An elevated troponin-I level conferred an increase in mortality during the 7 year follow-up period after major noncardiac surgery. This difference in mortality was mainly derived from the result within the first 6 months. (Int Heart J 2016; 57: 278-284)

Key words: Myocardial ischemia, Death, Surgical procedures

All surgical procedures elicit a stress response, although the extent of the response depends on the extent of the surgery and the use of anesthetics and analgesics that are used to reduce the response. The stress response can lead to increases in heart rate and blood pressure, which can precipitate episodes of myocardial ischemia.¹⁾

Individuals with intermediate to high cardiac risk for noncardiac surgery suffer from perioperative myocardial ischemic injury.²⁾ Cardiac troponins are a useful tool that help clinicians in making the diagnosis of perioperative myocardial infarction.³⁻⁵⁾ Many previous studies have investigated the role of cardiac troponins in the diagnosis of perioperative myocardial ischemic events and demonstrated the prognostic value of postoperative cardiac troponin elevation.⁶⁻⁹⁾ A recent meta-analysis of studies in predominantly high-risk surgery patients also showed that cardiac troponin elevation was a strong independent predictor of mortality within the first year after surgery.¹⁰⁾

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The development of perioperative cardiovascular complications not only affects the short-term period prognosis but may also influence the long-term consequences. However, few studies have explored the long-term, defined as beyond the first year after major noncardiac surgery, prognostic value of cardiac troponin elevation in the prediction of postoperative outcome. We undertook this study to evaluate the clinical outcome of cardiac troponin elevation after major noncardiac surgery. The present study extended the follow-up period to 7 years and attempted to obtain valuable data regarding longer-term mortality.

METHODS

Study populations: Patients aged ≥ 50 years who underwent major noncardiac surgery at Dong-A University Medical Cent-

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er from January 1, 2005 to December 31, 2007 were eligible for the study. Patients with preexisting troponin-I elevations were excluded, because this study aimed to evaluate the long-term clinical impact of post-operative troponin elevation. Day-case surgical procedures were considered to be of very low risk and postprocedural troponin-I values were unavailable. Thus, patients with day-case surgery were not included. The present study was approved by the institutional review board, which allowed the use of clinical data for this study.

Data collection: Data were collected retrospectively and consecutively. All data input was done by database managers and independent research nurses who were not aware of the study and had not participated in the management and care of the study patients. Clinical characteristics, cardiovascular risk factors, and medication on admission were documented. Data quality was assessed by reviewing a random sample of 10% of all medical records. All reported events were confirmed by reviewing hospital charts or by contacting the physicians. Follow-up was conducted in all patients using medical records or telephone interviews. To improve the completeness of follow-up, death data of all patients in this study were collected from the National Statistical Office of Korea.

Measurements: Troponin-I levels were collected from laboratory results. Study participants who consented to major non-cardiac surgery underwent pre- and postoperative serum enzyme sampling. Troponin-I concentrations were measured before and at day 1 and 2 after major noncardiac surgery. In addition, serial measurements of troponin-I were also performed if clinical events were suspicious for myocardial ischemia or troponin-I of the first 2 days after noncardiac surgery was elevated. Troponin-I was measured using an Abbott AxSYM analyzer (Abbott Laboratories, Abbott Park, IL, USA) by mass immunoassay with the normal upper limit of 0.10 ng/mL specified by the manufacturer. According to the manufacturer's recommendations and based on our analyses, troponin positive was defined as a troponin-I level higher than 0.10 ng/mL. The study population was classified into troponin positive (TnP) and negative (TnN) groups according to the troponin-I level.

Study endpoint and definitions: The primary endpoint was all-cause death at any point during the follow-up period. We defined all-cause death as death from any cause during follow-up. Operative mortality was defined as death occurring during hospitalization or within 30 days of surgery. Perioperative MI was defined according to the universal definition of MI.^{8,11} Major noncardiac surgery was defined by an expected hospital length of stay of at least 2 days,^{8,12} and one of the following: abdominal-aortic surgery, peripheral vascular surgery, laparotomy including abdominal and urogenital operations, major orthopedic surgery of the hip or spinal column, and thoracotomy. The study population was classified into vascular, included abdominal-aortic surgery and peripheral vascular surgery, and non-vascular surgery groups according to the type of surgery. Diabetes mellitus (DM) was defined as a history of diabetes, a fasting plasma glucose concentration above 126 mg/dL, or the presence of therapy. Dyslipidemia and hypertension were defined as a documented history of dyslipidemia or high blood pressure requiring diet or medical therapy, respectively. Chronic kidney disease (CKD) was defined as estimated glomerular filtration rate (eGFR) < 60 mL/minute per 1.73 m² using the modification of diet in renal disease (MDRD) formula or se-

rum creatinine (Cr) > 1.5 mg/dL. The MDRD formula was defined as follows:

$$\text{eGFR} = 186 \times \text{serum Cr}^{-1.154} \times \text{Age}^{-0.203} \times (0.742 \text{ if female})$$
 where Cr concentration is in mg/dL.

Statistical analysis: Continuous variables are expressed as the mean $\pm$ SD and were analyzed by the independent *t*-test to compare the differences with the control group. Categorical variables were compared by the chi-square test or Fisher exact test. To assess the cut-off values of the independent predictors of surgical outcomes, receiver-operating characteristic (ROC) curve analysis was used. The cut-off values were selected as one with the maximal sum of sensitivity and specificity. C-statistics analysis was performed to examine the independent prediction of troponin-I level when compared with the incorporation of other clinical variables. Baseline characteristics associated with all-cause death were estimated with univariate Cox regression models and reported as relative risk (RR) with the 95% confidence interval (CI). Those with a *P* value $\leq$ 0.05 were used in the multivariate Cox regression model to identify independent predictors for all-cause mortality. Variables that were identified to have statistical significance in multivariate regression underwent Kaplan-Meier survival analysis and were then compared with the log-rank test. Univariate and multivariate logistic regression models were used to define predictors of troponin positivity. All potential preoperative predictors with *P* < 0.1 on univariate logistic analysis were included in the multivariate logistic regression analysis, and a backward conditional selection method was used for variable selection by the model. In a supplementary analysis, we investigated the dose-response relation between cardiac troponin-I and 6-month mortality by stratifying peak cardiac troponin-I concentrations into 4 groups: < 0.10 ng/mL, 0.10 to 1.00 ng/mL, 1.10 to 2.00, and > 2.10 ng/mL. The < 0.10 ng/mL group was the reference category to which the other groups were compared. Statistical analysis was performed using IBM SPSS version 21.0 for Windows (SPSS Inc., Chicago, IL, USA). All statistical tests were carried out at the 0.05 significance level.

RESULTS

Baseline characteristics: A total of 750 subjects who underwent major noncardiac surgery were included. Baseline characteristics of the study population are presented in Table I. The proportion of men and DM patients was 405 patients (54.0%) and 208 patients (27.7%), respectively. The median follow-up was 1727 days (interquartile range: 663 to 2269 days). There were 92 (12.2%) patients in the TnP group. Univariate analysis showed that CKD (*P* < 0.001), heart failure (*P* = 0.007), previous PCI (*P* = 0.002), previous MI (*P* < 0.001), and vascular surgery (*P* < 0.001) were more frequent in the TnP group. Compared with the TnN group, patients in the TnP group showed a lower ejection fraction (*P* = 0.032). When clinical variables were taken into consideration, CKD (RR: 3.71, 95% CI: 2.35–5.86, *P* < 0.001), history of previous MI (RR: 2.25, 95% CI: 1.35–3.72, *P* = 0.002), and vascular surgery (RR: 1.96, 95% CI: 1.18–3.24, *P* = 0.009) emerged as independent predictors of troponin positivity in multivariate logistic regression analysis.

Clinical outcomes: In all patients, all-cause death occurred in 288 subjects (38.4%) during the 7-year follow-up. Among

Table I. Comparison of Baseline Clinical Characteristics Between Troponin Positive Group and Troponin Negative Group

Variables	Overall population (<i>n</i> = 750)	TnP group (<i>n</i> = 92)	TnN group (<i>n</i> = 658)	<i>P</i>
Clinical variables				
Age (years)	66.79 (± 8.6)	68.2 (± 8.9)	66.6 (± 8.6)	0.103
Male - No. (%)	405 (54.0)	147 (± 0.5)	146 (± 0.5)	0.880
Hypertension - No. (%)	233 (31.1)	33 (35.9)	200 (30.4)	0.288
Diabetes mellitus - No. (%)	208 (27.7)	32 (34.8)	176 (26.7)	0.107
Chronic kidney disease - No. (%)	98 (13.1)	32 (34.8)	66 (10.0)	< 0.001
Dyslipidemia - No. (%)	46 (6.1)	5 (5.4)	41 (6.2)	0.766
Atrial fibrillation - No. (%)	53 (7.1)	7 (7.6)	46 (7.0)	0.829
Heart failure - No. (%)	49 (6.5)	12 (13.0)	37 (5.6)	0.007
Previous MI - No. (%)	76 (10.1)	22 (23.9)	64 (8.2)	< 0.001
Previous stroke - No. (%)	28 (3.7)	5 (5.4)	23 (3.5)	0.358
Previous CABG - No. (%)	12	1 (1.1)	12 (1.8)	0.513
Previous PCI - No. (%)	45	12 (13.0)	33 (5.0)	0.002
Ejection fraction (%)	58.8	57.0	59.1	0.032
Heart rate (beats/minute)	78.2 (± 9.4)	81.5 (± 12.5)	77.8 (± 8.9)	0.007
Systolic blood pressure (mmHg)	121.2 (± 15.5)	121.6 (± 18.1)	121.2 (± 15.2)	0.799
Diastolic blood pressure (mmHg)	76.7 (± 9.3)	77.2 (± 11.8)	76.6 (± 8.9)	0.602
Medications - No. (%)				
Anti-platelet agent	152 (20.3)	30 (32.6)	122 (18.5)	0.002
Loop diuretic	48 (6.4)	7 (7.6)	41 (6.2)	0.613
Beta-blocker	118 (15.7)	19 (20.7)	99 (15.0)	0.167
ACEi	133 (17.7)	23 (25.0)	110 (16.7)	0.051
CCB	163 (21.7)	23 (25.0)	140 (21.3)	0.615
Statin	56 (7.5)	7 (7.6)	49 (7.4)	0.956
Laboratory findings				
Hemoglobin (g/dL)	12.1 (± 2.0)	11.8 (± 2.4)	12.2 (± 1.9)	0.082
Platelet (× 10 ³ /mm ³)	247.6 (± 92.1)	242.0 (± 84.8)	248.4 (± 93.1)	0.499
Urea nitrogen (mg/dL)	20.8 (± 15.1)	29.2 (± 23.3)	19.6 (± 13.1)	< 0.001
Serum creatinine (mg/dL)	1.4 (± 1.6)	2.5 (± 3.0)	1.2 (± 1.3)	< 0.001
Protein (g/dL)	6.5 (± 0.9)	6.4 (± 1.0)	6.6 (± 0.9)	0.060
Albumin (g/dL)	3.8 (± 0.6)	3.7 (± 0.6)	3.8 (± 0.6)	0.007
Total cholesterol (mg/dL)	176.1 (± 43.8)	164.3 (± 47.8)	177.8 (± 43.0)	0.006
Postoperative troponin-I (ng/mL)	0.31 (± 1.89)	2.52 (± 4.86)	0.01 (± 0.02)	< 0.001
Surgical kind - No. (%)				
Vascular surgery				
Abdominal-aortic surgery	31 (4.1)	9 (9.8)	22 (3.3)	0.004
Peripheral vascular surgery	52 (6.9)	15 (16.3)	37 (5.6)	< 0.001
Non-vascular surgery				
Laparotomy	434 (57.9)	50 (54.3)	384 (58.4)	0.466
Major orthopedic surgery	213 (28.4)	14 (15.2)	199 (30.2)	0.003
Thoracotomy	20 (2.7)	4 (4.3)	16 (2.4)	0.285
Anesthesia kind - No. (%)				
General	600 (80.0)	63 (68.5)	537 (81.6)	0.428
Local	131 (17.5)	24 (26.1)	107 (16.3)	0.321
Combine (local to general)	2 (0.3)	0 (0.0)	2 (0.3)	–
Spinal	17 (2.2)	5 (5.4)	12 (1.8)	0.584

ACEi indicates angiotensin-converting-enzyme inhibitor; CCB, calcium channel blocker; MI, myocardial infarction; TnN, troponin negative; and TnP, troponin positive.

these 288 patients, 50 in the TnP group died and thus all-cause mortality was estimated to be 54.3%. Among the patients in the TnN group, 238 died during the follow-up period, and all-cause mortality was estimated to be 36.2%. Operative mortality was 4.1% (31 subjects) and the incidence of perioperative MI was 3.1% (23 subjects) in the overall population. Of these 23 patients, 16 were in the TnP group and 7 were in the TnN group. The TnP group had a higher prevalence of perioperative MI ($P < 0.001$) and a higher mortality rate ($P < 0.001$) than the TnN group. Subjects with perioperative MI had a higher long-term mortality rate (RR: 4.28, 95% CI: 1.23–15.42, $P = 0.026$). The TnP group had a higher operative mortality rate (RR: 4.23, 95% CI: 2.67–11.31, $P < 0.001$). In the follow-up death group,

46 subjects (55.4% of 83) were in the vascular surgery group and 242 subjects (36.3% of 667) were in the non-vascular surgery group. The vascular surgery group had a higher mortality rate than the nonvascular group and the difference was statistically significant (RR: 2.18, 95% CI: 1.38–3.46, $P = 0.001$). Operative mortality was not significantly different between the vascular and non-vascular groups (RR: 1.67, 95% CI: 0.94–2.98, $P = 0.078$). Eleven subjects (1.5%) had perioperative MI. The incidence of perioperative MI was higher in the vascular surgery group (RR: 7.06, 95% CI: 2.11–23.68, $P = 0.004$).

Independent predictors of all-cause death in major noncardiac surgery: In univariate Cox regression analysis, age, sex, DM, CKD, previous MI, previous stroke, ejection fraction, use of

Table II. Univariate and Multivariate Cox Regression Analysis of Predictors of All-Cause Death

	Univariate analysis		Multivariate analysis	
	RR (95% CI)	P	RR (95% CI)	P
Age (over 70 years)	1.57 (1.23 – 1.99)	< 0.001	1.62 (1.28 – 2.04)	< 0.001
Male	1.56 (1.22 – 2.03)	0.001	1.67 (1.31 – 2.13)	< 0.001
Diabetes mellitus	2.12 (1.10 – 4.30)	0.011	1.12 (0.86 – 1.45)	0.390
Chronic kidney disease	2.46 (1.32 – 3.91)	< 0.001	1.14 (0.81 – 1.59)	0.460
Previous MI	2.38 (1.24 – 4.97)	0.038	1.87 (1.31 – 2.84)	0.511
Previous stroke	2.66 (1.59 – 5.87)	0.023	1.48 (0.88 – 2.49)	0.143
Ejection fraction (< 50%)	1.92 (1.26 – 2.93)	0.003	2.10 (1.45 – 3.04)	< 0.001
Loop diuretics	2.56 (1.20 – 4.562)	0.010	1.34 (0.87 – 2.06)	0.179
Dyslipidemia	0.69 (0.48 – 0.94)	0.011	0.89 (0.68 – 1.17)	0.401
Heart rate $\geq$ 80 beats/minute	2.12 (1.28 – 3.49)	< 0.001	1.49 (1.17 – 1.88)	0.001
Hemoglobin (< 12 g/dL)	2.92 (1.97 – 4.49)	< 0.001	1.78 (1.40 – 2.26)	< 0.001
Troponin positivity	2.56 (1.93 – 3.76)	< 0.001	1.73 (1.27 – 2.36)	< 0.001
Vascular surgery	2.31 (1.38 – 3.76)	0.001	1.02 (0.71 – 1.47)	0.901

MI indicates myocardial infarction.

Figure 1. ROC curve for postoperative troponin-I for prediction of all-cause mortality. The dotted line represents the non-discrimination line. The AUC is 0.813 (95% CI: 0.69–0.93, $P < 0.001$). ROC indicates receiver-operating characteristic; and AUC, area under curve.

loop diuretics, dyslipidemia, heart rate, hemoglobin, vascular surgery, and TnP were related to all-cause death. To determine independent factors related to all-cause death, we performed multivariate Cox regression analysis (Table II). In the multivariate Cox regression, age (RR: 1.62, 95% CI: 1.28–2.04, $P < 0.001$), male gender (RR: 1.67, 95% CI: 1.31–2.13, $P < 0.001$), ejection fraction (RR: 2.10, 95% CI: 1.45–3.04, $P < 0.001$), heart rate (RR: 1.49, 95% CI: 1.17–1.88, $P = 0.001$), hemoglobin (RR: 1.78, 95% CI: 1.40–2.26, $P < 0.001$), and TnP (RR: 1.73, 95% CI: 1.27–2.36, $P < 0.001$) were independent predictors of all-cause death. Elevated troponin-I was associated with death in both univariate and multivariate analyses. In the ROC curve, the elevation of postoperative troponin-I above 0.1 ng/mL was the point of both the highest sensitivity and specificity to predict long-term mortality (Figure 1). The mean event-free survival rate estimated by Kaplan-Meier analysis

Figure 2. Seven-year cumulative incidence of all-cause death in patients in troponin-I positive and negative groups. Numbers of patients at risk are shown below each graph. Abbreviations as in Table II.

was longer in the TnN group ($P < 0.001$) (Figure 2). Such differences in long-term mortality during the 7-year follow-up period between the two groups were derived mainly from the results within the first 6 months by landmark analysis. Within the first 6 months, a difference in the all-cause death rate was observed between the TnP and TnN groups (27.1% versus 8.5%, RR: 1.63, $P < 0.001$ at Log Rank) (Figure 3). However, there was no difference in the rate of all-cause death ($P = 0.102$) from the survival curve beyond 6 months (Figure 3).

In each ROC analysis for the other independent factors, we found that a heart rate above 80 beats per minute (sensitivity 51.4%, specificity 63.2%, $P < 0.001$, area under the curve = 0.58), age above 70 years (sensitivity 53.8%, specificity 62.1%, $P < 0.001$, area under the curve = 0.61), and ejection fraction below 50% (sensitivity 86.5%, specificity 11.9%, $P = 0.020$, area under the curve = 0.45) effectively predicted all-

Figure 3. Landmark analysis of study population. Cumulative risk of all-cause death during the first 6 months and thereafter for patients with troponin-I positive (> 0.10 ng/mL) versus negative (< 0.10 ng/mL) level. Numbers of patients at risk are shown below each graph. Abbreviations as in Table II.

cause mortality. In the present study, mean hemoglobin was 12.4 ± 2.2 g/dL in men and 11.8 ± 1.7 g/dL in women. ROC curve analysis for hemoglobin was used in both males and females. The respective ROC cut-off values, yielding maximum sensitivity and specificity, were found at a cut-off point of 12.0 g/dL for both the male and female groups, as well as for the overall population (sensitivity 60.8%, specificity 56.2%, $P < 0.001$, area under the curve = 0.61). Comparison of the C-statistics showed a value of 0.61 for age, 0.53 for gender, and 0.81 for postoperative troponin-I. Postoperative troponin-I performed significantly better ($P < 0.001$) as compared with age and gender.

There was a dose-response relationship between the cardiac troponin-I concentration and 6-month mortality (Figure 4). Peak cardiac troponin-I levels were < 0.10 ng/mL in 87.7% ($n = 658$), between 0.10 and 1.00 ng/mL in 7.1% ($n = 53$), between 1.10 and 2.00 ng/mL in 2.7% ($n = 20$), and > 2.10 ng/mL in 2.5% ($n = 19$) of the patients. Six-month mortality rates in these groups were 9%, 19%, 20%, and 58%, respectively. Cardiac troponin-I > 0.10 ng/mL was associated with a significantly increased risk for 6-month mortality compared with the lowest level group.

DISCUSSION

The purpose of this study was to evaluate the value of troponin-I in long-term mortality after major noncardiac surgery in practice. The major findings of the study were as follows: 1) Patients with troponin-I elevation after major noncardiac surgery had a poor prognosis in the 7-year follow-up period. This result was mainly derived from the difference within the first 6 months. Moreover, we observed a dose-re-

Figure 4. Dose-response relation between cardiac troponin-I concentration and 6-month mortality. Peak cardiac troponin-I concentrations are categorized into 4 groups and presented with 6-month mortality rates. Numbers inside bars indicate number of deaths divided by total number of patients in each group. Odds ratios and 95% confidence intervals for mortality are shown above bars. The < 0.10 ng/mL group is the reference category to which the other groups were compared.

sponse relationship between the cardiac troponin-I concentration and 6-month mortality. There were no differences in mortality beyond 6 months. 2) Postoperative troponin-I had better prognostic accuracy than age or gender for all-cause death. Age over 70 years, male gender, lower ejection fraction less than 50%, lower hemoglobin level below 12 g/dL, and resting heart rate over 80 beats per minute were independent predictors of long-term mortality after major noncardiac surgery. However, these thresholds of heart rate, age, and hemoglobin in our study were of little use in predicting all-cause mortality considering a sensitivity of about 50%.

Cardiac troponin testing is a key diagnostic element for the diagnosis and management of patients with acute coronary syndromes. Both cardiac-specific troponin-I and troponin-T are specific and sensitive biomarkers of myocardial damage.¹¹⁾ Direct comparison of the performance of cardiac-specific troponin-I and troponin-T revealed small differences in patients with ACS, but potentially important differences that may be amplified in patients with chronic renal failure.^{13,14)} In previous studies, abnormal levels of cardiac biomarkers were proven to be statistically significant independent predictors of intermediate and long-term outcomes of cardiac events.^{4,6,8-10)} Our study showed that a postoperative troponin-I level above 0.10 ng/mL was an independent factor for long-term mortality. It is notable that there were significant differences between the TnP and TnN groups in the rate of all-cause death until 6 months. The 6-month all-cause mortality rate after major noncardiac surgery in patients with TnP and TnN was 27.1% and 8.5%, respectively. This finding was consistent with that of previous reports.^{9,15)} However, these differences were no longer significant after 6 months. This may be because stress due to noncardiac surgery might not last over 6 months,^{9,15)} and most patients that had fatal perioperative MI may die within the first 6 months.¹⁶⁾

Previous studies have suggested that the first 48 to 72 postoperative hours have the highest risk for cardiac complications after major vascular surgery.^{17,18)} Therefore, as suggested previously, the introduction of postoperative monitoring of troponin as a standard protocol might be feasible.¹⁹⁾

Troponin-I elevation can occur after noncardiac surgery in patients without coronary artery disease. In one angiographic study, nearly 50 percent of patients with perioperative acute coronary syndrome had no evidence of plaque rupture.²⁰⁾ Perioperative catecholamine changes and hypercoagulable status were present during the postoperative period.^{21,22)} The development of hypertension, hypotension, or tachycardia during surgery may lead to a myocardial oxygen supply-demand mismatch. In addition, the anemia due to surgical bleeding may cause troponin elevation. Thus, an elevated troponin level after noncardiac surgery may be a finding that represents the likely occurrence of type 2 MI.

The results of our evaluation of the data are comparable to those of recent trials.^{6,15,19)} The present cohort study estimated the incidence of troponin-I elevation after major noncardiac surgery, and troponin-I positivity above 0.10 ng/mL was found in 12.2% of the patients. Studies with vascular and other high-risk but elective surgery showed an incidence of postoperative troponin elevation of 10 to 45 percent.²³⁻²⁶⁾ The incidence of perioperative MI, as found in the present study, was 3.1%, which was not comparable to the recent observational study.¹⁹⁾ With regard to the definition, the incidence of perioperative MI is directly related to the sensitivity of the biomarker used.^{11,15)} Recently, the study by Weber, *et al* suggested that high-sensitive troponin assay provides strong prognostic information in patients undergoing noncardiac surgery incremental to the widely accepted revised cardiac index.²⁷⁾

Many trials have sought prognosticating factors in noncardiac surgery.^{4,5,6,10,21,22,27-42)} In these studies, poor functional capacity, recent MI and unstable angina, decompensated heart failure, significant arrhythmia, diabetes mellitus, renal insufficiency, cerebrovascular disease, advanced age, tachycardia, anemia, surgical kind, and elevated troponin-I level were determined to be independent prognostic factors after noncardiac surgery, most of which were in agreement with our study. While the results of those studies had been generated after short-term follow-up, the present study extended the follow-up period to 7 years and attempted to provide valuable data regarding longer term mortality. To the best of our knowledge, this study included the longest registry of patients undergoing major noncardiac surgery. Because the present study had complete follow-up in all subjects using data from the National Statistical Office of Korea, our results would be more directly applicable to routine clinical practice and may provide important insight into different clinical courses between early and late follow-up periods. In addition, patients with preexisting troponin-I elevations were excluded, because all-cause mortality can be influenced by myocardial injury which may already have occurred before major noncardiac surgery.⁶⁾ Therefore, the present study focused on postoperative troponin-I at higher levels, and could exclude the effect of preexisting troponin-I elevations.

There are several limitations to our study that should be addressed. First, the present study was conducted at a single center and employed a retrospective design. Therefore, the major limitation was possible selection bias. The high prevalence

of DM and CKD may be the result of selection bias, therefore, our cohort was a relatively high-risk population. The second major limitation was the lack of information regarding cause-specific mortality in individual patients. As a result, this study could not demonstrate the clinical relevance of troponin-I level in association with cardiac death after noncardiac surgery. We attempted to overcome this limitation by conducting follow-up for all patients. Third, because troponin-I was measured during the first 2 days after and before noncardiac surgery, myocardial damage that may have occurred after that time interval was missed. Previous research has shown that myocardial injury may occur on postoperative day 3.²⁷⁾ Furthermore, the troponin assay used was a relatively old one in a time of high sensitive troponin measures. Fourth, adverse events during noncardiac surgery were not considered, which may have affected operative mortality and all-cause mortality.

Conclusion: Patients with troponin-I elevation after major noncardiac surgery had higher mortality during the 7-year follow-up period, which was mainly derived from the result within the first 6 months. However, there were no differences in mortality beyond 6 months.

DISCLOSURE

Statement of competing interests: The authors state there are no competing interests to declare.

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