Research Paper

Diagnostic and prognostic value of minor elevated cardiac troponin levels for percutaneous coronary intervention-related myocardial injury: a prospective, single-center and double-blind study

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Abstract

Cardiac troponin-I (cTnI) and -T (cTnT) are sensitive and specific markers of myocardial injury. However, the role of increased cTnI and cTnT in percutaneous coronary intervention (PCI)-related myocardial injury remains controversial. In this prospective, single-center and double-blind study, we aimed to determine the diagnostic and prognostic value of cTnI as well as cTnT (cTns) in PCI-related myocardial injury in a Chinese population. A total of 1,008 patients with stable angina pectoris and non-ST-segment elevation acute coronary syndrome were recruited. The levels of cTnI and cTnT were examined before and after PCI. All patients were followed up for 26 ± 9 months to observe the incidence of major adverse cardiac events (MACEs). Our results showed that post-PCI cTnI and/or cTnT levels were increased to more than the 99th percentile upper reference limit (URL) in 133 (13.2%) patients, among which 22 (2.2%) were more than 5×99th percentile URL. By univariate analysis, an elevation in cTns after PCI was not an independent predictor of increased MACEs, HR 1.35 ($P = 0.33$, 95%CI: 0.74−2.46). In conclusion, our data demonstrate that the incidence of PCI-related myocardial injury is not common in a Chinese population and minor elevated cTns levels may not be a sensitive prognostic marker for MACEs.

Keywords: percutaneous coronary intervention (PCI), troponins, PCI-related myocardial injury, major adverse cardiac events, diagnosis, prognosis

INTRODUCTION

According to the universal definition of myocardial infarction (MI), the increased level of cardiac troponins (cTns) from normal baseline value to above the 99th percentile upper reference limit (URL) could be assumed as an indicator for PCI-myocardial necrosis. Elevation of more than three times of the 99th percentile

URL is defined as a PCI-related MI (MI type 4a)[1]. However, the latter is redefined by elevation of cTn values ($\geqslant 5 \times 99^{th}$ percentile URL) in patients with normal baseline value ($< 99^{th}$ percentile URL) or a rise of cTn values $> 20\%$ if the baseline values are elevated, stable or falling. In addition, either of the following symptoms are required: (i) symptoms suggestive of myocardial ischemia; (ii) new ischemic ECG changes; (iii) angiographic findings consistent with a procedural complication; (iv) imaging demonstration of new loss of viable myocardium or new regional wall motion abnormality[2].

CTns (-I and-T) are particularly sensitive and specific markers of myocardial injury[3,4]. They are superior to creatine kinase muscle-brain (CK-MB) fraction in sensitivity, specificity and long-term prognostic significance in acute coronary syndromes (ACS)[3−7]. Post-procedural elevations of CK-MB or cTns levels occur in 5–50% of patients undergoing PCI[8]. It has been proved that the elevation of CK-MB with more than 3 to 8 $\times$ URL has prognostic implications, especially when accompanied by the development of Q waves on electrocardiogram[9,10]. In addition, many studies have demonstrated that significant elevation of CK-MB levels is associated with reduced long-term survival rate of post-PCI patients[11−13]. To date, however, the association between the increase of cTns levels after PCI and the follow-up cardiac events remains controversial[14−25]. Previous studies showed no prognostic role of increased post-PCI cTnI levels for mortality in ACS patients[14−20]. However, recent reports have suggested that elevated cTnI level may be a predictor of long-term mortality[21−25]. The aim of this prospective, single-center and double-blind study was to determine the diagnostic and prognostic value of cTnI as well as cTnT in PCI-related myocardial injury in a Chinese population.

PATIENTS AND METHODS

Patients

The present study was a prospective, single-center and double-blind study. The protocol was approved by the local institutional board at the authors′ affiliated institution and written informed consents were obtained from all patients. We reviewed hospital charts of patients to verify the data. From January 2010 to November 2012, patients who underwent elective PCI for the treatment of stable and unstable angina pectoris or non-ST-segment elevation myocardial infarction at the Cardiology Center of our institution were selected. Patients with myocardial infarction one week before PCI or with an elevation in pre-pro-cedure cTns were excluded. Before PCI, all patients were pre-treated with aspirin 75 mg/day and clopidogrel 75 mg/day (or loaded with clopidogrel 300 to 600 mg if not already at least six hours before PCI) for at least three days. During PCI, patients received unfractionated heparin (100–150 IU/kg and additional heparin, occasionally). Nitroglycerin or platelet glycoprotein IIb/IIIa inhibitors (tirofiban) were used at the discretion of the operator. Dual antiplatelet therapy was recommended to those who received bare metal stents at least four weeks and to those who were treated with drug-eluting stents at least 12 months by use of aspirin and clopidogrel after PCI. Coronary angiography was performed by the femoral or radialis approach. Diseased vessel was defined as the number of coronary arteries with $\geqslant 50\%$ diameter stenosis (including the left anterior descending, circumflex or right coronary arteries; or bypassable branches thereof) or the number of lesions as $\geqslant 50\%$ diameter stenosis in the target vessel[26]. Multivessel disease was defined as the presence of $> 70\%$ lesion in three major coronary arteries and bypassable branches thereof. Modified Gensini index system was applied to assess the extent of coronary artery disease. The stenosis weights were (percentage stenosis, weight): 0–25, 2; 26–50, 4; 51–75, 8; 76–90, 16; 91–99, 32; 100, 64. All patients undergoing primary PCI of the symptomatic or infarction related arteries were performed according to standard techniques. Residual stenosis $<20\%$ and thrombolysis in myocardial infarction (TIMI) flow reaching grade three indicated the success of procedure. Complication of dissection and major branch vessel occlusion was induced by coronary implantation.

Measurement of laboratory biomarkers

Blood samples for cardiac biomarkers testing were drawn in each patient before and 18–24 hours after PCI. Further measurements were performed if patients had post-procedural symptoms suggesting myocardial ischemia. The peak values of cTns were used for analysis. The samples were inserted into tubes with a heparin anticoagulant agent, centrifuged at 3,000 g for 10 minutes, and then stored at -40°C until analysis. CK-MB was quantified with automated chemiluminescent immunoassay techniques in the clinical laboratory of the authors′ afiiliated institution. The CK-MB assay has a 99th percentile URL of 25 μmol/L. Plasma levels of cTnT were analyzed using the access two immunochemiluminometric assay (Roche Diagnostics GmbH, Mannheim, Germany). The upper limit of normal for the assay was < 0.1 ng/mL. Plasma levels of cTnI were measured by enzyme linked immunosorbent assay

(ELISA: Institute of Cardiovascular Disease, the First Affiliated Hospital of Nanjing Medical University, China), and the upper limit of normal for the assay was < 0.5 ng/mL.

Clinical outcomes

Follow-up were performed by E-mail or telephone interviews with the patients or their relatives, or by inviting patients to complete a standardized question–naire. All adverse events were confirmed by reviewing the medical records of the patients after discharge. The primary endpoint of follow-up was defined as major adverse cardiovascular events (MACEs), including a composite of death, hospitalization due to nonfatal myocardial infarction, unplanned revascularization or heart failure. Nonfatal myocardial infarction was defined as the presence of chest pain lasting 20 min–uets or longer, new ST-T wave changes or Q waves on the electrocardiogram, or increased cardiac biomarker greater than five times of the 99th percentile URL in patients with normal baseline levels, or as an elevation of > 20% in CK-MB or troponins in patients with raised baseline levels[2]. Unplanned revascularization included coronary artery bypass grafting surgery (CABG) or repeated PCI of the target vessel(s). Heart failure was based on the diagnosis of local hospital diagnosis.

Statistical analysis

Continuous data were expressed as mean $\pm$ standard deviation (SD) and categorical variables as frequencies (%). The highest post-procedural value of cTnI or cTnT was used for analysis. Comparisons between groups were performed by using the Chi-quare or Fisher′s exact test for categorical variables. Normally distributed continuous variables were compared with Student′s t test. The incidence of MACEs were calcu–lated and plotted according to Kaplan-Meier methods, and comparisons between the groups were performed using log-rank statistic. The impact of prognostic fac–tors on survival was assessed by the Cox proportional hazards model. Associations between variables of interest with long-term outcomes were tested on uni–variate analysis. Variables with a P-value of <0.05 on univariate testing as covariate were subjected to multivariate Cox regression analysis. The value of $P < 0.05$ was considered to be significant. All statis–tical evaluations were performed with the SPSS soft–ware package (version 13.0, SPSS, Chicago, IL, USA).

RESULTS

The study flowchart is shown in *Fig. 1*. We selec–ted data from 2,589 consecutive patients who had
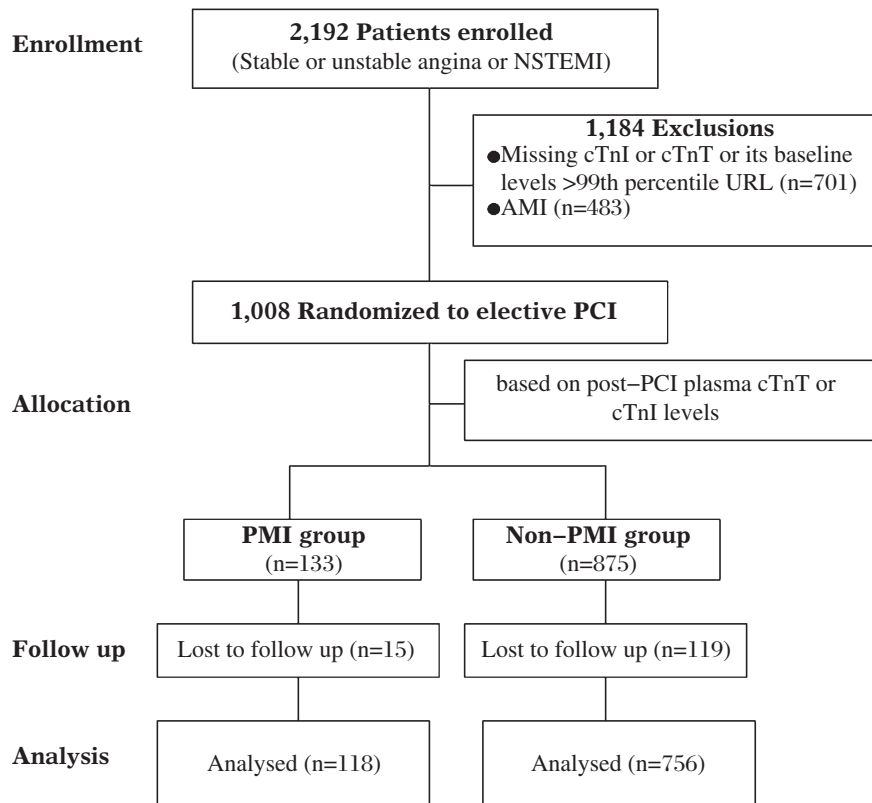

Fig. 1 **The study flowchart.** NSTEMI: Non-ST-segment elevation myocardial infarction.

undergone PCI at our institution. A total of 2,192 patients fulfilled the inclusion criteria but 701 (27%) patients were excluded because of missing cTnI or cTnT or its baseline levels $> 99^{th}$ percentile URL; 483 (19%) patients were excluded for acute ST-segment elevation myocardial infarction requiring emergency intervention. The remaining 1,008 (39%) patients were included in the final analysis. The clinical and procedure characteristics of the 1,008 selected patients were homogeneous to those who were excluded. According to the newest universal definition of myocardial infarction[2], these patients were divided into two subgroups based on post-PCI plasma cTnT or cTnI levels. The non- PCI-related myocardial injury (PMI) group was defined as cTnT levels < 0.1 ng/mL and cTnI < 0.5 ng/mL, the PMI group was defined as cTnT > 0.1 ng/mL (99th percentile URL), or cTnI > 0.5 ng/mL (99th percentile URL).

Characteristics of study subjects

Baseline characteristics of patients with and without cTns elevation are summarized in **Table 1**. Most baseline characteristics were comparable between the two groups. The mean age of the cohort was 63 ± 10 years, and 73.3% of the patients were male. Patients with a rise in cTns had more adverse clinical charac–teristics; they were older, higher baseline systolic blood pressure and heart beats, but lower pre-procedural eGFR. There was no statistical difference in the use of aspirin, beta-blocker, angiotensin-converting enzyme inhibitors (ACEI) or angiotensin-converting enzyme-receptor blockers (ARB) and statins between the groups.

Angiographic and procedural characteristics

Table 2 summarizes the angiographic and proce–dural characteristics. Each patient was treated with

Table 1 **Demographic and clinical characteristics of the study population**

Baseline characteristics	Subgroup 1 (N=875)	Subgroup 2 (N=133)	P value
Mean age, years	62 ± 10	65 ± 10	0.008
Male sex	641 (73.3%)	97 (72.9%)	1.000
BMI (Kg/cm²)	24.81 ± 3.03	24.36 ± 2.97	0.144
Stable angina	109 (12.5%)	15 (11.3%)	0.778
Unstable angina	690 (78.9%)	100 (75.2%)	0.365
NSTEMI	12 (1.4%)	4 (3.0%)	0.149
History of hypertention	585 (66.9%)	101 (75.9%)	0.045
History of hyperlipidemia	63 (7.2%)	8 (6.0%)	0.719
History of diabetes	214 (24.5%)	40 (30.1%)	0.165
History of smoking	380 (43.4%)	51 (38.4%)	0.071
Prior MI	68 (7.8%)	10 (7.5%)	1.000
Prior PCI	89 (10.2%)	10 (7.5%)	0.434
Prior CABG	8 (0.9%)	4 (3.0%)	0.061
SBP (mmHg)	132.4 ± 14.8	135.5 ± 16.9	0.026
Heart rate (bpm)	69.8 ± 11.2	71.7 ± 12.4	0.065
LDL-C (mmol/L)	2.59 ± 0.81	2.66 ± 0.89	0.329
Pre-procedural			
eGFR (mL/min)	89.03 ± 20.21	84.26 ± 24.16	0.015
GLU (mmol/L)	5.63 ± 1.59	5.64 ± 1.78	0.933
LVEF (%)	63.94 ± 6.59	63.46 ± 6.86	0.484
Medication at discharge number, (%)			
Aspirin	873 (99.8%)	132 (99.2%)	0.346
Beta-blockers	659 (75.8%)	98 (73.7%)	0.589
Statins	860 (98.4%)	129 (97.0%)	0.281
ACEI /ARB	637 (72.8%)	100 (79.4%)	0.130

Data are presented as mean $\pm$ SD, absolute n (%), or median (inter quartile range). BMI: Body mass index (Kg/cm²); NSTEMI: Non-ST-segment elevation myocardial infarction; MI: Myocardial infarction; CABG: Coronary artery bypass grafting; SBP: Systolic blood pressure; LDL-C: Low density lipoprotein cholesterol; eGFR: estimated glomerular filtration rate; GLU: Glucose; LVEF: Left ventricular ejection fraction; ACEI/ARB: Angiotensin - converting enzyme inhibitors/receptor antagonists

Table 2 **Procedural and periprocedural characteristics**

	Non-PMI	PMI	P value
No. of diseased arteries			
LM or LM + single	11 (1.3 %)	0 (0 %)	0.377
LM + double or triple	18 (2.1 %)	6 (4.5 %)	0.116
Single	271 (31.0 %)	19 (14.3 %)	<0.001
Double	281 (32.1 %)	38 (28.6 %)	0.484
Triple	216 (24.7 %)	47 (35.3 %)	0.011
Multiple	80 (9.1 %)	22 (16.5 %)	0.013
Lesions	3.17±1.81	4.10±1.91	<0.001
Gensini score	89.02±65.40	116.04±75.61	<0.001
No. of treated arteries			
Single	545 (62.3 %)	62 (46.6 %)	0.001
Double	257 (29.4 %)	54 (40.6 %)	0.012
Triple	77 (8.8 %)	17 (12.8 %)	0.150
LM	16 (1.8 %)	1 (0.8 %)	0.714
LAD	640 (73.1 %)	103 (77.4 %)	0.341
LCX	266 (30.4 %)	55 (41.4 %)	0.013
RCA	352 (40.2 %)	61 (45.9 %)	0.220
No. of stent	2.15±1.27	2.70±1.38	<0.001
Total stent lenghth (mm)	50.50±32.30	63.83±35.04	<0.001
Tirofiban use	5 (0.6 %)	6 (4.5 %)	0.001
Cardiac biomarker levels at baseline and after PCI			
Baseline cTnI (ng/mL)	0.32±0.16	0.35±0.33	0.30
Baseline cTnT (ng/mL)	< 0.1	< 0.1	
Baseline CK-MB (μmol/L)	12.58±7.78	11.32±5.60	0.10
Post-procedure cTnI (ng/mL)	0.30±0.13	0.54±0.67	<0.001
Post-procedure cTnT (ng/mL)	0.10±0.00	0.33±0.36	<0.001
Post-procedure CK-MB (μmol/L)	14.29±9.80	29.78±39.51	<0.001
Dissection	5 (0.6 %)	5 (3.8 %)	0.005
Branch vessel occlusion	3 (0.3 %)	3 (2.3 %)	0.033
Length of stay (days)	8.3±4.2	9.8±7.5	0.001

Value are given as number of patients (percent) or mean±SD. LM: Left main; LAD: Left anterior descending; LCX: Left circumflex; RCA: Right coronary artery; Single, double, triple: number of diseased and treated arteries vessel; Tirofiban: glycoprotein IIb/IIIa inhibitors.

stent placement after balloon pre-dilation. Procedural success and post-procedure TIMI grade three flows were achieved in all patients. Patients with a rise of cTns had more extensive coronary artery disease with a greater incidence of 3-vessel ($P = 0.011$) and multivessel ($P = 0.013$) coronary artery disease than patients with normal cTns. Gensini scores were signif-icantly higher in the PMI group compared with the non-PMI group ($116.04±75.61$ vs. $89.02±65.40$, $P < 0.001$). Additionally, there was a marked difference in the number of target coronary lesions between the two groups, respectively ($3.17±1.81$, $4.10±1.91$, $P < 0.001$). In concert with more extensive coronary disease and adverse baseline clinical characteristics, PMI patients underwent more 2 vessels ($P = 0.012$), left circumflex artery ($P = 0.013$) PCIs, and had more complicated procedural outcomes, including dissection

(3.8%, $P = 0.005$) and branch vessel occlusion (2.3%, $P = 0.033$). Moreover, these patients had greater total implanted stent length ($63.83±35.04$ mm, $P < 0.001$) and a higher number of stents implanted ($2.70±1.38$, $P < 0.001$). Glycoprotein IIb/IIIa inhibitors were used more frequently in patients with increased cTns (respectively, 4.5% vs 0.6%, $P = 0.001$), likely in keeping with the more complex nature of the procedures.

Comparison of cTns and CK-MB defined PMI

Baseline cTnI, cTnT and CK-MB values were not significantly different between the groups and lower 99th percentile upper reference limit. Compared with the non-PMI group, the average level of cTnI, cTnT and CK-MB were higher in the PMI group, respectively, ($0.54±0.67$ ng/mL, $0.33±0.36$ ng/mL, and $29.78±39.51$ μmol/L; $P < 0.001$, for all) after PCI (**Table 2**).

An elevation of post-PCI cTns was detected in 133 (13.2 %) patients (cTnT > 0.1 ng/mL: 11.4%, 96/841; median, 0.22 ng/mL; inter quartile range, 0.15 to 0.43 ng/mL; cTnI > 0.5 ng/mL: 8.6%, 48/559, cTnI median, 0.58 ng/mL; inter quartile range, 0.52 to 0.70 ng/mL). Among them, 22 (2.2%) patients (cTnT $\geqslant$ 0.5 ng/mL: 2.6 %, 2/841; median, 0.86 ng/mL; inter quartile range, 0.65 to 1.23 ng/mL; cTnI $\geqslant$ 2.5 ng/mL: 0.2%, 1/512, cTnI 5.95 ng/mL) were clinically relevant for diagnosing MI type 4a[2]. In addition, when the CK-MB definition was applied, 84 of 799 patients (10.5%) showed evidence of injury (CK-MB > 25 μmol/L) and six of 799 patients (0.8%) were considered to conform to PCI-related MI (CK-MB > 125 μmol/L).

Clinical outcomes

Follow-up data, including the survival status, were available for 874/1,008 (86.7%) patients. There was no statistical difference between groups regarding loss ratio of follow-up time (**Fig. 2**). During 26±9 months (inter quartile range, 17 to 34 months) of follow-up, 25 (25/1,008, 2.5%) patients died (including: cardiac death, 17/25, 68%; cancer death, 5/25, 20%; cerebral hemor–rhage death, 2/25, 8%; other causes of death, 1/25, 4%). In addition, the incidences of non-fatal myocardial infarction, heart failure and unplanned revascularization were higher in the PMI group than those in the non-PMI group (0.8% vs 0.7%, 1.7% vs 0.9% and 5.9% vs 4.2%), but no significant difference was found (P = 0.913, 0.080 and 0.444). Additionally, there is no correlation

between a PCI-related cTns elevation and MACEs by log-rank test (11.0% vs 7.8%, P = 0.331) (**Fig. 2** and **3**).

There was no evidence of a nonlinear or threshold effect for the association between post-PCI cTns > 99th URL and the time to MACEs, HR 1.35 (95% CI: 0.74–2.46, P = 0.33) in univariate analysis (**Table 3**). However, by univariate analysis, an elevation in post-PCI CK-MB > 99th URL was an independent predictor of increased long-term MACEs. However, the relation–ship between the incidence of PCI-related myocardial injury and MACEs was insignificant, when the con–founding variables were adjusted by multivariate Cox regression analysis. In addition, Cox model revealed that previous PCI, pre-procedure eGFR < 60 (mL/minute), multiple vessel lesion and LVEF < 40% were indepen–dently associated with a higher incidence of MACEs in patients who underwent elective PCI, even after adjust–ment for confounders (**Table 3**).

DISCUSSION

The major findings of the present study are that fol–lowing PCI in patients with normal baseline cTnT and cTnI: (1) the incidence of PMI is not common in Chinese population, which occurrs in about 13.2% of patients. Among them, the number in MI type 4a is in 2.2 % (22/1,008); (2) cTns, minor elevation after successful PCI, are probably associated with the elderly, more serious coronary disease and more com–plicated procedure characteristics; (3) previous PCI, pre-procedure eGFR < 60 (mL/minute), multiple ves–sels lesion and LVEF < 40% rather than minor PMI provide long-term prognostic information regarding MACEs.

In our study, an addition of 3 biomarkers (cTnT, cTnI and CK-MB) to establish prognostic factors pro–vided incremental prognostic information regarding MACEs in patients undergoing primary percutaneous coronary intervention for NSTE-ACS. However, the data shows an elevation in post-PCI cTns is signifi–cantly low. An elevation of post-PCI cTns was detected in 13.2% of patients. Among them, 2.2% of them are clinically relevant in diagnosing MI type 4a. However, when the CK-MB definition was applied, 10.5% of patients showed evidence of injury and 0.8% of them were considered to conform to PMI. Lim et al.[27] analyzed elevation in cTnI and CK-MB with late gadolinium enhancement (LGE) cardiac magnetic resonance (CMR) imaging post-PMI. Twenty six patients were defined as MI type 4a judging by cTnI. But only a minority of patients showed evidence of abnormality on CMR-LGE; furthermore, only three of them were defined as cardiac necrosis. Consequently,
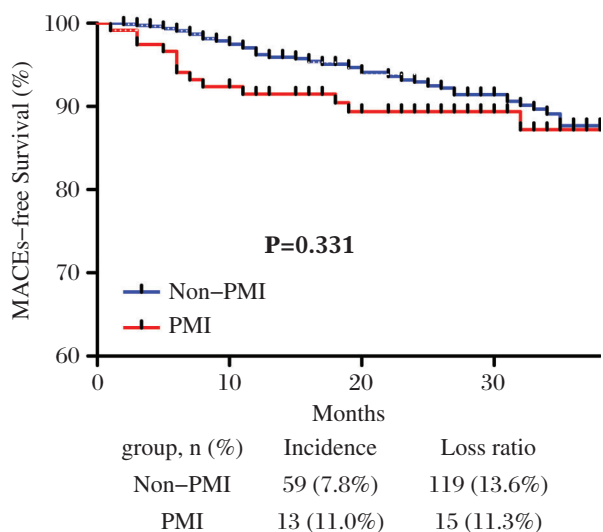

group, n (%)	Incidence	Loss ratio
Non–PMI	59 (7.8%)	119 (13.6%)
PMI	13 (11.0%)	15 (11.3%)

Fig. 2 Kaplan-Meier estimates for survival free of the com–posite endpoint-MACEs for patients with and without PMI. There were 59 and 13 MACEs observed during follow-up, respectively.
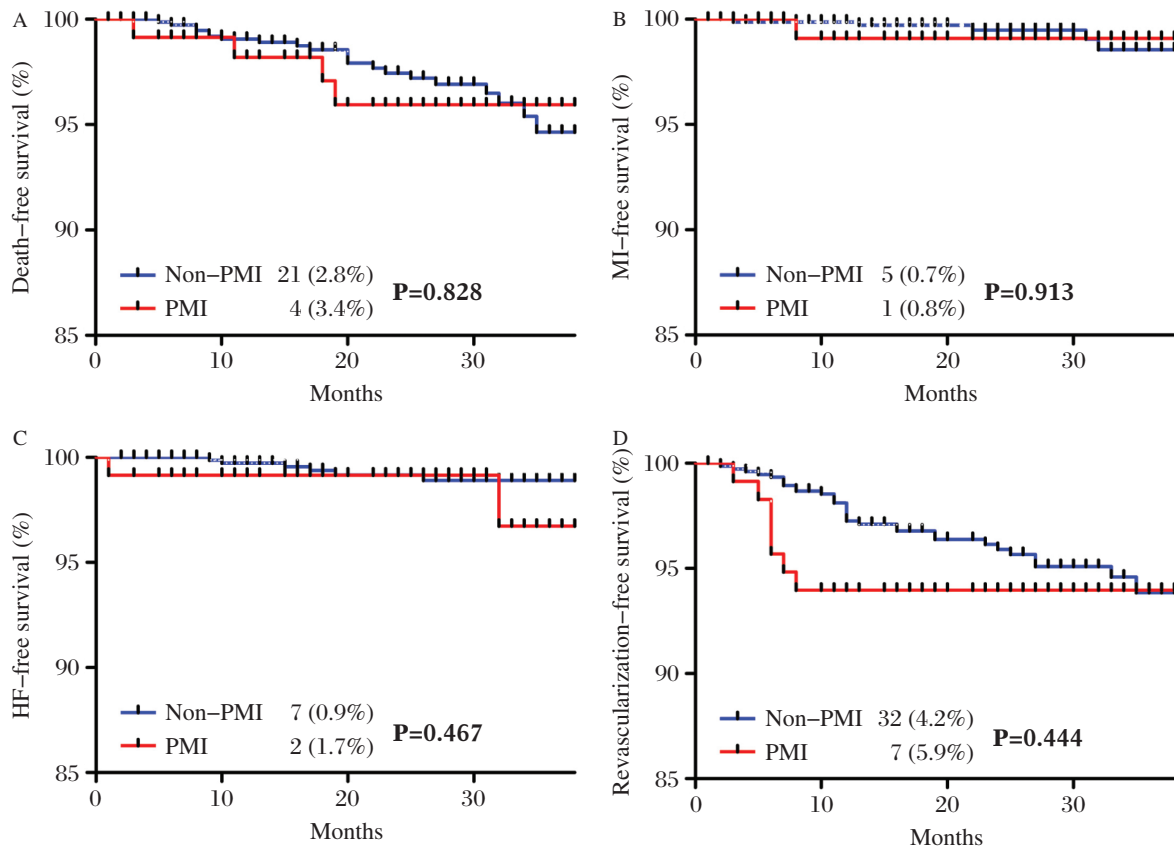
Fig. 3 Kaplan-Meier estimates for survival free of death, non-fatal myocardial infarction, heart failure and unplanned revascularization for patients with and without PMI. A: Graphs represent death-free survival during follow-up in patients with and without PMI. B: Graphs represent non-fatal myocardial infarction-free survival during follow-up in patients with and without PMI. C: Graphs represent heart failure-free survival during follow-up in patients with and without PMI. D: Graphs represent unplanned revascularization-free survival during follow-up in patients with and without PMI.

they inferred that CK-MB differentiates PMI better than troponins. More than half of the patients with slight rise in CK-MB showed no evidence of PMI, one third of them showed evidence of PCI-related myocardial necro-sis, and roughly 15% can be classified as PMI. Cardiac troponin radically alters this distribution, with the vast majority of the patients ($> 80\%$) fulfilling the criteria of PMI. The study by Cavallini et al.[28] defined cTnI thresholds (0.15 ng/mL) and MI type 4a with a rise in cTnI > 0.45 ng/mL. The incidence of MI type 4a, which is 19.7 % (467/2,362) higher than this study. Furthermore, the new definition of MI[2] offers the threshold level of troponin > 5 times 99th percentile of URL and a clinical setting consistent with myocardial ischemia as MI after PCI. A small troponin increase after a successful elective PCI was not infrequent.

Elevation in cTns or CK-MB may be a marker for severe atherosclerosis, aggravated plaque burden[29], presence of vulnerable plaques, endothelial dysfunc-tion, microvascular injury and inflammation. Patients who suffered from PMI had more extensive coronary artery disease. For example, the greater incidence of

3-vessel and multivessel coronary artery disease are 35.3% and 16.5%, respectively. Besides, the number of lesions in the target coronary artery (4.10 ± 1.91) is larger than that without PMI (3.17 ± 1.81, $P < 0.001$). Earlier studies have implicated branch vessel occlusion and dissection as the mechanisms for ischemic injury after PCI[30–32]. Patients with a rise of cTns had more complicated procedural outcomes, including dissection (3.8%, $P = 0.005$) and branch vessel occlusion (2.3%, $P = 0.033$). In addition, sev-eral studies suggested that microvascular hypoperfu-sion, due to thrombus embolization may be another underlying mechanism in a significant proportion of patients[33–35]. Glycoprotein IIb/IIIa inhibitors were used more frequently in patients with increased cTns (4.5% vs 0.6%, respectively; $P = 0.001$). In conclusion, either undetectable element by routine angiographic evaluation in the catheterization laboratory or slow-reflow caused elevation in cardiac biomarkers.

Increased levels of cTns, especially in concomitant with CK-MB, led to the unaddressed issue of the prog-nostic significance of milder isolated elevations in

Table 3 Hazard ratios for MACEs in the univariate risk factor and adjusted mulitivariate risk factor model

Age (years)	HR (95% CI)	P value	Adjusted Model HR (95% CI)	P value
<56	reference			
56–69	1.46 (0.76–2.80)	0.25		
≥70	1.48 (0.73–2.99)	0.28		
History of diabetes	1.27 (0.72–2.25)	0.40		
History of hypertension	0.83 (0.52–1.34)	0.46		
Previous CABG	5.95 (1.87–18.93)	0.003	2.42 (0.50–11.76)	0.27
Previous PCI	2.37 (1.36–4.14)	0.002	2.60 (1.30–5.21)	0.007
CTns				
<99% URL	reference			
>99% URL	1.35 (0.74–2.46)	0.33		
CK-MB				
<99% URL	reference			
≥99% URL	2.31 (1.21–4.41)	0.011	1.85 (0.91–3.73)	0.09
eGFR (mL/min)				
≥90	reference			
60–89	1.15 (0.69–1.89)	0.59	0.89 (0.47–1.67)	0.71
<60	2.38 (1.12–5.04)	0.024	2.55 (1.09–5.96)	0.032
LVEF (%)				
≥55	reference			
40–54	1.59 (0.68–3.70)	0.28	0.96 (0.34–2.72)	0.93
<40	8.47 (3.06–23.47)	<0.001	7.73 (2.68–22.28)	<0.001
Multiple	1.99 (1.07–3.69)	0.03	3.35 (1.68–6.69)	0.001
Gensini score				
<46	reference			
46–119	0.99(0.55–1.77)	0.96		
≥120	1.44 (0.77–2.69)	0.26		

The scale of cTns, CK-MB, eGFR, LVEF are according to the new guidelines recommend range, and age, Gensini score are according to inter quartile range. We adjusted confounders (variables with a P value of <0.05 on univariate testing) in the multivariate model.

cTns. Several previous studies in view of the universal definition of MI have revealed the relationship between cTnI[27–28,36] and long-term mortality. The study by Damman et al.[36] demonstrated that the ratio of death increased along with rising levels of cTnT, (HR 2.78, 95% CI: 1.82–4.24, $P < 0.001$) in univariate analysis. Nevertheless, multivariate analysis indicated that ele‒vated cTnT was not associated with a higher risk of mortality. Their data suggested that the use of multiple biomarkers instead of cTnT alone including established risk factors improved the prediction of mortality in STEMI patients undergoing primary PCI. Studies with CMR imaging have confirmed that an elevation in cTns after PCI is related to myocardial necrosis. In addi‒tion, there is a positive correlation between the magni‒tude of injury and the extent of CK-MB, rather than cTns[27]. Similarly, our data showed that an elevation in post-PCI CK-MB instead of cTns > 99th URL was an independent predictor of long-term MACEs, (HR 2.31, 95% CI: 1.21–4.41). However, this relationship was

insignificant when the confounding factors were adjusted by multivariate Cox regression analysis. From the current point, the definition of periprocedural MI may be too strict and minor elavated cTns levels may not be a sensitive prognostic marker for MACEs.

In addition, apart from previous PCI, multiple-vessel lesion and LVEF < 40%, our data reveals the impor‒tance of renal disease as a risk factor for MACEs after PCI. The eGFR < 60 mL/minute was associated with higher incidence of MACEs in patients undergoing elective PCI, (HR 2.38, 95% CI: 1.12–5.04, $P = 0.024$). Although after adjustment for confounders, the relationship persisted in these patients, (HR 2.55, 95% CI: 1.09–5.96, $P = 0.032$). Possible mechanisms may be a high prevalence of coronary events among patients with chronic kidney disease (CKD). Post-pro‒cedural serum creatinine was ineffective to evaluate the risk of contrast-induced acute kidney injury (CI-AKI). Moreover, further research should focus on the effect of reperfusion therapy on renal function, as well as

the efficacy and safety of cardiovascular medication in these patients[36].

There are several potential limitations in our study. Firstly, the clinical study was limited to a small size of sample because of the short periods and single center observation. Large volume of samples and multiple centers are needed to confirm our findings. Secondly, we measured cTnT and cTnI at 18–24 hours after the procedure. Furthermore, measurements were performed if patients had post-procedural symptoms suggesting myocardial ischemia. So the peak values, rather than repeated 4–6 hourly values of cTns, were used for ana-lysis. Thus, we may not be sure that the measured levels of cTnT and cTnI are at the true peak. However, the recognized optimal time to detect peak cTnI has been reported to be at 12–24 hours[37]. So as a result, we do not think that it greatly affects the validity of our find-ings. Thirdly, shorter time of follow-up concerning MACEs of patients was performed 1.5 years or longer after PCI. Thus, longer time evaluation is indispensable to demonstrate the reasonable results. Finally, the new PMI definition stresses the importance of imaging evidence of new loss of viable myocardium or presence of new regional wall motion abnormality. Further research is needed to select reasonable imaging for assessing myocardial injury after PCI.

In conclusion, this study shows that the incidence of PMI is not common in Chinese population and minor elevated cTns levels may not be a sensitive prognostic marker for long-term MACEs after elective PCI.

Acknowledgments

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