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# Association of major adverse cardiovascular events and cardiac troponin-I levels following percutaneous coronary intervention: a three-year follow-up study at a single center

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**Abstract. – OBJECTIVE: Major adverse cardiovascular events occurrences of patients with different cardiac troponin-I (cTnI) levels following percutaneous coronary intervention (PCI) remained controversial. The prognostic relevance and risk factors of PCI-related myocardial infarction (MI) were not very clear as well.**

**PATIENTS AND METHODS: Our study included 249 coronary artery disease patients without preoperative cTnI elevation who successfully accepted PCI from 2013 to 2014. A three-year follow-up was conducted for each patient. The patients were divided into PCI-related MI group and non-PCI-related MI group. Risk factors of PCI-related MI were first explored. The occurrence of MACE was recorded. The prognostic relevance between PCI-related MI (PMI) group and non-PCI-related MI group, as well as different postoperative cTnI levels, were compared.**

**RESULTS: Low-density lipoprotein cholesterol (LDL-C), age, Gensini Score, total stent length, and intra-operative complication were found positively correlated with PCI-related MI occurrence, while hemoglobin and prior PCI history were negatively correlated. After 3-year follow-up, the Kaplan-Meier survival curve showed MACE occurrence was significantly increased in PCI-related MI group. Comparing to patients with normal postoperative cTnI, MACE occurrence was increased in patients with a 10×upper limit of normal (ULN)≤cTnI<70×ULN and cTnI≥70×ULN, while there was no difference in patients with 1×ULN≤cTnI<5×ULN and 5×ULN≤cTnI<10×ULN. Cox proportional hazard regression analysis revealed PMI, NT-proBNP, and left ventricular ejection function (LVEF)<50% were positively correlated with MACE occurrence, while maximum inflation pressure and apoA-I were negatively correlated.**

**CONCLUSIONS: Prognosis of PCI-related MI was poor, as well as in patients with postoperative cTnI≥10×ULN. Among the risk factors of PMI, LDL-C, age, Gensini Score, total stent length, and intra-operative complication were positively correlated with PCI-related MI occurrence, while hemoglobin and prior PCI history were negatively correlated.**

*Key Words:*
Percutaneous coronary intervention (PCI), PCI-related myocardial infarction (PMI), Cardiac troponin I, Major adverse cardiovascular events.

## Introduction

Revascularization procedures, including percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG), are the major therapies of coronary artery disease (CAD)[1]. Peri-procedural myocardial infarction (MI) may occur after PCI or CABG, and remains one of the most common complications of revascularization procedures[2-4]. As we know, PCI is the dominant method of revascularization in China now. Therefore, our study focused on PCI-related MI, which was classified into type 4a myocardial infarction according to the Third Universal Definition of MI[4]. In this paper, type 4a MI was defined as elevation of cardiac troponin (cTn) > 5×99$^{th}$ percentile upper reference

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limit (URL) within 48 h after the procedure, and added clinical evidence of myocardial ischemia [prolonged chest pain more than 20 min, ischemic electrocardiogram (ECG) changes, angiographic evidence of a flow-limiting complication or imaging evidence of newly happened MI]. The term "myocardial injury" should be used for situations of elevation postoperative cTn without these manifestations.

Over the years, the definition of PCI-related MI (PMI) has been changing, and the biomarker has also changed from creatine kinase-MB (CK-MB) to cTn, which was more sensitive[5]. Although some reports[6] on the predictors and clinical significance of PCI-related MI used CK-MB as MI biomarker, cTn was widely used in studies exploring the prognosis of PCI[7-9]. Due to the different diagnostic criteria, risk factors and prognostic significance of peri-procedural myocardial infarction or peri-procedural myocardial injury, especially a small area of myocardial injury, remains controversial[10-14]. Even the writing Committee of Universal Definition of MI noted that the definition of PCI-related MI mentioned above was of an uncertain clinical relevance. Moreover, the new universal definition and cardiovascular magnetic resonance (CMR) for the diagnosis of small-size periprocedural myocardial damage after complex PCI was lacking of a substantial agreement according to one study[15]. Afterwards, another expert consensus proposed by the Society for Cardiac Angiography and Intervention (SCAI) defined a "clinically relevant MI" after PCI as CK-MB≥10x upper limit of normal (ULN) or cTn≥70x ULN after the operation[16].

Furthermore, risk factors of PCI-related MI remained unclear. It was not known yet whether the recognized cardiovascular risk factors such as hypertension, diabetes, and hyperlipidemia, as well as their therapeutic drugs, would affect the outcome of the operation and cause PCI-related MI. It is important to clarify the influence factors and long-term outcomes of PCI-related MI so as to develop better treatment strategies. Therefore, our work first explored the risk factors of PCI-related MI. Then, a 3-year follow-up was conducted to explore the long-term outcome of PCI-related MI and other factors influencing the prognosis after PCI. As the clinical significance of different postoperative cTn levels remained controversial, we further analyzed the 3-year outcomes of patients with different cardiac troponin I (cTnI) levels after PCI.

## Patients and Methods

### Study Population

Five hundred and eighty-eight consecutive patients undergoing PCI at the Third Affiliated Hospital of Sun Yat-sen University from January 1, 2013, to December 31, 2014, were examined. Exclusion criteria included: (1) acute myocardial infarction (AMI) occurred in 8 weeks; (2) level of preoperative cardiac troponin I (cTnI) was higher than ULN; (3) New York Heart Association (NYHA) class IV heart failure; (4) complicating with other severe disease such as severe infection, cancer, renal failure and so on; (5) severe bleeding complications such as cerebral hemorrhage or gastrointestinal hemorrhage occurred; (6) insufficient clinical data. Among these patients, 339 patients were excluded and 249 patients were eventually included in the present study (Figure 1). This research was approved by the Ethics Committee of the Third Affiliated Hospital of Sun Yat-sen University. Signed written informed consents were obtained from all the participants before the study.

### Laboratory Measurements

Fasting blood samples were collected within 3 days before PCI. Blood routine, serum biochemical items, glycosylated hemoglobin, lipid profile [including total cholesterol (TC), triglyceride (TG), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), non-high density lipoprotein choles-

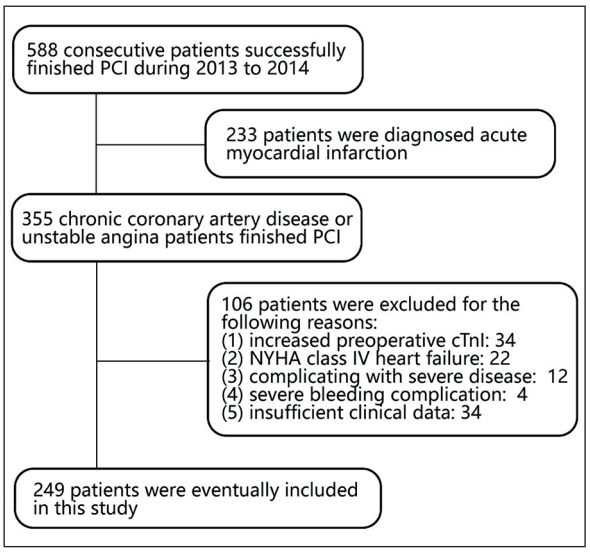


**Figure 1.** Flow chart of study population.

terol (non-HDL-C), apolipoprotein-A I (apoA-I), apolipoprotein-B100 (apoB100) and lipoprotein a (Lp(a))], N-terminal pro-brain natriuretic peptide (NT-proBNP), and high-sensitivity C-reactive protein (hsCRP) were examined. CTnI levels were determined before PCI and 24 h after PCI using the chemiluminescence method through the ADVIA Centaur chemiluminescence immune assay system. The upper limit of normal (ULN), which was defined as the 99$^{th}$ percentile of the normal population was used to replace URL. ULN of cTnI was 0.04 ng/mL of our test.

### Echocardiography and Electrocardiography

ECG was recorded before PCI and immediately after the procedure for each patient. While ischemic symptoms, such as chest pain or chest tightness appeared, ECG was checked again. Results were compared to detect the development of new ST-T changes or pathological Q wave. Ultrasonic cardiogram (UCG) was finished before PCI. Left ventricular ejection fraction (LVEF) reflecting systolic cardiac function and E/A ratio reflecting cardiac diastolic function were recorded. After PCI, UCG was performed only if PMI was highly suspected, but the diagnostic evidence was insufficient.

### Drug Therapy

Each patient received sufficient dose of aspirin, clopidogrel, and statin before the procedure (aspirin 0.1 g daily for at least 5 days or a loading dose of 0.3 g, clopidogrel 75 mg daily for at least 5 days or a loading dose of 300 mg). Dual antiplatelet was received for at least 1 year after PCI. The secondary prevention for CAD, such as angiotensin-converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB), beta-blockers, calcium channel blocker (CCB), trimetazidine or nitrates was given according to the particular condition of each patient.

### Coronary Angiography and PCI

Patients accepted coronary angiography first and PCI indication was decided by 2 experienced interventional cardiologists. PCI was performed by 3 different experienced interventional cardiologists, respectively. The severity of coronary artery lesion was evaluated by the Gensini Score[17]. Calculation of the Gensini score was initiated by giving a severity score to each coronary stenosis as follows: 1 point for ≤25% narrowing, 2 points for 26 to 50% narrowing, 4 points for 51 to 75% narrowing, 8 points for 76 to 90% narrowing, 16 points for 91 to 99% narrowing, and 32 points for total occlusion. Then, each lesion score is multiplied by a factor that takes into account the importance of the lesion's position in the coronary circulation (5 for the left main coronary artery, 2.5 for the proximal segment of the left anterior descending coronary artery, 2.5 for the proximal segment of the circumflex artery, 1.5 for the mid-segment of the left anterior descending coronary artery, 1.0 for the right coronary artery, the distal segment of the left anterior descending coronary artery, the posterolateral artery, and the obtuse marginal artery, and 0.5 for other segments). Finally, the Gensini score was calculated with the sum of the individual coronary segment scores. Parameters of PCI including intervention vessels, number of stents, total stent length, balloon expansion pressure after the procedure, and intra-operative complications (e.g., slow-flow, no-reflow, coronary artery dissection, branch artery occlusion, and malignant arrhythmia) were recorded. All stents were drug-eluting stents (DES).

### Postoperative Follow-Up and Study End Points

Follow-up was conducted every 1 year after PCI for each patient until 3 years after the operation. The occurrence of major adverse cardiovascular events (MACE) was set as the study endpoint and the occurrence time was recorded. MACE was defined as acute heart failure, recurrent MI, recurrent angina pectoris, and cardiac death[18]. Patients who died of non-cardiovascular diseases were classified into loss to follow-up.

### Statistical Analysis

Continuous data were expressed as mean ± standard deviation (SD) and categorical data were presented as a percentage. Student's *t*-test was performed to determine the differences in continuous data between groups, while the Pearson chi-square test or Fisher exactness method was performed to determine the differences in categorical data. Multivariate logistic regression analysis was used to explore the correlations between variables and PCI-related MI. Kaplan-Meier survival curves and Log-rank tests were used for the comparisons of the event-free survival rate. Cox proportional hazard regression model was performed to investigate the influence factors of prognosis after PCI. Variables selections of both multivariate logistic and Cox proportional hazard

regression analysis were made by the stepwise forward method. Threshold values for *F*-to-enter and *F*-to-remove were 0.05 and 0.1, respectively. All analyses were performed using Statistical Product and Service Solutions (SPSS) Statistics 17.0 (SPSS Inc., Chicago, IL, USA). *p*-values of <0.05 were considered significant.

## Results

### Patient Characteristics

PCI-related MI was diagnosed according to the criteria in the Third Universal Definition of MI. Among the 249 patients included, postoperative cTnI≥1×ULN, ≥5×ULN, ≥10×ULN, ≥70×ULN was detected in 160 (64.3%), 87 (34.9%), 51 (20.5%), 23 (9.2%) patients, respectively. Among them, 43 patients (17.3%) were diagnosed PCI-related MI (PMI), including 26 with prolonged chest pain, 23 with ischemic ECG changes, 6 with angiographic evidence of flow-limiting complication, and 7 with new regional wall motion abnormality detected by UCG. The baseline clinical characteristics and drug therapy of PCI-related MI (PMI) and non-PCI-related MI (non-PMI) patients are shown in Table I. In the univariate analysis, hemoglobin was lower in PCI-related MI patients while LDL-C and TC were significantly higher in PCI-related MI patients.

### PCI Parameters

CAG and PCI parameters were compared between PCI-related MI and non-PCI-related MI patients as shown in Table II. Mean Gensini Score was higher in PCI-related MI patients than in non-PCI-related MI patients. PCI-related MI patients were more likely to receive more stents and longer total stent length implanted. Operative complications, including coronary artery dissection, malignant arrhythmia, slow flow, branch artery occlusion, coronary artery spasm, and allergic shock occurred more frequently in PCI-related MI patients. Intervention vessel number, intervention vessel location, and maximum inflation pressure were not significantly different.

### Influence Factors of PMI

Influence factors of PCI-related MI were explored by multivariate logistic regression analysis. Covariates included gender, age, body mass index (BMI), type of CAD (unstable angina or not), NYHA functional class, prior PCI history, diabetes mellitus, hypertension, smoking history, family history of CAD, hemoglobin, lipid profile, creatinine, uric acid, glycosylated hemoglobin, hsCRP, NT-proBNP, LVEF, E/A ratio, mean arterial pressure, drugs, Gensini Score, number of intervention vessels, intervention vessel location, number of stents, total stent length, maximum inflation pressure, intraoperative complication, and operation doctors. Eventually, LDL-C (OR per 1-SD: 1.44, 95%CI: 1.03-2.02, $p$=0.032), age (OR per 1-SD: 1.52, 95% CI: 1.04-2.23, $p$=0.028), Gensini Score (OR per 1-SD: 1.84, 95% CI: 1.34-2.53, $p$<0.001), total stent length (OR per 1-SD: 1.62, 95%CI: 1.19-2.21, $p$=0.002), and intra-operative complication (OR: 9.08, 95% CI: 2.53-32.55, $p$=0.002) were found positively correlated with PCI-related MI occurrence, while hemoglobin (OR per 1-SD: 0.66, 95%CI: 0.47-0.94, $p$=0.021) and prior PCI history (OR: 0.20, 95%CI: 0.04-0.98, $p$=0.047) were found negatively correlated with PCI-related MI occurrence (Figure 2).

### Three-Year Outcome

During the 3 years, 2 patients in PCI-related MI group (4.6%) and 6 patients in non-PCI-related MI group (2.9%) were lost to follow-up. Among them, 2 patients (1 in PCI-related MI group and 1 in non PCI-related MI group) lost contact in the first-year follow-up, 1 patient in non PCI-related MI group lost contact in the second-year follow-up, 4 patients (1 in PCI-related MI group and 3 in non PCI-related MI group) lost contact in the third-year follow-up, and 1 patient in non PCI-related MI group died of lung cancer 20 months after PCI. Among the 241 patients finishing our 3-year follow-up, MACE occurred in 19 patients of PCI-related MI group and 24 patients of non-PCI-related MI group (44.2% *vs.* 11.7%, $p$<0.001). Patients in PCI-related MI group had significant higher cardiogenic mortality (7.0% *vs.* 1.0%, $p$=0.03) and recurrent angina pectoris rate (27.9% *vs.* 7.3%, $p$<0.001) than those in non-PCI-related MI group. Rates of acute heart failure (7.0% *vs.* 2.4%, $p$=0.288) and recurrent MI (2.3% *vs.* 1.0%, $p$=0.498) were not significantly different between the two groups. (Figure 3)

MACE occurrence was used as the endpoint in our survival analysis. Kaplan-Meier survival curve was built and the log-rank test was used to compare the different event-free survival rate of the PCI-related MI and non-PCI-related MI patients. Eventually, results showed that event-free survival rate of the PCI-related MI patients was significantly

**Table I.** Baseline clinical characteristics and drug therapy.

| | PMI (n = 43) | non-PMI (n = 206) | *p*-value |
|---|---|---|---|
| Male, n (%) | 27 (62.8%) | 146 (70.9%) | 0.295 |
| Age, y | 68.14 ± 10.37 | 65.73 ± 10.12 | 0.159 |
| BMI, kg/m$^2$ | 24.35 ± 3.21 | 24.21 ± 3.62 | 0.813 |
| Hypertension, n (%) | 36 (83.7%) | 148 (71.8%) | 0.107 |
| Diabetes mellitus, n (%) | 11 (25.6%) | 72 (35.0%) | 0.236 |
| Prior PCI, n (%) | 2 (4.7%) | 31 (15.0%) | 0.067 |
| Smoking, n (%) | 14 (32.6%) | 73 (35.4%) | 0.719 |
| Family history of CAD, n (%) | 3 (7.0%) | 19 (9.2%) | 0.860 |
| Unstable angina, n (%) | 11 (25.6%) | 60 (29.1%) | 0.640 |
| NYHA functional class | | | 0.506 |
| NYHA I class, n (%) | 13 (30.2%) | 63 (30.6%) | |
| NYHA II class, n (%) | 22 (51.2%) | 118 (57.3%) | |
| NYHA III class, n (%) | 8 (18.6%) | 25 (12.1%) | |
| Hemoglobin (g/L) | 130.35 ± 16.25 | 135.99 ± 15.65 | 0.033* |
| TC (mmol/L) | 4.77 ± 1.11 | 4.31 ± 1.30 | 0.034* |
| TG (mmol/L) | 1.49 ± 1.03 | 1.78 ± 1.72 | 0.288 |
| HDL-C (mmol/L) | 1.10 ± 0.28 | 1.03 ± 0.29 | 0.104 |
| LDL-C (mmol/L) | 3.09 ± 0.99 | 2.63 ± 1.05 | 0.009* |
| non-LDL-C (mmol/L) | 3.67 ± 1.08 | 3.29 ± 1.25 | 0.066 |
| apoAI (g/L) | 1.30 ± 0.23 | 1.28 ± 0.25 | 0.613 |
| $apoB_{100}$ (g/L) | 1.17 ± 0.23 | 1.17 ± 0.76 | 1.000 |
| Lp(a) (mg/L) | 277.38 ± 289.94 | 235.74 ± 273.38 | 0.370 |
| Creatinine (μmol/L) | 91.14 ± 32.37 | 91.03 ± 70.90 | 0.993 |
| Uric Acid (μmol/L) | 399.52 ± 99.13 | 406.90 ± 122.88 | 0.691 |
| Glycosylated hemoglobin (%) | 6.26 ± 1.06 | 6.42 ± 1.32 | 0.525 |
| HsCRP (mg/L) | 5.21 ± 6.71 | 5.05 ± 11.30 | 0.950 |
| NT-proBNPa | | | 0.386 |
| Normal, n (%) | 34 (79.1%) | 175 (85.0%) | |
| Grey zone, n (%) | 4 (9.3%) | 19 (9.2%) | |
| High, n (%) | 5 (11.6%) | 12 (5.8%) | |
| LVEF < 50%, n (%) | 5 (11.6%) | 19 (9.2%) | 0.627 |
| E/A ratio < 1, n (%) | 25 (58.1%) | 102 (49.5%) | 0.303 |
| MAPb (mmHg) | 94.37 ± 13.14 | 95.63 ± 10.70 | 0.501 |
| Drug therapy | | | |
| ACEI, n (%) | 6 (14.0%) | 25 (12.1%) | 0.743 |
| ARB, n (%) | 15 (34.9%) | 73 (35.4%) | 0.945 |
| β-blocker, n (%) | 25 (58.1%) | 96 (46.6%) | 0.169 |
| CCB, n (%) | 18 (41.9%) | 88 (42.7%) | 0.918 |
| Trimetazidine, n (%) | 26 (60.5%) | 123 (59.7%) | 0.927 |
| Nitrates, n (%) | 21 (48.8%) | 76 (36.9%) | 0.144 |

BMI, body mass index; ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker. [a]: NT-proBNP was calculated using the following classification: "normal" was < 300 pg/mL; "grey zone" was 300-450 pg/mL for < 50 years, 300-900 pg/mL for 50-75 years and 300-1800 pg/mL for > 75 years; "high" was > 450 pg/mL for <50 years, > 900 pg/mL for 50-75 years and >1800 pg/mL for > 75 years. [b]: Mean arterial pressure (MAP)=1/3* (systolic pressure) +2/3*(diastolic pressures). *$p$<0.05.

lower than the non-PCI-related MI patients ($p$<0.001) (Figure 4A). Additionally, the outcomes of different postoperative cTnI levels were explored. Patients with normal postoperative cTnI were set as control group, while patients with elevated postoperative cTnI were divided into 1×ULN≤cTnI<5×ULN, 5×ULN≤cTnI<10×ULN, 10×ULN≤cTnI<70×ULN, and cTnI≥70×ULN four groups. Survival curve showed event-free survival rates of patients with 10×ULN≤cTnI<70×ULN ($p$=0.027), and cTnI≥70×ULN ($p$=0.002) were significantly lower, while there was no significant difference between 5×ULN≤cTnI<10×ULN ($p$=0.204), 1×ULN≤cTnI<5×ULN ($p$=0.388) patients and those with normal cTnI (Figure 4B).

Multivariate analysis including covariates mentioned above and PCI-related MI showed that PCI-related MI(HR 10.32, 95%CI: 3.418-31.176, $p$<0.001), NT-proBNP (HR 3.65, 95%CI:

**Table II.** CAG and PCI parameters.

| | PMI (n = 43) | non-PMI (n = 206) | *p*-value |
|---|---|---|---|
| Gensini Score | 58.98 ± 35.09 | 38.80 ± 26.94 | 0.001* |
| Number of intervention vessels | 1.56 ± 0.67 | 1.34 ± 0.56 | 0.055 |
| Intervention vessel location | | | |
| LM, n (%) | 3 (7.0%) | 4 (1.9%) | 0.190 |
| LAD, n (%) | 32 (74.4%) | 127 (61.7%) | 0.113 |
| LCX, n (%) | 11 (25.6%) | 62 (30.1%) | 0.554 |
| RCA, n (%) | 19 (44.2%) | 69 (33.5%) | 0.182 |
| OM, n (%) | 1 (2.3%) | 7 (3.4%) | 1.000 |
| D1, n (%) | 0 (0%) | 5 (2.4%) | 0.591 |
| D2, n (%) | 0 (0%) | 1 (0.5%) | 1.000 |
| PDA, n (%) | 1 (2.3%) | 2 (1.0%) | 0.435 |
| Number of stents | 2.00 ± 0.98 | 1.58 ± 0.83 | 0.004* |
| Total stent length, mm | 57.37 ± 32.18 | 41.66 ± 27.34 | 0.004* |
| Maximum inflation pressure, atm | 15.86 ± 2.45 | 15.67 ± 2.73 | 0.672 |
| Complication, n (%) | 7 (16.3%) | 5 (2.4%) | 0.001* |
| Coronary artery dissection, n (%) | 1 (2.3%) | 3 (1.5%) | |
| Malignant arrhythmia, n (%) | 1 (2.3%) | 1 (0.5%) | |
| Slow flow, n (%) | 2 (4.7%) | 1 (0.5%) | |
| Branch artery occlusion, n (%) | 1 (2.3%) | 0 (0%) | |
| Coronary artery spasm, n (%) | 1 (2.3%) | 0 (0%) | |
| Allergic shock, n (%) | 1 (2.3%) | 0 (0%) | |
| Operation Doctor | | | 0.815 |
| Doctor A, n (%) | 8 (18.6%) | 47 (22.8%) | |
| Doctor B, n (%) | 13 (30.2%) | 62 (30.1%) | |
| Doctor C, n (%) | 22 (51.2%) | 97 (47.1%) | |

LM, left main coronary artery; LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery; OM, obtuse marginal; D1, first diagonal branch; D2, second diagonal branch; PDA, posterior descending artery. *$p$<0.05.

1.85-7.20, $p$<0.001) and LVEF<50% (HR 19.76, 95%CI: 3.48-112.23, $p$=0.001) were positively correlated with MACE occurrence, while maximum inflation pressure (HR per 1-SD 0.35, 95%CI: 0.18-0.68, $p$=0.002) and apoA-I (HR per 1-SD 0.40, 95%CI: 0.23-0.70, $p$=0.001) were negatively correlated with MACE occurrence (Figure 5).

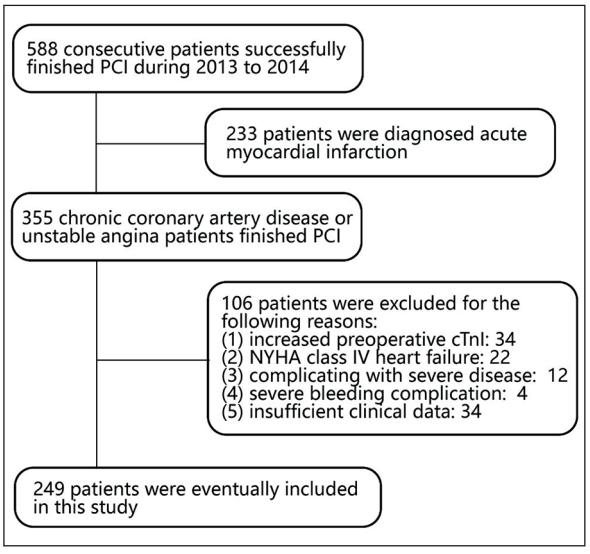


**Figure 1.** Flow chart of study population.

## Discussion

We revealed that an elevated cTnI level after PCI was relatively common, regardless of the definition of PCI-related MI. More than half of the patients had postoperative cTnI≥1×ULN and one-fifth of the patients had cTnI≥10×ULN. According to the Third Universal Definition of MI, PCI-related MI was diagnosed in 17.3% patients in our study, which was not unusual. After 3-year survival analysis, patients with PCI-related MI had a significantly worse prognosis, indicating this definition of PMI was "clinically relevant". Thus, the first part of our work exploring the influence factors of PCI-related MI became more meaningful. Finally, we found LDL-C, age, Gensini Score, total stent length, and intra-operative complication might be risk factors, while hemoglobin and prior PCI history might be protective factors.

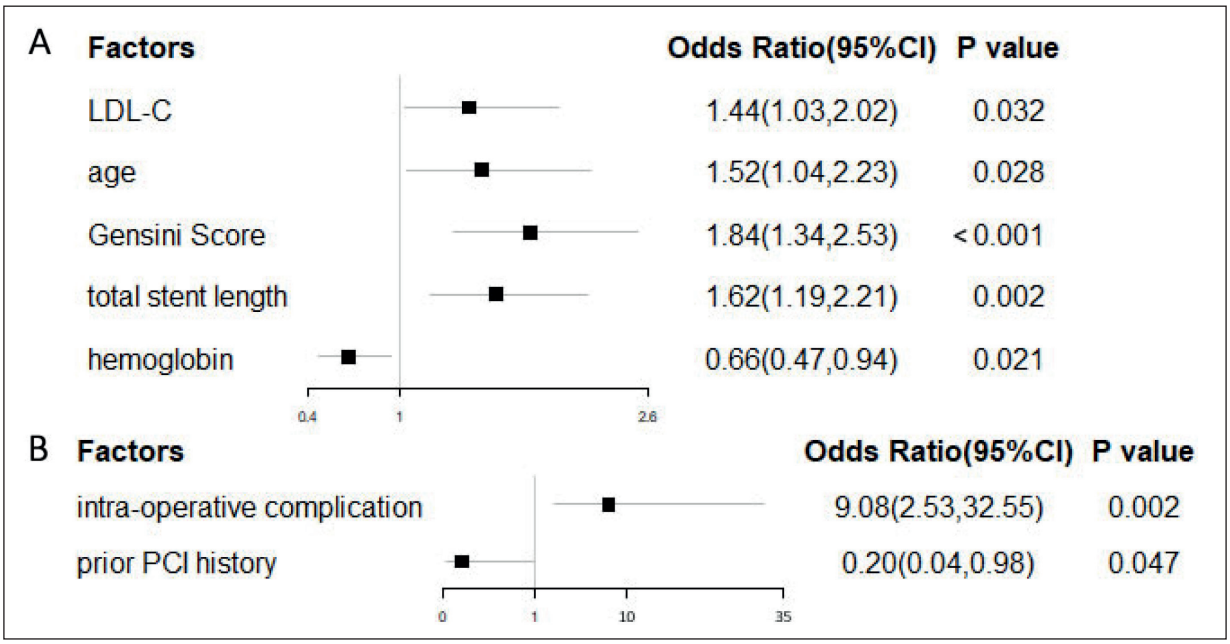


**Figure 2.** Influence factors of PCI-related MI explored by multivariate logistic regression analysis. **A,** Continuous variables (1 SD changed). **B,** Categorical variables.

As we know, LDL-C plays a key role in the development and progression of atherosclerotic plaque and coronary heart disease[19]. Although several studies[20-22] have demonstrated that preoperative statin treatment was beneficial to prevent PCI-related MI, there is yet no direct evidence to prove the correlation of LDL-C level and occurrence of PCI-related MI. The multivariate logistic regression analysis in our study showed that as LDL-C increased 1-SD, the risk of PCI-related MI increased 44%, indicating that LDL-C was a risk factor of PCI-related MI. We suggested

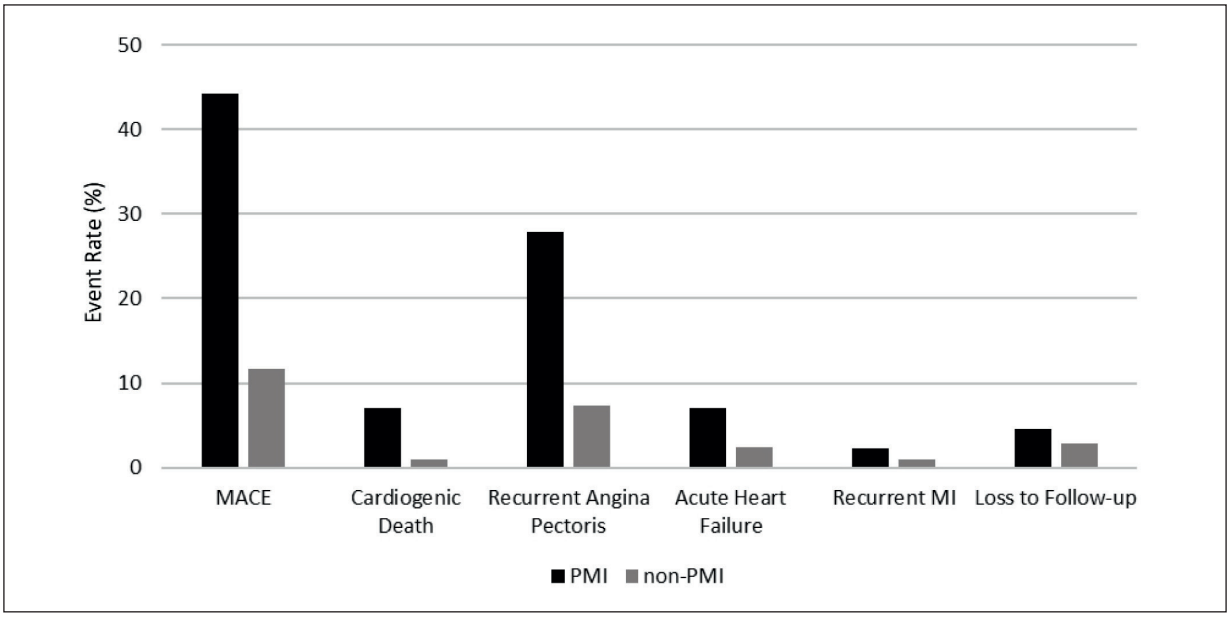


**Figure 3.** Three-year outcomes in the PCI-related MI and non-PCI-related MI patients.

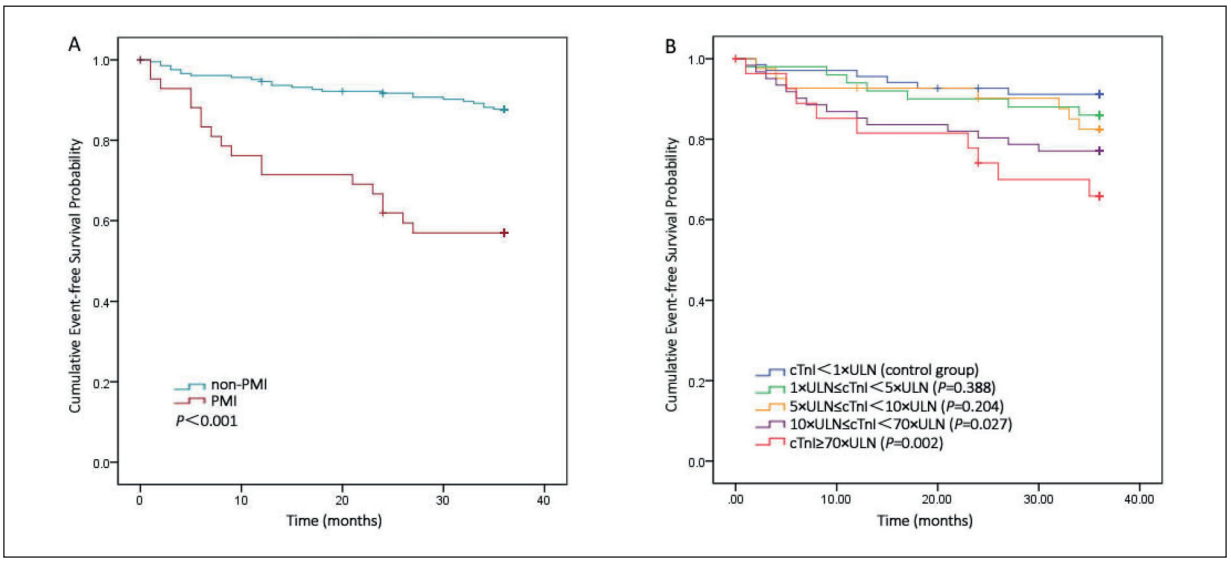


**Figure 4.** Kaplan-Meier survival curves for MACE occurrence among patients successfully accepted PCI. **A,** PCI-related MI and non-PCI-related MI patients. **B,** Patients with different postoperative cTnI levels.

that oxidative low-density lipoprotein (ox-LDL) played an important role. Phagocytosis of ox-LDL by macrophages and smooth muscle cells under endarterium through scavenger receptors could induce the cells to collect, proliferate, and differentiate into foam cells, which could further promote the development the atherosclerotic plaques[23]. Ox-LDL could also induce the expressions of various inflammatory mediators and cytotoxic constituents. These substances lead to the exacerbation of inflammation in atherosclerotic plaques and make the plaques evolve and unstable[24]. Moreover, lipid pools in the atherosclerotic plaques are likely to be more abundant in patients with increased LDL-C. Distal small vessels embolism caused by decomposed atherosis particles from the rich lipid pools in the ruptured plaques during stent implantation also account for the perioperative myocardial injury. In addition, the more complex coronary lesions of patients with increase LDL-C may raise the risk of small vessel occlusions during PCI[25]. Unlike LDL-C, we found there was no correlation between non-HDL-C and PCI-related MI. Non-HDL-C was

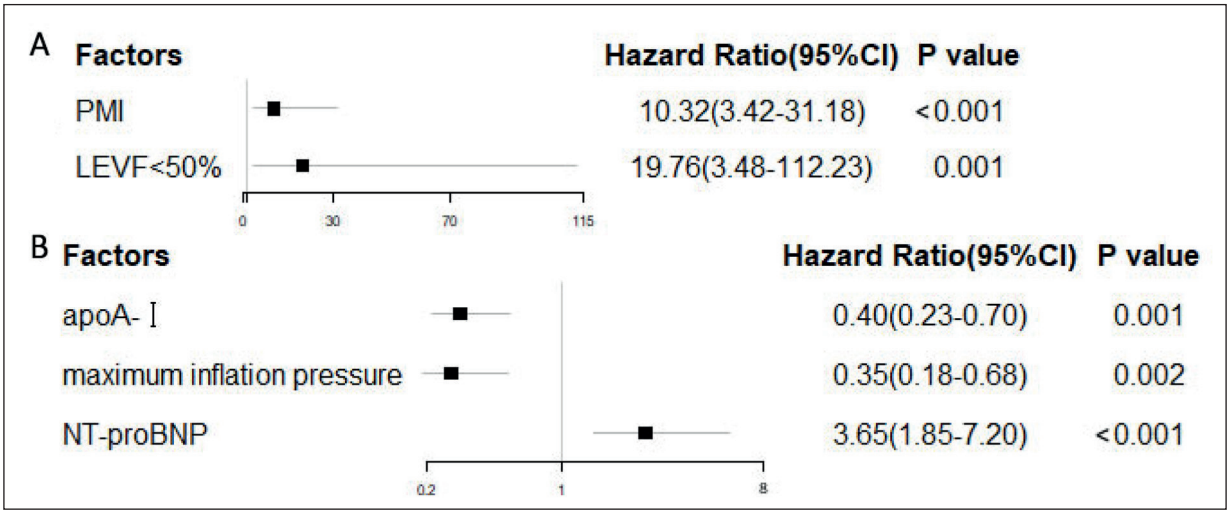


**Figure 5.** Influence factors of MACE occurrence after PCI explored by Cox proportional hazard regression model. **A,** Categorical variables. **B,** Continuous variables (1 SD changed).

set as the secondary target for cholesterol control consists of very-low-density lipoprotein cholesterol (VLDL-C), intermediate-density lipoprotein cholesterol (IDL-C), and LDL-C[19]. Accordingly, we speculate that the effects of VLDL-C in prompting PCI-related MI and peri-procedural myocardial injury are inferior to LDL-C.

Other than LDL-C, age, operative complications, and total stent length were found as risk factors of PCI-related MI, while hemoglobin was negatively correlated with PCI-related MI occurrence, as previous articles reported[4,26-28]. The severity of coronary artery lesions was also found as a definite risk factor of PCI-related MI. In the previous researches[29], the severity of coronary artery lesions was represented by lesion vessels number, lesion classifications, lesion length, degree of stenosis, plaque feature, etc. The latter are complex and quite inconvenient for clinical practice. In our study, therefore, the severity of coronary artery lesions was synthesized as the Gensini score, which revealed a positive correlation with PCI-related MI. As Gensini score increased 1-SD, the risk of PCI-related MI occurrence was to increase by 84%. These data suggested that the Gensini score could be used to evaluate the risk of PCI-related MI before the operation. Besides, our work found that patients undergone PCI before had a lower risk of PCI-related MI. It might be explained that patients of prior PCI history had better remote ischemic preconditioning which had already been observed reducing PCI-related MI in elective PCI[30].

As for the prognosis of PCI-related MI and postoperative myocardial enzymes increase, there are still great arguments in the world[10-14]. In our 3-year follow-up report, we found that the event-free survival rate was significantly lower in PCI-related MI patients through the Kaplan-Meier survival curve. The results of multivariate analysis similarly held that the occurrence risk of MACE was distinctly elevated in the PCI-related MI patients. Thus, the prognosis of PCI-related MI was proved to be poor according to our results, which strongly suggested the necessity to control the risk factor of PCI-related MI to prevent the occurrence of MACE. For postoperative cTnI level, regardless of clinical manifestations, our study found there were no differences in the event-free survival rates between patients with 1×ULN≤cTnI<5×ULN, 5×ULN≤cTnI<10×ULN and those with normal cTnI. While patients with cTnI≥10×ULN showed a significantly decreased event-free survival rate. Furthermore, as reported in the previous reswearch[31], to help diagnose myocardial infarction, the increased extent of cTnI could also predict the range of myocardial injury. Thus, major postoperative myocardial injury is presumed to generate poor prognosis rather than minimal myocardial necrosis. Since the elevation of cTnI after PCI was relatively common, it could be speculated that at least postoperative cTnI≥10×ULN was of prognostic significance according to our results.

In addition to PCI-related MI and different cTnI levels, other independent predictors of MACE in CAD patients were worth to be identified and several studies had been carried out. Meta-analyses have already demonstrated that PCI-based strategy improved long-term survival compared with a medical treatment-only strategy in patients with stable coronary artery disease[32], while CABG might be a better choice in patients with complex coronary lesions and anatomy[33]. In patients with non-ST-segment elevation acute coronary syndrome, a strategy of the very early invasive coronary evaluation was benefited in those with GRACE risk score >140, which indicated a high risk for adverse cardiovascular events compared to an invasive strategy conducted within 2 to 3 days[34]. Tsai et al[35] found that having triple vessel disease, stent implantation, hypertension, and estimated glomerular filtration rate (eGFR) or uric acid independently predicted MACE in coronary artery disease patients. Our work focused on the prognosis of patients undergoing PCI. We found NT-proBNP and LVEF<50% might be risk factors of MACE occurrence after PCI in the multivariate analysis by Cox proportional hazard regression model, while maximum inflation pressure and apoA-I might be protective factors. As NT-proBNP and LVEF both reflect heart function, we can conclude that patients with cardiac insufficiency have a greater MACE prevalence after PCI. The reason why maximum inflation pressure was negatively correlated with MACE occurrence after PCI remained unclear yet. It was suspected to be related to the reduction of in-stent thrombosis. ApoA-I is widely known as the major apolipoprotein of HDL to reversely transport the cholesterol and cooperate with HDL-C to protect the cardiovascular system[19]. Furthermore, high HDL-C/apoA-I value increases the risk of mortality in coronary heart disease patients[36]. While HDL-C transfers to other subclasses and fail to protect the cardiovascular system anymore, apoA-I will not transfer together, becoming a cardiovascular protective

factor independently of HDL-C[37]. However, not a significant relationship between HDL-C and PCI prognosis was found and apoA-I turned out to be a strong protective factor in favor of reducing the occurrence of MACE. However, there was still a lack of medicine increasing apoA-I defining safety and efficacy[38,39], as well as evidence certifying the cardiovascular protective effects of apoA-I elevation. Therefore, apoA-I is not yet included in the therapeutic goal. Focusing on the preoperative apoA-I level, it is still beneficial to assess the long-term prognosis of patients.

### Study Limitation

As a single-center study, the sample size was relatively small, which decreased the power of the test. Some patients were excluded at the beginning of study due to insufficient clinical data. Some patients were lost to follow-up in survival analysis, that may cause bias of the results. Some information was missing in a few patients and this may also affect the results. Finally, although we had already included more than 40 covariate variables, there were still some factors that might be related to PCI-related MI occurrence or influent prognosis after PCI. Also, some variables had not been measured due to the limitation of equipment. Moreover, the risk scores including TIMI, GRACE, and PURSUIT scores[40] were not suitable for our study since they were mainly used in patients suffering from acute coronary syndrome (ACS), while our study included stable CAD patients and ACS patients.

## Conclusions

We showed that prognosis of PCI-related MI was poor, as well as in patients with postoperative cTnI≥10×ULN. Among risk factors of the PCI-related MI, LDL-C, age, Gensini Score, total stent length, and intra-operative complication were positively correlated with PCI-related MI occurrence, while hemoglobin and prior PCI history were negatively correlated. In addition to PCI-related MI, NT-proBNP and LVEF<50% were also found positively correlated with MACE occurrence after PCI, while the maximum inflation pressure and apoA-I were nnegatively correlated.

### Conflict of Interest

The Authors declare that they have no conflict of interests.

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