Novel insights in reperfusion therapy and stent thrombosis in the drug eluting stent era

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Chapter 5

Usefulness of Peak Troponin-T to Predict Infarct Size and Long- Term Outcome in Patients with First Acute Myocardial Infarction after Primary Percutaneous Coronary Intervention

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Am J Cardiol. (in press)

ABSTRACT

Background: In acute myocardial infarction (MI) cardiac troponin-T (cTnT) is the preferred biomarker to detect myocardial necrosis. Our aim was to investigate the prognostic value of peak plasma cTnT in patients with ST-elevation myocardial infarction (STEMI) treated by primary percutaneous coronary intervention (PPCI).

Methods: One hundred sixty eight consecutive patients with first STEMI were studied. Patients were eligible if STEMI symptoms started <9 h before the PPCI. During the first 48 hours post PPCI cTnT and creatine kinase (CK) were measured repeatedly. Main outcome measures were left ventricular ejection fraction (LVEF) assessed by myocardial scintigraphy at 90 days, and clinical outcomes through 1 year follow-up post PPCI in a dedicated out-patient clinic.

Results: Peak cTnT values were reached within 24 hours post PPCI in all patients. The enzymatic infarct size, measured by cumulative 48-h CK release, correlated positively with peak cTnT ($r = 0.73$, $p < 0.001$). LVEF at 3 months was negatively correlated with peak cTnT ($r = -0.52$, $p < 0.001$). A peak plasma cTnT $\geq$ 6.5 µg/L predicts a LVEF $\leq$ 40% at follow-up with 86% sensitivity and 74% specificity. Multivariable Cox regression analysis identified peak cTnT as an independent predictor of major adverse cardiac events (HR = 1.07, 95% CI = 1.01-1.12) and heart failure (HR = 1.12, 95% CI = 1.05-1.20) assessed through clinical follow-up.

Conclusions: Peak cardiac troponin-T after primary PCI for STEMI offers a good estimation of infarct size and is prognostic indicator in patients with first acute myocardial infarction.

INTRODUCTION

The current guidelines for ST-elevation myocardial infarction (STEMI) stress that primary percutaneous coronary intervention (PPCI) should be the treatment of choice in patients presenting in a hospital with catheterization facility and an experienced team[1]. As a result, PPCI has become for many centers the first option therapy in acute myocardial infarction (MI). This is mainly the consequence of the superior outcome of PPCI when compared to thrombolysis.[2-4]

Cardiac troponin T (cTnT) has become the golden standard for the MI documentation[5,6] mainly because its specificity: it belongs to the proteins of the contractile apparatus and its structure is unique for cardiac muscle.[7] After ischemic injury, cTnT serum concentrations display a biphasic curve with an early peak within the first 24 hours followed by a plateau at 72-96 hours after the onset of symptoms.[8, 9]

Since the beginning of the troponin era, numerous studies have linked troponin T or I levels to the evolution of myocardial infarction. These studies mainly assessed STEMI patients treated by thrombolysis[10-12] or combined (PPCI or thrombolysis) populations.[13]

However, the past years have brought updated definitions for STEMI[5] and little information is available about the prognostic role of troponins in patients diagnosed and treated according to the recent guidelines.

The main aim of our study was therefore to verify the prognostic importance of the early cTnT peak on LV ejection fraction 90 days post PPCI and on major adverse cardiac events through one year follow-up in patients with STEMI treated by PPCI.

METHODS

Study design

This is a single center prospective study, conducted according to the institutional STEMI protocol (MISSION!) implemented at Leiden University Medical Centre (LUMC) since February 2004.[14] This protocol includes standardized pre-hospital, in-hospital and outpatient clinical framework for decision making and treatment. Our hospital provides a round-the-clock service of PPCI with 6 trained PCI physicians and dedicated nurses.

Patients selection

Main results of MISSION! study are published elsewhere.[14] One hundred sixty-eight consecutive patients with first acute myocardial infarction (MI) were enrolled in this sub-study. Patients were eligible if STEMI symptoms started < 9 hours before the procedure, the electrocardiogram (ECG) demonstrated STEMI (ST-segment elevation ≥ 0.2 mV in ≥ 2 contiguous leads in V1 through V3 or ≥ 0.1 mV in other leads), and received abciximab prior to PPCI. Exclusion criteria were previous history of MI, previous PCI or bypass surgery, left bundle branch block, recent surgery, recent stroke, recent spinal trauma, hemorrhagic diatheses, severe liver or kidney failure and known contraindications for therapy with abciximab, aspirin, clopidogrel or heparin.

No informed consent is required, since the MISSION! protocol is the standard STEMI care regimen in the region Hollands-Midden, The Netherlands.

Electrocardiographic data analysis

All patients had a high quality 12-lead ECG recorded at presentation and within 90 min after PPCI. ST segment elevation was measured manually 20 ms after the end of the QRS complex (the J point) using a hand-held caliper. We have considered a resolution of the ST-segment of ≥ 70% when the sum of the ST-segment elevations measured at 90 minutes after PPCI decreased by more than 70% of the initial sum of ST-segment elevations.

Medications

Were prescribed according to MISSION! protocol.[14] All patients received abciximab (Centocor, Leiden, The Netherlands) before PPCI, an equivalent of 300 mg of acetylsalicylic acid, 600 mg clopidogrel as a loading dose, and heparin given as a bolus of 5000 IU at the start of the PCI procedure. After the procedure, all patients received aspirin (75 mg/day) indefinitely and clopidogrel (75 mg/day) for one year.

Laboratory data

Cardiac troponin-T (cTnT) concentration in serum was measured on an 3rd generation Elecsys 2010 analyzer (Roche Diagnostics, Almere, The Netherlands).The detection limit of the assay is 0.01 μg/l. The decision limit used for diagnosis of MI is 0.03 μg/l, with an imprecision of < 10%. Creatine kinase (CK) activity in plasma was measured on a Roche Hitachi Modular P800 (Roche Diagnostics) having an upper limit of normal of 200 U/L.

Blood samples were collected according to MISSION! protocol at admission and every 6 h in the first 48 h after PPCI. Subsequently these levels were determined every day up to discharge, unless clinical events suggested repeat measurements. After collection, blood samples were centrifuged immediately and serum was stored at -20°C until analysis. The laboratory staff responsible for measurements was blinded to the patient data.

Peak TnT and CK were determined retrospectively from serial samples in first 48 h. A value was defined as peak if it was the highest in the 48 h time period and if there was at least 1 lower value before and after this peak value.

Enzymatic infarct size measurement

The cumulative release of CK in the first 48 h (48-h CumCK) was calculated as a measure of infarct size in each patient by an investigator blinded to the assigned treatment.[15] For this purpose the two-compartment model is used, which has been verified for several enzymes. The model has been described in detail by van der Laarse et al.[16] This model can be used in all patients with MI, whether or not they received reperfusion therapy.

Invasive procedure and angiographic evaluation

Coronary angiography was performed by the femoral approach. All patients underwent PPCI and stenting of the infarction related artery (IRA) according to standard techniques. Stent implantation was successfully completed in all patients. Procedural success was defined as residual stenosis < 20% and TIMI flow grade 3. Initial and post procedural TIMI flow grade of the IRA[17] were assessed off-line.

Myocardial perfusion imaging

An ECG gated SPECT acquisition at rest using intravenous Technetium 99m Tetrofosmin (MYOVIEW, Amersham, Buckinghamshire, UK) was used to measure the LV ejection fraction (LVEF) 90 days after PPCI in a total of 160 patients. LVEF was calculated using an automated and validated method (QGS software, version 2.0, Cedars-Sinai Medical Center, Los Angeles, CA, USA). Detailed methods have been described elsewhere.[18] Eight patients (5%) in the study group had no perfusion study at follow-up (2 patients died and 6 patients had incomplete analysis due to technical difficulties). LVEF assessment was done by an investigator blinded to the patient data.

Clinical outcome

According to the MISSION! protocol, patients were scheduled at a dedicated out-patient clinic after 1, 3, 6 and 12 months. Clinical outcome was evaluated through the monitoring of major adverse cardiac events (MACE) occurring at any time during the follow-up. Only the most serious event of MACE was used to calculate the cumulative MACE per patient according to the following sequence: death> MI> heart failure (HF)> target vessel revascularization (TVR). Death was defined as "all-cause" death at follow-up. MI during follow-up was defined as a troponin-T rise > 0.03 µg/l with symptoms or PCI, or a re-rise of troponin-T > 25% after recent MI in the presence of symptoms or re-PCI, or the development of new Q waves on ECG.[19,20] Heart failure during follow-up was defined as either the presence of rales in more than one third of the lung fields that did not clear with coughing or evidence of pulmonary edema on chest X-ray. Target vessel revascularization was defined as any revascularization procedure of the target vessel.

Statistical analysis

Categorical variables are presented as counts and proportions (percentages) and compared by Chi-square or Fisher exact test. Normal distribution of continuous data was tested using a Kolmogorov-Smirnov test.

Normally distributed continuous data are presented as mean ± 1 SD and were compared by unpaired *t* test or one-way analysis of variance (ANOVA) as appropriate. Not-normally distributed data are expressed as median with interquartile range (IQR), and the Kruskal-Wallis test was used to compare differences between groups.

For comparison of multiple groups with ordinal categorization, the trend in the binomial proportions of categorical variables was analyzed using Chi-square for trend analysis (linear-by-linear association test), and one-way ANOVA was used to test for linear trends across the means of continuous variables with logarithmic transformation of outcome variables. Correlation between continuous variables was tested using Pearson correlation test.

Linear regression analyses were performed to characterize predictors of LVEF and peak TnT. Univariable and multivariable Cox proportional –hazards regression models were performed to characterize predictors of MACE and heart failure. Categorical variables included age > 75y, gender, hypertension, diabetes, hypercholesterolemia, smoking habit, Killip class ≥ 2, site of MI, IRA, initial TIMI 2-3 flow, multi-vessel disease, drug-eluting stents use, multiple stent implantation, ST-segment resolution ≥ 70% within 90 minutes and LVEF ≤ 40% at follow-up. Continuous variables included age, time from symptoms to treatment, sum of ST-segment elevation on admission ECG, basal, peak and cumulative 48-h CK release, basal

and peak cTnT, and LVEF at follow-up. Multivariable Cox regression was performed using only variables with a probability value < 0.05 at univariable regression analysis. Significant variables analysed were reported with their respective hazard ratios (HR) and 95% confidence intervals (CI). The cut-off value of early cTnT peak that identifies with the highest sensitivity and specificity patients with an ejection fraction ≤ 40% at 90 days was analyzed by the receiver operating characteristic curve.

All p-values are two-tailed, and statistical significance was defined if $p < 0.05$. All analyses were performed with SPSS version 14.0 statistical software (SPSS Inc., Chicago, IL, USA).

RESULTS

The study population consists of 168 consecutive patients who underwent PPCI and were treated with abciximab according to the MISSION! protocol.

Baseline characteristics

Data on peak cTnT was available in all patients included in the study. For all patients the peak cTnT value occurred within the first 24 hour after admission. For analysis of baseline clinical characteristics and procedural results, patients were stratified by peak cTnT into three tertiles (< 2.69 μg/L, 2.69-6.34 μg/L, > 6.34 μg/L, table I). Patients with higher peak cTnT values were more likely to be elderly (age ≥ 75 year) and presented with Killip class ≥ 2.

Procedural related characteristics

The median time between onset of symptoms and first balloon inflation was significantly longer in the highest peak cTnT tertile (172 min, IQR 116-264 min) than in the other cTnT tertiles (p trend = 0.04) (table 1).

For the entire study population, mean peak cTnT was 5.83 ± 5.79 μg/L. The peak cTnT occurred at the first measurement before PPCI (baseline) in 2% of patients, at 6 h post-PPCI in 40% of patients, at 12 h in 39% of patients, at 18 h in 14% of patients, and at 24 h in 5% of patients. If this categorization was done for the three peak cTnT tertiles, it was found that the higher the peak cTnT, the earlier the time the peak was achieved (p trend = 0.02, figure 2). By multivariable linear regression analysis including all variables listed in table 1, the independent correlates of peak cTnT after PPCI were anterior MI, sum of ST elevation on admission ECG, TIMI 2-3 pre-PPCI and Killip class ≥ 2 on admission (table 2). Of the variables listed in Table 1, none of the post-procedural angiographic findings were independently predictive of peak cTnT level.

Table 1 Baseline and procedural characteristics of patients stratified by peak troponin-T level

	Lowest < 2.69 (n = 56)	Medium 2.69-6.34 (n = 56)	Highest > 6.34 (n = 56)	p Trend
Age (years)	58 ± 11	56 ± 12	64 ± 12	0.002*
Age ≥ 75 yrs, n (%)	6 (11)	5 (9)	15 (27)	0.016**
Male gender, n (%)	44 (79)	43 (77)	46 (82)	NS**
Risk factors, n (%)				
Hypertension	19 (34)	19 (34)	20 (36)	NS**
Diabetes mellitus	10 (18)	3 (6)	5 (9)	NS**
Hypercholesterolemia	27 (48)	22 (39)	23 (42)	NS**
Current Smoking	37 (66)	31 (56)	31 (56)	NS**
Positive Family history	25 (45)	25 (46)	24 (44)	NS**
Killip class ≥ 2, n (%)	0	1 (2)	4 (7)	0.046**
Anterior MI, n (%)	34 (61)	13 (23)	33 (59)	NS **
Symptoms to balloon (min)	131 (105-165)	160 (113-258)	172(116-264)	0.04†
IRA is LAD, n (%)	32 (57)	11 (20)	30 (54)	NS**
Initial TIMI 2-3 flow, n (%)	33 (60)	18 (33)	9 (16)	< 0.001**
Post-PPCI TIMI 2-3 flow, n (%)	56 (100)	56 (100)	54 (96)	NS**
3-vessel disease, n (%)	7 (13)	7 (13)	10 (18)	NS**
DES, n (%)	29 (52)	30 (54)	24 (43)	NS**
Multiple stents implantation, n (%)	20 (36)	21 (38)	21 (38)	NS**
ST- resolution ≥ 70%, n (%)	40 (71)	36 (64)	32 (57)	NS**
Initial sum of ST- deviation (mm)	14 ± 8	19 ± 11	20 ± 10	< 0.001*
Basal CK (U/L)	192 ± 156	180 ± 177	447 ± 792	NS*
Basal TnT (µg/L)	0.17 ± 0.43	0.12 ± 0.31	1.42 ± 3.88	NS*
Peak CK (U/L)	641 ± 514	1929 ± 1810	3520 ± 1680	< 0.001*
Cumulative 48-h CK (U/L)	2996 ± 2990	8371 ± 3911	16306 ± 7859	< 0.001*

*Data are presented as mean ± standard deviation, number (%) of patients or median (Interquartile range). MI= myocardial infarction, IRA= infarction related artery, LAD= left anterior descending, TIMI= thrombolysis in myocardial infarction, PPCI= primary percutaneous coronary intervention, DES= drug eluting stents, CK= creatine kinase, TnT= troponin-T. *one way ANOVA for trend, ** Chi-square for trend,† Kruskal-Wallis test*

TIMI 2-3 flow pre-PPCI was present more frequently in patients of the lowest peak cTnT tertile. However, post-procedural TIMI flow was not significantly different between the tertiles (table 1).

The sum of ST-segment deviation on admission ECG is highest in patients with highest peak cTnT tertile. However, there were no significant differences between the tertiles with respect to occurrence of complete ST segment resolution. Peak CK was significantly higher in the highest peak cTnT tertile than in the other tertiles (table 1).

Cumulative 48-h CK release was highest in the highest peak cTnT tertile (table 1).

Assessment of the relationship between peak cTnT and enzymatic infarct size measured with cumulative CK in first 48-h post-PPCI, revealed a positive correlation between cTnT peak and enzymatic infarct size ($r = 0.73$, $p < 0.001$) (figure 1).

Table 2 Correlates of peak troponin-T level determined by multivariable linear regression analysis

Peak troponin-T level	Beta	B (95% CL)	P
Anterior MI	0.26	3.28 (1.3-5.2)	0.001
Sum of ST-deviation on admission ECG	0.34	0.19 (0.10-0.28)	< 0.001
TIMI 2-3 flow pre-PPCI	-0.35	-4.73 (- 7.0- -2.4)	< 0.001
Killip class ≥ 2	0.40	5.79 (3.5-8.1)	< 0.001

B= un-standardized regression coefficients, Beta= standardized regression coefficients, CL= confidence limits, ECG = electrocardiogram, MI = myocardial infarction, TIMI = thrombolysis in myocardial infarction.

Myocardial scintigraphy results

The LV function was analyzed for 160 patients at 3 months after PPCI. LVEF was highest in the lowest peak cTnT tertile (61 ± 8%), and lowest in the highest tertile (52 ± 13%, $p < 0.001$). LVEF was negatively correlated to peak cTnT values ($r = -0.52$, $p < 0.001$, figure 3). Mean value of peak cTnT was significantly higher in patients with LVEF ≤ 40% (14.1 ± 7.4 µg/L) compared to those with LVEF > 40% (5.1 ± 5.0 µg/L, $p< 0.001$).

Multivariable linear regression analysis revealed that the independent correlates of LVEF 3 months after PPCI were peak cTnT, TIMI 2-3 flow pre-PPCI and male gender (table 3).

Table 3 Correlates of left ventricular ejection fraction at 3 months follow-up, determined by multivariable linear regression analysis

LVEF	Beta	B (95% CL)	P
Peak troponin-T (µg/L)	-0.49	-0.94 (-1.3- -0.5)	< 0.001
Male gender	-0.22	-7.27 (-12.1- -2.4)	0.004
TIMI 2-3 flow pre-PPCI	0.22	5.49 (1.25-9.72)	0.01

B= un-standardized regression coefficients, Beta= standardized regression coefficients, CL= confidence limits, LVEF = left ventricular ejection fraction, TIMI = thrombolysis in myocardial infarction, PCI = percutaneous coronary intervention.

The highest sensitivity (86%) and specificity (74%) for the identification of patients with a LVEF ≤ 40% at 90 days was attained for an early cTnT peak cut-off value of 6.5 µg/L. The area under the curve for this cut-off value was 0.86 (95% CI = 0.77-0.95, figure 4).

Figure 1 Timing of peak levels in patients stratified by troponin-T level.

Patients were divided in three tertiles according to their peak plasma troponin-T level, per tertile, patients were categorized according to time-of-peak TnT at the pre-PPCI blood sample (baseline), and at the samples taken at 6, 12, 18 and 24 hours post-PPCI.

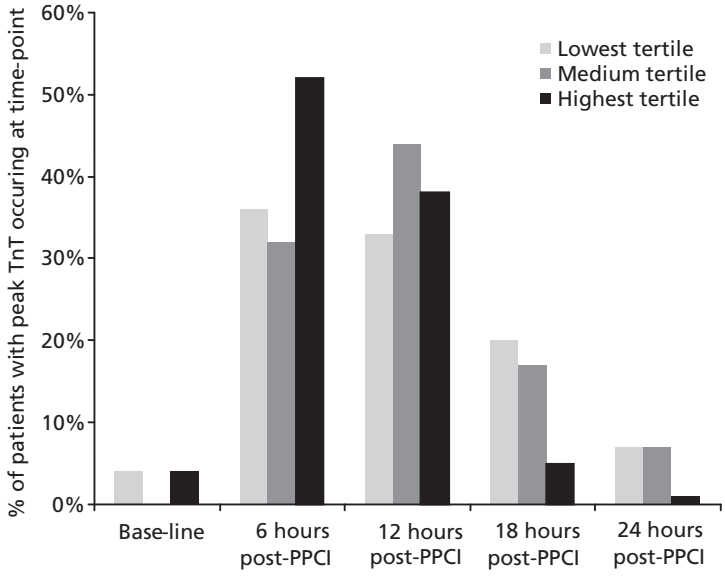


Figure 2 Relation between cumulative 48-h CK release and peak troponin-T level in 168 patients admitted with first acute myocardial infarction.

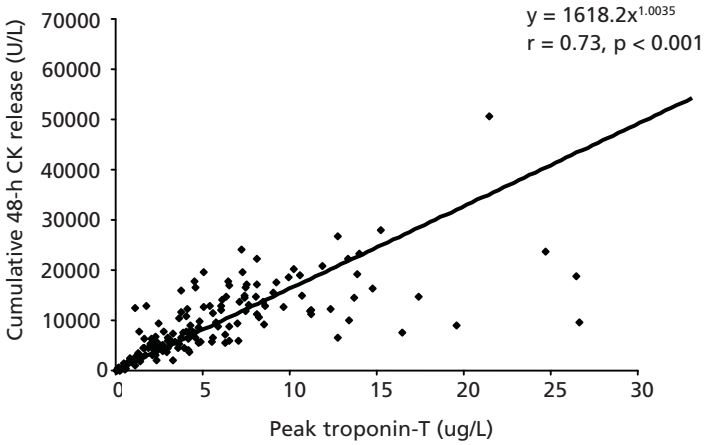


Figure 3 Relation between LV ejection fraction determined at 3 months follow-up and peak plasma troponin-T level in 168 patients admitted with first acute myocardial infarction.

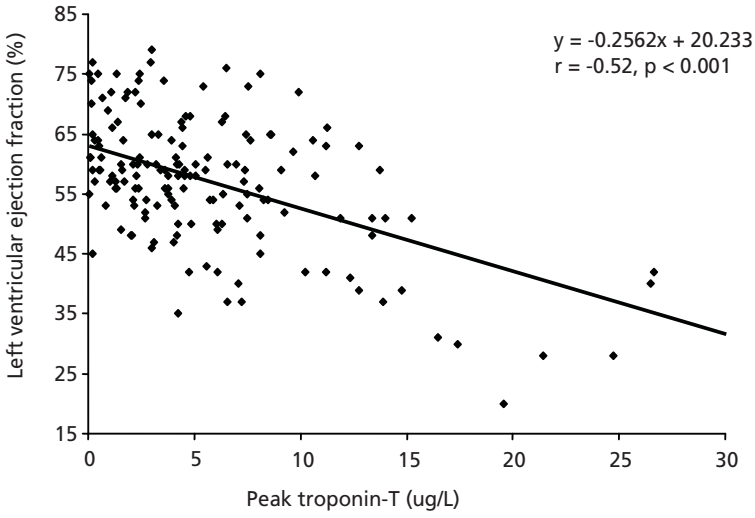
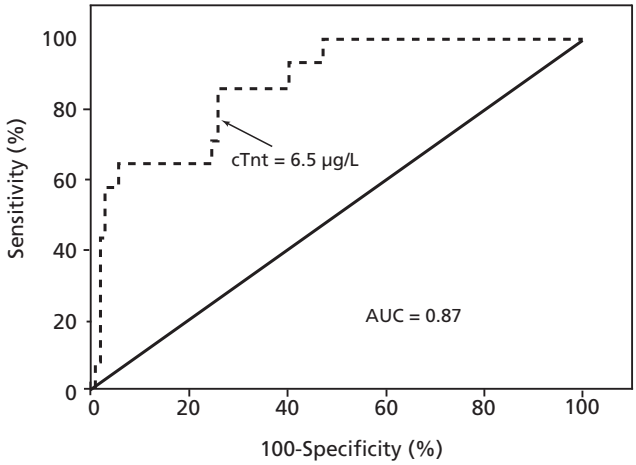


Figure 4 Receiver operator characteristic (ROC) curve analysis for peak troponin-T as a predictor of left ventricular ejection fraction ≤ 40% at 3 months follow-up.

AUC= Area under the ROC curve, cTnT= cardiac troponin T. Best decision threshold is shown (sensitivity is 86% and specificity is 74%).



Clinical follow-up

All patients were followed for a median of 210 days (interquartile range (IQR) 90-330 days). Cumulative MACE occurred in 27 (16%) patients. Mean peak cTnT was significantly higher in patients who developed a MACE (7.9 ± 8.9 µg/L) than in patients who did not develop any MACE (5.4 ± 4.9 µg/L, p = 0.03). Six (4%) patients died, and their mean peak cTnT (12.0 ± 14.9 µg/L) was higher that that of survivors (5.6 ± 5.1 µg/L, p = 0.007). Seven (4%) patients

had recurrent MI and 12 (7%) patients had a TVR during follow-up. Their mean peak cTnT values did not differ significantly from that of patients who had no recurrent MI or TVR.
Eight (5%) patients developed heart failure on follow-up, and had higher mean peak cTnT (14.2 ± 12.5 µg/L) than those without heart failure (5.4 ± 4.9 µg/L, p < 0.001).
Univariable Cox proportional-hazards regression analysis for prediction of MACE including all variables listed in table I, revealed that sum of ST segment deviation on admission ECG, peak cTnT, and LVEF at 3 months post-PPCI were significantly correlated with the incidence of MACE (table 4). A similar analysis for prediction of heart failure showed that peak cTnT and LVEF ≤ 40% were significantly correlated with the incidence of heart failure.
LVEF ≤ 40% was associated with 6 times higher incidence of heart failure compared to patients with LVEF > 40% (table 4).
By multivariable Cox regression analysis, including only variables that had p < 0.05 in univariable regression analysis, only peak cTnT was identified as independent predictor of incidence of MACE and heart failure (table 4).

Table 4 Predictors of major adverse cardiac events and heart failure determined by Cox proportional-hazards regression analysis

	Univariable			Multivariable		
	HR	95% CL	P	HR	95% CL	P
MACE						
Sum of ST-deviation on admission ECG	1.05	1.01-1.09	0.01	1.04	0.99-1.08	0.07
Peak TnT level (µg/L)	1.07	1.02-1.12	0.005	1.07	1.01-1.12	0.01
LVEF at 3 months follow-up (%)	0.96	0.93-0.99	0.03	--	--	--
Heart Failure						
Peak TnT level (µg/L)	1.13	1.06-1.21	< 0.001	1.12	1.05-1.20	0.001
LVEF ≤ 40%	6.03	1.4- 25.3	0.01	--	--	--

MACE = major adverse cardiac events, LVEF = left ventricular ejection fraction, HR = hazards ratio, CL = confidence limits.

DISCUSSION

In the present study we demonstrated that the location of myocardial infarction, the sum of ST-segment deviations on admission ECG, the pre-PPCI TIMI flow, and the Killip class at admission were determinants of peak cTnT levels. Furthermore, the peak cTnT was an independent predictor for left ventricular function at three month and for major adverse cardiac events including heart failure through one-year clinical fllow-up.

Basal CK, peak CK and cumulative 48-h CK

CK is an established non-invasive measure of infarction size and severity[21-23] and recently CK was also proved to be a good prognostic marker for patients undergoing primary PCI.[24] Despite its wide use in clinical studies, it is still difficult to decide which of the values from the CK dynamics reflects the real infarct size and is not corrupted by the early reperfusion process.[25,26] We have therefore analyzed in our study several CK levels: (1) the basal (admission)

value did not demonstrate a similar trend as peak cTnT, (2) the peak CK demonstrated a significant trend with the peak cTnT tertiles and (3) the cumulative 48-h CK [27,28] was strongly correlated with the peak cTnT values. Tzivoni et al.[29] have recently showed that peak levels of cTnT are as accurate as CK in estimating the myocardial infarction size in patients who undergo primary PPCI.

Determinants of peak TnT

Rasoul et al.[30] have reported that presentation delay, anterior location of the MI, and higher age were independent predictors of peak cTnT levels. The longer delay found by Rasoul et al.[30] may explain the higher sum of the ST-deviation on admission, the lower pre-PPCI TIMI flow and the higher Killip class which were found to be peak cTnT determinants in our study cohort. Although we did not find age to be an independent determinant of peak cTnT levels, we have observed significant age differences among the cTnT tertiles: patients in the highest peak cTnT tertile were older than patients in the lowest cTnT tertile (64 vs. 58 years, p-trend = 0.002); patients older than 75 years were also more frequent in the highest cTnT tertile than in the lowest cTnT tertile (27% vs. 11%, p-trend = 0.016).

Troponin-T and infarction size

In our study population all patients displayed their peak cTnT within the first 24 hours after admission. Early peak cTnT is known for some time[31] and relates to the troponin release dynamics in myocardial infarction patients who benefitted from early reperfusion therapy. Therefore we consider that: (1) a good prognostic indicator based on peak cTnT can be obtained for patients with MI treated with PPCI as early as the end of their first day in-hospital; (2) for risk stratification it appears to save time and money when serial cTnT measurements are limited to the first 24 hours in patients with MI treated with PPCI.

In our study, the patients within the highest (> 6.34 μg/L) peak cTnT tertile had an approximately five-times higher cumulative 48-h CK than patients within the lowest (< 2.69 μg/L) peak cTnT tertile. This group with the largest infarct size (highest peak cTnT tertile) presented a significantly higher delay between the onset of symptoms and PPCI when compared to the other two cTnT peak tertiles. All three cTnT tertiles had similar TIMI grades and ST-segment resolutions (≥ 70%) after PPCI, indicating no differences between groups in terms of epicardial or myocardial reperfusion (or impaired myocardial reperfusion known as "no-reflow" phenomenon[32,33]). Therefore, the difference in infarction size and the subsequent worse prognosis are to be explained only by the longer delay between symptoms and PPCI (and therefore the delay in abciximab administration) and not by a higher incidence of the "no reflow" phenomenon. This aspect is of particular interest and may be related to the abciximab administration prior to PPCI for all the patients. Periprocedural administration of abxicimab or the pre-procedural administration of tirofiban have been associated with a better myocardial perfusion and a significant reduction in one-year mortality.[4,34] In the present study we did not adjust for the time of abciximab administration because we intended to investigate the prognostic value of cTnT regardless of the medication received prior to PPCI.

Troponin-T in relation to left ventricular ejection fraction and heart failure

Peak cTnT was correlated negatively with the LVEF measured by myocardial scintigraphy after

three months. Previously, several studies have shown a relation between peak troponins and LV function in follow-up.[35-38]

We have also found that TIMI 2-3 flow pre-PCI was correlated with a better LV function at 3 months follow-up. Secondly, male gender was a strong independent negative predictor of LVEF at 3 months.

The peak cTnT at index event and the LVEF ≤ 40% at three month were significantly correlated with the incidence of heart failure through follow-up. LVEF ≤ 40% was associated with 6 times higher incidence of heart failure compared to patients with LVEF > 40%. Peak cTnT was identified as independent predictor of heart failure development at one year follow up. To the best of our knowledge, this is the first study to show that peak cTnT at the index event predicts heart failure through one year follow-up in STEMI patients who underwent PPCI.

In our study we showed that a cut-off point for early cTnT peak of 6.5 µg/L had a high sensitivity (86%) in prediction of patients with low ejection fraction at 90 days follow-up with a specificity of 74%. The screening ability of cTnT for detection of low ejection fraction was previously suggested. Tzivoni et al.[29] presented a cut-off value of 3.5 µg/L with a sensitivity of 90% but low specificity, 31% and Panteghini et al.[39] showed that cTnT > 2.98 µg/L predicts low ejection fraction at 3 months with a sensitivity of 86.7% and specificity of 81.4%.

Troponin-T and MACE

At follow-up, peak cTnT predicted major cardiac events such as death, myocardial infarction, target vessel revascularization and heart failure. These findings are in agreement with previous studies that demonstrated a relation between peak troponins and clinical outcomes in short and long-term follow-up.[35-38]

Based on the results of this study we suggest that a peak cTnT value obtained in the first 24 hours after PPCI may be routinely used as a sole cardiac marker in patients with ST-elevation myocardial infarction.

Limitations

In our view, a possible limitation is that we could not extend cTnT measurements beyond 48 hours because this was not included in the MISSION protocol. We could therefore not calculate a cumulative troponin release in analogy with cumulative CK values. However, the peak cTnT was successfully used in previous work and we do not expect that a cumulative cTnT value would have changed any of the presented findings.

CONCLUSIONS

Peak cardiac troponin-T in the first 24 after primary PCI offers a good estimation of infarct size and a long-term prognostic indicator in patients with first acute myocardial infarction.

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