

Prognostic Value of High Sensitive Troponin T in Patients with Chronic Ischemic Heart Disease Undergoing Percutaneous Coronary Intervention

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SOUHRN

Cíl: Několik studií zkoumalo různé srdeční biomarkery jako prediktory prognózy po perkutánní koronární intervenci (PCI) u pacientů s chronickou ischemickou chorobou srdeční; výsledky těchto studií jsou však rozporuplné. Stanovování troponinu T vysoce citlivou metodou (high-sensitive troponin T, hs-TnT) představuje novou a přesnější možnost. Cílem této studie bylo zjistit, zda mohou hodnoty hs-TnT sloužit jako prediktor závažných kardiovaskulárních příhod (major adverse cardiovascular events, MACE) v prvním roce po úspěšné plánované PCI u pacientů se stabilní anginou pectoris (SAP).

Materiál a metody: Do studie bylo zařazeno 100 pacientů s diagnózou SAP a úspěšně provedenou plánovanou PCI. Ze studie byli vyloučeni nemocní se zvýšenými hodnotami troponinu I (> 0,1 ng/ml) před výkonem. Hodnoty hs-TnT se stanovovaly před výkonem a v rozmezích 3–4 hodin (časné období) a 12–24 hodin (pozdní období) po výkonu, přičemž za pozitivní byla považována hodnota hs-TnT > 14 pg/ml. Byla rovněž zaznamenávána incidence MACE v prvním roce.

Výsledky: Hodnoty hs-TnT byly pozitivní u 36 % pacientů v prvním období a u 54 % pacientů v pozdním období. Incidence MACE v prvním roce byla významně vyšší u pacientů s pozitivními hodnotami hs-TnT v časném, ne však v pozdním období (36,1 % vs. 15,6 %; $p = 0,026$); logistická regresní analýza prokázala poměr šancí ve výši 3,36.

Závěr: Hodnoty hs-TnT naměřené 3–4 hodiny po úspěšné elektivní PCI u pacientů se SAP mohou predikovat incidenci MACE v prvním roce. Tyto výsledky musí nicméně potvrdit větší studie.

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ABSTRACT

Objective: Several studies have investigated different cardiac biomarkers as predictors of the prognosis after percutaneous coronary interventions (PCI) in patients with chronic ischemic heart disease; nevertheless, the results of these studies are conflicting. High sensitive troponin T (Hs-TnT) measurement is a novel and sensitive method. The aim of this study was to investigate if Hs-TnT levels are a predictor of major adverse cardiovascular events (MACE) in the first year after a successful elective PCI in patients with stable angina pectoris (SAP).

Material and methods: 100 patients who presented with SAP and underwent successfully elective PCI were included in the study. Patients with elevated troponin I levels (>0.1 ng/mL) before the procedure excluded from the study. Hs-TnT levels were measured before the procedure and at 3–4 hours (h) (early period) and 12–24 hours (late period) after the procedure and Hs-TnT level >14 pg/mL was considered positive. The incidence of MACE during the first year was recorded.

Results: Hs-TnT levels were positive in 36% of the patients in the early period and in 54% of the patients in the late period. The incidence rate of MACE for the first year was significantly higher in the patients with positive Hs-TnT levels in the early period but not the late period (36.1% vs. 15.6%; $p = 0.026$) and logistic regression analysis yielded an odds ratio of 3.36.

Conclusion: Hs-TnT levels measured 3–4 h after a successful elective PCI in patients with SAP can predict the incidence of MACE within the first year. Nonetheless, these results must be corroborated by other larger studies.

Keywords:

Chronic ischemic heart disease

High sensitive troponin T

Major adverse cardiovascular events

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Introduction

Many studies have investigated changes in concentrations of cardiac biomarkers, both before and after PCI, as predictors of short-term and long-term prognosis. These biomarkers are usually troponin T and I, creatine kinase-muscle/brain (CK-MB), and high sensitive C-reactive protein (Hs-CRP). Cardiac troponin T and I are components of the contractile apparatus of cardiomyocytes and used as biomarkers of myocardial necrosis in patients suspected of having an acute coronary syndrome (ACS).¹ Moreover, there is a documented relationship between troponin levels and recurrent ischemic coronary events in patients with acute coronary syndromes.^{2–4} It is known that serum troponin levels increase not only during ACS but also the following PCI.⁵ Troponin increases in about one-third of the patients who undergo PCI and is associated with abnormal microvascular perfusion and necrosis, as determined by cardiac magnetic resonance imaging (MRI).^{6,7} The degree of troponin elevation following PCI is related to the duration of the procedure, lesion length, development of complications during the procedure, stent implantation, presence of chronic kidney disease, and interventions in more than one artery.^{8,9} Studies on the prognostic value of troponin elevation following PCI report varying outcomes. Some studies state that even slight elevations in cardiac troponin levels unfavorably influence PCI outcome while others report that only high levels of cardiac troponin are associated with a poor outcome.^{10–12} Importantly, some studies have failed to determine a relation between troponin positivity after PCI and poor cardiovascular outcomes.^{13,14} High sensitive troponin T (Hs-TnT) measurement is more sensitive than the conventional method and allows measurement of up to 10-fold lower concentration of troponin T.¹⁵ High Hs-TnT levels have been associated with long-term adverse events in both NSTEMI-ACS patients and in stable, high-risk populations.^{16,17} Although Hs-TnT is a sensitive biomarker of cardiac injury that is used in risk stratification, the prognostic significance of post-PCI Hs-TnT levels remains unclear in patients who have undergone elective PCI for stable angina. Thus, evaluating post-PCI Hs-TnT levels may be beneficial in identifying patients who may require closer monitoring and more intensive antiaggregant treatment. Therefore, the present study aimed to investigate the prognostic value of pre- and post-procedure Hs-TnT levels on poor cardiovascular outcomes within a one-year follow-up period in the patients undergoing successful elective PCI for stable angina.

Material and methods

Patients

A total of 103 patients had undergone successful elective percutaneous coronary intervention for stable angina was enrolled in the study. The final study population was 100 patients as three patients discontinued the follow-up in the first year. All patients were informed about the study and their informed consent was obtained. The study was approved by the Faculty of Medicine Ethics Committee. Patients presenting with acute coronary syndromes, pre-

vious unsuccessful percutaneous coronary intervention, high cardiac troponin levels at presentation, heart failure with reduced ejection fraction, renal insufficiency (estimated glomerular filtration rate; eGFR <30 mL/min/1.73 m²), liver insufficiency, metastatic carcinoma, pulmonary embolism, cor pulmonale, moderate/severe pulmonary hypertension, pericardial disease, and patients with less than one-year survival expectancy were excluded from the study.

Sample collection and measurements of high sensitive troponin T

In total three blood samples were drawn for Hs-TnT measurement; i.e., before PCI, between 3–4 hours (h) and between 12–24 h after PCI. Samples immediately centrifuged at 3000 rpm for 15 min to separate serum and the serum stored at –20 °C till use. After the completion of patient enrollment (approximately six months), all serum samples were analyzed at the laboratory using an “Eleclys® Troponin T high sensitive assay” kit (RocheDiagnostics Limited) according to manufacturer's instructions. The measurement range of the kit is 3–10000 ng/L (pg/mL), and Hs-TnT was measured by electrochemiluminescence on a Cobas e 411 analyzers (Roche Diagnostics). An Hs-TnT level >14 pg/mL (above the upper limit of the reference range) was scored as positive. CK-MB and cTn-I were measured both before and after PCI in all patient samples, and cTn-I >0.1 ng/mL (above the upper limit of the reference range) and CK-MB >4.96 ng/mL (above the upper limit of the reference range) scored as positive. Patients who presented with stable angina and with no previous coronary angiography (CAG) primarily underwent CAG at the Coronary Angiography Unit. CAG of patients reviewed and those with a lesion causing 70% or higher stenosis on CAG evaluated for PCI suitability. PCI performed by experienced cardiologists on suitable patients. Transthoracic echocardiography was performed and ejection fraction (EF) values were recorded. In addition, the EuroSCORE (European System for Cardiac Operative Risk Evaluation) was calculated for each patient. Prior to PCI, each patient received 300 mg aspirin and 300–600 mg clopidogrel. Unfractionated heparin was administered at a dose of 100 U/kg during the procedure and additional doses were administered, as necessary, during the prolonged procedures. After the procedure, the patients have prescribed a maintenance therapy of 100 mg aspirin and 75 mg clopidogrel for one year, in addition to other necessary medications such as statins, ACE inhibitors, and β -blockers. The procedure considered successful if TIMI III flow was observed after PCI, the residual lesion was \leq 20%, and stent thrombosis was absent in the first hour after the procedure. Procedural details such as type (DES or BMS), length, and diameter of the stents implanted, number of diseased vessels, and number of vessels with interventions recorded (interventions grouped as either 1 vessel or \geq 2 vessels). In the event of more than one stent is implanted, stent length was considered as the sum of all stents used and stent diameter was that of the narrowest used stent. Stent type was considered as DES even if one of the used stents was DES. Balloon angioplasty was not taken into account for stent-related data (seven patients). The CAG of the patients was reviewed and SYNTAX scores (SYNergy between

Table 1 – Comparison of demographic variables, clinical data and percutaneous coronary intervention data according to the post-procedural 3–4 h and 12–24 h Hs-TnT value

	3–4 h Hs-TnT		p-value	12–24 h Hs-TnT		p-value
	Negative (n = 64)	Positive (n = 36)		Negative (n = 46)	Positive (n = 54)	
Age (year)	55 (37–82)	59 (33–90)	0.337	55 (37–75)	58 (33–90)	0.036*
	n (%)	n (%)		n (%)	n (%)	
Gender (n [%])						
Female	19 (29.7)	7 (19.4)	0.344	14 (30.4)	12 (22.2)	0.370
Male	45 (70.3)	29 (80.6)		32 (69.6)	42 (77.8)	
Family history (n [%])						
No	34 (53.1)	18 (50.0)	0.836	24 (52.2)	51 (51.9)	1.000
Yes	30 (46.9)	18 (50.0)		22 (47.8)	26 (48.1)	
Hypertension (n [%])						
No	25 (39.1)	6 (16.7)	0.025*	18 (39.1)	13 (24.1)	0.131
Yes	39 (60.9)	30 (83.3)		28 (60.9)	41 (75.9)	
Diabetes mellitus (n [%])						
No	40 (62.5)	21 (58.3)	0.831	28 (60.9)	33 (61.1)	1.000
Yes	24 (37.5)	15 (41.7)		18 (39.1)	21 (38.9)	
Smoking (n [%])						
No	33 (51.6)	15 (41.7)	0.155	23 (50.0)	25 (46.3)	0.073
Yes	19 (29.7)	8 (22.2)		16 (34.8)	11 (20.4)	
Quitted	12 (18.8)	13 (36.1)		7 (15.2)	18 (33.3)	
Hyperlipidemia (n [%])						
No	32 (50.0)	15 (41.7)	0.532	18 (39.1)	29 (53.7)	0.164
Yes	32 (50.0)	21 (58.3)		28 (60.9)	25 (46.3)	
History of MI (n [%])						
No	43 (67.2)	21 (58.3)	0.394	31 (67.4)	33 (61.1)	0.538
Yes	21 (32.8)	15 (41.7)		15 (32.6)	21 (38.9)	
Ejection fraction (%)	57.5	53.1	0.160	54.8	52.4	0.606
Body mass index (kg/m²)	28.2	28.1	0.600	28.4	28.1	0.874
eGFR (mL/min/1.73 m²)	111.1	108.6	0.586	116.7	100.7	0.121
Pre-procedure Hs-TnT (pg/mL)	3.1 (3.0–11.5)	9.8 (10.5–19.1)	0.0001*	3.1 (3.0–11.5)	8.0 (3.0–19.1)	0.0001*
EuroSCORE	1 (0–7)	3 (0–8)	0.047*	1 (0–7)	2 (0–8)	0.099
SYNTAX score	8 (2–35)	10 (1–31)	0.191	7 (2–35)	10 (1–31)	0.003*
Number of diseased vessels						
1 vessel	45 (70.3)	20 (55.6)	0.190	34 (73.9)	31 (57.4)	0.096
≥2 vessels	19 (29.7)	16 (44.4)		12 (26.1)	23 (42.6)	
Number of intervened vessels						
1 vessel	53 (83)	27 (75)	0.436	39 (84.8)	41 (75.9)	0.322
≥2 vessels	11 (17)	9 (25)		7 (15.2)	13 (24.1)	
	n = 58	n = 35		n = 42	n = 51	
Stent length (mm)	18 (9–79)	28 (9–92)	0.032*	18 (9–79)	28 (9–92)	0.004*
Stent diameter (mm)	2.7 (2.2–4.5)	2.7 (2.5–4.5)	0.473	2.7 (2.2–4.5)	2.7 (2.2–4.5)	0.788
Stent type						
BMS	24 (41.4)	17 (48.6)	0.525	19 (45.2)	22 (43.1)	1.000
DES	34 (58.6)	18 (51.4)		23 (54.8)	29 (56.9)	

BMS – bare metal stent; DES – drug-eluting stent; eGFR – estimated glomerular filtration rate; Hs-TnT – high sensitive troponin T; MI – myocardial infarction; * p-value <0.05 – statistically significant.

PCI with TAXUS™ and Cardiac Surgery) were calculated. Patients were followed up at 1, 6 and 12 months after the procedure to determine the predictive value of Hs-TnT for major adverse cardiovascular events (MACE). Cardiac death, acute coronary syndrome [ST-elevation MI (STEMI), NSTEMI, and unstable angina pectoris (USAP)], and stroke defined as MACE. All patients with acute coronary syndrome after the initial PCI underwent CAG (20 patients). The CAGs of the patients reviewed and the type and severity of the lesions (stent thrombosis, stent restenosis and other vascular lesions) recorded. Only patients with critical lesions ($\geq 70\%$) on CAG were considered as USAP. Stent thrombosis defined as complete occlusion of the stent by thrombotic lesions inside the target vessel and stent restenosis defined as $\geq 70\%$ stenosis of the stent inside the target vessel. In patients with more than one MACE within the first year, the first event considered as MACE.

Statistical analysis

The SPSS 17.0 (Chicago, IL) package program was used for statistical analyses of data. Categorical measurements were summarized as number and percentage, whereas continuous variables were represented as a median. The Chi-square test or the Fisher test used for comparing categorical variables (demographic data, gender, cut-off values of Hs troponin etc.). Distributions compared between groups for continuous variables and the Mann Whitney U-test was used as the data were found to be non-normally distributed (age, stent length, stent diameter, SYNTAX score etc.). Factors influencing the study endpoint (incidence of MACE) were determined using logistic regression analysis.

The level of statistical significance was set at ' $p < 0.05$ ' for all tests.

Results

The study population consisted of a total of 100 patients of whom 26 (26%) were female and 74 (74%) were male. The age of the participants ranged between 33 and 90 years and the mean age was 57.31 ± 10.3 years. Hs-TnT was positive in 36 (36%) patients between 3–4 h and in 54 (54%) patients between 12–24 h post-PCI. During the course of the one-year follow-up, the incidence of MACE was 23% ($n = 23$) involving cardiac death ($n = 1$), ACS ($n = 20$; $n = 5$ STEMI, $n = 5$ NSTEMI, $n = 10$ USAP), and stroke ($n = 2$). The distribution of lesions causing MACE in patients who developed ACS was as follows: stent thrombosis ($n = 4$), stent restenosis ($n = 12$), new lesions in other than target vessel ($n = 4$). Comparison of demographic variables, clinical data, and percutaneous coronary intervention (PCI) data according to the post-procedural 3–4h and 12–24h Hs-TnT value, the prevalence of hypertension ($p = 0.025$), age ($p = 0.036$), pre-procedure Hs-TnT value ($p = 0.0001$), EuroSCORE ($p = 0.047$), longer stent length ($p = 0.032$) and SYNTAX score ($p = 0.003$) were significantly higher in the patients with positive Hs-TnT (Table 1). There are no significant differences except male gender in the comparison of demographic variables, clinical data, and percutaneous coronary intervention data according to the presence of one-year MACE have been found (Table 2). Positive Hs-TnT value at 3–4 h post-procedure was statisti-

Table 2 – Comparison of demographic variables, clinical data, and percutaneous coronary intervention data according to the presence of one-year major adverse cardiovascular events

	MACE (–) $n = 77$	MACE (+) $n = 23$	p-value
	Median (min–max)	Median (min–max)	
Age (year)	56 (33–90)	56 (37–68)	0.431
	n (%)	n (%)	
Gender			
Female	25 (32.5)	1 (4.3)	0.006*
Male	52 (67.5)	22 (95.7)	
Family history			
No	36 (46.8)	16 (69.6)	0.062
Yes	41 (53.2)	7 (30.4)	
Hypertension			
No	25 (32.5)	6 (26.1)	0.618
Yes	52 (67.5)	17 (73.9)	
Diabetes mellitus			
No	46 (59.7)	15 (65.2)	0.808
Yes	31 (40.3)	8 (34.8)	
Smoking			
No	41 (53.2)	7 (30.4)	0.142
Yes	18 (23.4)	9 (39.1)	
Quitted	18 (23.4)	7 (30.4)	
Hyperlipidemia			
No	34 (44.2)	13 (56.5)	0.346
Yes	43 (55.8)	10 (43.5)	

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Table 2 – Comparison of demographic variables, clinical data and percutaneous coronary intervention data according to the presence of one-year major adverse cardiovascular events (Continued)

	MACE (–) <i>n</i> = 77	MACE (+) <i>n</i> = 23	<i>p</i> -value
	Median (min–max)	Median (min–max)	
History of MI			
No	49 (63.6)	15 (65.2)	0.999
Yes	28 (36.4)	8 (34.8)	
History of PCI			
No	42 (54.5)	14 (60.9)	0.639
Yes	35 (45.5)	9 (39.1)	
History of CABG			
No	71 (92.2)	22 (95.7)	1.000
Yes	6 (7.8)	1 (4.3)	
Systolic blood pressure (mmHg)	130 (85–185)	130 (100–170)	0.879
Diastolic blood pressure (mmHg)	75 (45–115)	80 (45–95)	0.317
Heart rate (beat/min)	72 (48–110)	70 (56–120)	0.667
Body mass index (kg/m²)	28.1 (19.6–48.0)	27.7 (21.3–38.8)	0.870
eGFR (mL/min/1.73 m²)	110.9 (37.4–144.0)	111.8 (77.7–140.0)	0.353
Ejection fraction (%)	60 (36–70)	58 (25–66)	0.083
Score of EuroSCORE	1 (0–8)	2 (0–8)	0.910
Hemoglobin (mg/dL)	13.5 (8.2–17.3)	14.4 (11.2–16.8)	0.128
Creatinine (mg/dL)	0.84 (0.4–1.5)	0.8 (0.6–1.2)	0.611
Fasting blood glucose (mg/dL)	102 (64–254)	101 (82–300)	0.606
LDL (mg/dL)	105 (33–197)	94 (34–218)	0.550
HDL (mg/dL)	36 (23–59)	31 (18–51)	0.131
Triglyceride (mg/dL)	136 (32–404)	157 (27–648)	0.210
Total cholesterol (mg/dL)	168 (80–290)	179 (78–313)	0.912
	<i>n</i> = 72	<i>n</i> = 21	
Stent diameter (mm)	2.7 (2.2–4.5)	2.7 (2.2–4.5)	0.803
Stent length (mm)	22 (9–79)	28 (9–92)	0.568
Stent count	1 (1–3)	1 (1–4)	0.766
	<i>n</i> = 77	<i>n</i> = 23	
SYNTAX score	8 (1–35)	10 (2–28)	0.447
	<i>n</i> (%)	<i>n</i> (%)	
Number of diseased vessels			
1 vessel	54 (70.1)	11 (47.8)	0.079
≥ 2 vessels	23 (29.1)	12 (52.2)	
Number of intervened vessels			
1 vessel	64 (83.1)	16 (69.6)	0.232
≥ 2 vessels	13 (16.9)	7 (30.4)	
	<i>n</i> = 72	<i>n</i> = 21	
Stent type			
BMS	30 (41.7)	11 (52.4)	0.457
DES	42 (58.3)	10 (47.6)	

BMS – bare metal stent; CABG – coronary artery bypass grafting; DES – drug eluting stent; eGFR – estimated glomerular filtration rate; HDL – high-density lipoprotein; Hs-TnT – high sensitive troponin T; LDL – low-density lipoprotein; MI – myocardial infarction; PCI – percutaneous coronary intervention; * *p*-value <0.05: statistically significant.

cally significant in patients who developed MACE within one year (*p* = 0.026). Among other cardiac biomarkers, post-procedure CK-MB value at 12–24 h was significantly higher in the MACE group (*p* = 0.008) (Table 3). A regression model was created using variables that were statistically significant during univariate analysis. Logistic re-

gression analysis was performed to identify independent risk factors for the development of MACE within one year (odds ratio = 11.31, 95% CI 1.35–94.64; *p* = 0.025) and it determined that positive Hs-TnT at 3–4 h post-procedure is a significant risk factor (odds ratio = 3.36, 95% CI 1.09–10.33; *p* = 0.034) (Table 4).

Table 3 – Comparison of post-procedural cut-off values of Hs-TnT and other cardiac biomarkers according to the presence of one-year major adverse cardiovascular events

	MACE (–) (n = 77) n (%)	MACE (+) (n = 23) n (%)	p-value
Hs-TnT (3–4 h)			
Negative	54 (70.1)	10 (43.5)	0.026*
Positive	23 (29.9)	13 (56.5)	
Hs-TnT (12–24 h)			
Negative	38 (49.4)	8 (34.8)	0.243
Positive	39 (50.6)	15 (65.2)	
cTn-I (3–4 h)			
Negative	64 (83.1)	16 (69.6)	0.232
Positive	13 (16.9)	7 (30.4)	
cTn-I (12–24 h)			
Negative	49 (63.6)	13 (56.5)	0.626
Positive	28 (36.4)	10 (43.5)	
CK-MB (3–4 h)			
Negative	66 (85.7)	18 (78.3)	0.516
Positive	11 (14.3)	5 (21.7)	
CK-MB (12–24 h)			
Negative	60 (77.9)	11 (47.8)	0.008*
Positive	17 (22.1)	12 (52.2)	

CK-MB – creatine kinase isoenzyme MB; cTn-I – cardiac troponin I; Hs-TnT – high sensitive troponin T; MACE – major adverse cardiovascular event; * p-value <0.05: statistically significant.

impaired microvascular perfusion⁶ and necrosis.⁷ Elevated cTn following PCI is also associated with duration of the procedure, lesion length, development of complications during the procedure (dissection, lateral branch occlusion, distal embolization, no-reflow phenomenon), stent usage, chronic kidney disease, and interventions in more than one vessel(8,9). Prolonged balloon inflation time, complex vascular structure, and left ventricle dysfunction are other causes of cTn elevation after PCI(19,21). Post-PCI, the number of hypertensive patients, and the EuroSCORE were significantly higher in patients with positive Hs-TnT only in the early period, while age and SYNTAX score were significantly higher in those with positive Hs-TnT in the late period. Earlier studies have reported the presence of higher cTn values before PCI in patients who show post-procedure cTn positivity. Miller et al. reported higher cTn-T values at 8–16 h post-procedure in those with high initial cTn-T values (≥ 0.03 ng/mL) compared to those with low initial cTn values (< 0.03 ng/mL) (22). A relationship between post-procedure cTn-I and cTn-T values and long-term mortality has been established(11–13, 18–20). While some studies showed that elevated cTn after PCI is an independent predictor of mortality(11,12,18), others did not report such an association(13,19,20). It is important to mention here that some of these studies also had patients with MI who had higher levels of cardiac biomarkers before PCI(12,18,20). Kini et al.(13) reported a 16.1% increase in the rate of CK-MB elevation (≥ 16 U/L) and 38.9% cTn-I positivity (≥ 2 ng/mL) after elective PCI in a study population of 2873 patients (not including high-risk patients). They also suggested that, after an average follow-up period of 12 ± 6 months,

Table 4 – Logistic regression analysis for the development of major adverse cardiovascular events in one year

	B	S.E.	Wald	Df	p	Odds ratio	95% CI for EXP(B)	
							Lower	Upper
Age	–0.040	0.026	2.407	1	0.121	0.96	0.91	1.01
Gender (male)	2.426	1.084	5.008	1	0.025*	11.31	1.35	94.64
Hs-TnT (3–4 h)	1.212	0.573	4.474	1	0.034*	3.36	1.09	10.33
CK-MB (12–24 h)	–0.006	0.032	0.030	1	0.862	0.99	0.93	1.06
Constant	–1.485	1.689	0.773	1	0.379	0.23		

CK-MB – creatine kinase isoenzyme MB; Hs-TnT – high sensitive troponin T; M – male; * p-value <0.05: statistically significant.

Discussion

Minor myocardial injury after successful PCI is quite common and cardiac biomarkers used to assess the extent of injury include CK-MB and cTn. The prevalence of elevated cTn after PCI has been reported to be between 17% and 48%.^{11–13,18–20} However, some of these studies have included MI patients with high levels of cardiac biomarkers prior to PCI.^{12,18,20} The present study comprised patients without ACS and with normal pre-procedure cTn-I levels (≤ 0.1 ng/mL) in whom Hs-TnT was elevated (> 14 pg/mL) in 36% of the patients at 3–4 h post-procedure and in 54% at 12–24 h. Post-procedure elevated cTn is associated with

there is a relationship between more than five-fold elevation in CK-MB and cardiac mortality, however post-procedure elevated cTn-I levels do not predict cardiac mortality. Likewise, Natarajan et al.(19), in a study on 1128 low-risk patients observed 17% cTn-I positivity but without CK-MB elevation after PCI and observed no relation with adverse cardiovascular outcomes at the end of one-year follow-up. Contrary to these studies, there are studies that suggest a significant relationship between post-procedure cTn levels and adverse cardiovascular outcomes. Prasad et al.(23) have reported cTn-T positivity (≥ 0.03 ng/mL) without CK-MB elevation after PCI in 19.6% of 1949 patients with normal CK-MB and cTn-T values before the procedure and found that post-procedure cTn-T

positivity was associated with adverse cardiovascular events during a median follow-up period of 26 months. In another report, Prasad et al.⁽²⁴⁾ divided 5487 patients into groups, who underwent elective PCI, according to pre-procedure and post-procedure cTn-T levels with a 28-month median follow-up period, and suggested that pre-procedure elevated cTn-T levels (≥ 0.01 ng/mL) are a predictor of mortality within one month and that post-procedure elevated cTn-T levels (≥ 0.01 ng/mL) are associated with 30-day mortality. The present study consisted of patients who presented with stable angina, had normal cTn-I levels (cTn-I ≤ 0.1 ng/mL) before the procedure and underwent successful, elective PCI. MACE development was analyzed at one year and significant relationship was determined between post-procedure early Hs-TnT positivity (36.1% vs. 15.6%; $p=0.026$). Further, even though the incidence of MACE at one year was higher in patients with post-procedure late Hs-TnT positivity, this was not statistically significant (27.8% vs. 17.4%; $p=0.243$). A regression model used to identify factors that independently affected MACE occurrence and it was found that post-procedure early Hs-TnT positivity was a significantly associated with MACE (odds ratio=3.36, 95% CI 1.09-10.33; $p=0.034$). Further analyses of MACE development during the first year using a cTn-I cut-off value of greater than 0.1 ng/mL revealed no significant differences between these two groups. This may be attributed to the fact that Hs-TnT is more sensitive than cTn-I. These results imply that Hs-TnT is a better biomarker than cTn-I in predicting risk of MACE development after PCI and also provides better prognostic information. A similar analysis for CK-MB revealed post-procedure late CK-MB positivity was significantly higher in the group that developed MACE at one year ($p = 0.008$). Such a significant elevation in post-procedure late period is probably due to the fact that CK-MB is detectable only in the later periods following myocardial injury. Nonetheless, this significance disappeared during logistic regression analysis. Two potential explanations exist for the observed elevations in cardiac biomarkers after PCI and the incidence of MACE. The first uses a positive correlation between the magnitude of myocardial injury, and cTn secretion and the fact that cTn is known to be elevated after PCI and myocardial injury, as documented by MRI. Consequently, myocardial injury may impair left ventricle function and lead to life-threatening arrhythmia. The alternative explanation is that elevated CK-MB and cTn values may also be markers of severe atherosclerosis, increased plaque burden, presence of sensitive plaque, endothelial dysfunction, microvascular injury, and inflammation, and that inflammation is an independent predictor of long-term adverse events after PCI.²³ Given this, we can conclude that both post-procedure early (3–4 h) Hs-TnT positivity and late (12–24 h) CK-MB positivity are associated with one-year MACE development in patients with stable angina undergoing successful, elective PCI. Importantly, separating the effects of post-PCI Hs-TnT positivity on MACE development in early and late periods is unique to this report and, to the best of our knowledge, is the first of its kind. In our study, the only clinical risk factor affecting MACE development in 1 year was male gender. In a meta-analysis involving 13 randomized controlled trials published by

Chen et al.⁵). It has been reported that MACE rates are more common in female gender in the short-term and long-term after coronary stenting. The reason for this inconsistent finding in our study may be the low number of female patients in the study population (74% male, 26% female). There are some limitations of our study must be emphasized. The number of patients in the present study is only 100 and the prognostic usefulness will be better understood with larger studies. Also the follow-up period was limited to one year and it is possible that Hs-TnT after PCI is relevant for long-term prognosis as well. Prognostic assessment for mortality could not be performed as death was an infrequent outcome during follow-up. The distribution of risk factors among the groups with and without Hs-TnT positivity after PCI was not homogenous and only the global effects of these factors on MACE development, rather than their individual effects, may be evident. Some of the patients did not complete all follow-up visits, had to be reached by phone, and evaluated at the closest health center. Thus, it is possible that information so obtained may not be completely accurate. Secondary endpoints such as incidence and degree of angina pectoris, hospitalization for heart failure, and asymptomatic stent restenosis were not included and therefore, follow-up visits did not specifically address these issues.

Conclusion

In conclusion, post-procedure early period Hs-TnT measurement may provide prognostic benefit (prognostic marker of MACE incidence) in the patients who undergo PCI for stable angina, but larger studies are required to adequately verify this information.

Conflict of interest

All authors declare that they do not have conflict of interest.

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None.

Ethical statement

Cukurova University, Faculty of Medicine, ethics committee – (09.02.2012/5).

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