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ALANINE AMINOTRANSFERASE LEVELS AND MONOCYTE COUNT INDEPENDENTLY PREDICT 30-DAY OUTCOMES IN ST-ELEVATION MYOCARDIAL INFARCTION PATIENTS WITH SUCCESSFULLY RESTORED CORONARY TIMI-3 FLOW BY PRIMARY PERCUTANEOUS CORONARY INTERVENTION

Alanin Aminotransferaz Düzeyleri ve Monosit Sayısı Primer Perkutan Koroner Girişim ile Başarılı TIMI-3 Koroner Akım Sağlanan ST Yükselmeli Miyokard İnfarktüsünde 30 Günlük Sonuçları Bağımsız Olarak Öngörür

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ABSTRACT

Aim: To investigate the relationship of various hematological and biochemical parameters besides the cardiac enzymes with 30-day outcomes in patients with successfully restored coronary TIMI-3 flow by primary percutaneous coronary intervention (p-PCI).

Materials and methods: Two hundred patients with ST elevation myocardial infarction (STEMI), with no history of prior myocardial infarction (MI), who underwent p-PCI and had TIMI-3 flow, were enrolled, consecutively. The primary endpoint of the study was defined as the composite of death, fatal and non-fatal MI, target vessel revascularization and cerebrovascular event.

Results: Only ALT concentration (OR: 1.010, 95% CI: 1.003-1.018, P = 0.008), monocyte count (OR: 1.002, 95% CI: 1.001 - 1.004, P = 0.005), hypertension (OR: 3.010, 95% CI: 1.081 - 8.384, p = 0.035) and lower LVEF (OR: 0.926, 95% CI: 0.875 - 0.981, P = 0.008) were independent predictors of primary endpoint in multivariate logistic regression analysis.

Conclusion: We found that elevated liver enzymes as determined by serum Alanine aminotransferase levels and monocyte count as well as hypertension and lower LVEF independently predicted 30-day outcomes in patients with successfully restored coronary flow by p-PCI. These parameters may provide new aspects, to identify the pathophysiology and prognosis of acute vascular events, which in turn may facilitate discovery of new treatment modalities.

Key words: STEMI; Liver enzymes; Alanine aminotransferase; Monocyte count; Primary PCI; Major adverse cardiac events.

ÖZET

Amaç: Primer perkutan koroner girişim (p-PKG) ile başarılı TIMI-3 koroner akım sağlanan hastalarda 30 günlük sonuçlar ile kardiyak enzimlerin yanında değişik hematolojik ve biyokimyasal parametreler arasındaki ilişkinin araştırılması amaçlandı.

Materyal ve metod: Çalışmaya daha önceden miyokard infarktüsü geçirmeyen, p-PKG uygulanan ve TIMI-3 koroner akım sağlanan ST yükselmeli miyokart enfarktüslü (STYMI) 200 hasta alındı. Çalışmanın birincil son noktası bileşik ölüm, ölümcül ve ölümcül olmayan miyokard infarktüsü, hedef damara tekrar girişim ve serebrovasküler olaydı.

Bulgular: Çok değişkenli analizde birincil son noktanın bağımsız öngörücüleri olarak sadece alanin aminotransferaz konsantrasyonu (OR: 1.010, 95% CI: 1.003-1.018, P = 0.008), monosit sayısı (OR: 1.002, 95% CI: 1.001 - 1.004, P = 0.005), hipertansiyon (OR: 3.010, 95% CI: 1.081 - 8.384, p = 0.035) ve düşük sol ventrikül ejeksiyon fraksiyonu (OR: 0.926, 95% CI: 0.875 - 0.981, P = 0.008) bulundu.

Sonuç: Hipertansiyon ve düşük sol ventrikül ejeksiyon fraksiyonu kadar serum alanin aminotransferaz düzeyi olarak tanımlanan yükselmiş karaciğer enzimleri ve monosit sayısı p-PKG ile başarılı koroner akım sağlanan hastalarda 30 günlük sonuçları bağımsız olarak öngördü. Bu parametreler akut vasküler olayların patofizyolojisini ve prognozunu anlamak için yeni bakış açısı sağlayabilir.Bu da yeni tedavi seçeneklerinin bulunmasını kolaylaştırabilir.

Anahtar kelimeler: Miyokart enfarktüsü; Karaciğer enzimleri; Alanin aminotransferaz; Monosit sayısı; Primer PKG; Major istenmeyen kardiyak olaylar.

Introduction

ST segment elevation myocardial infarction (STEMI) is a major public health problem and the leading cause of death in developed countries. Primary percutaneous coronary intervention (p-PCI) is the best reperfusion therapy due to improved survival and reduction of combined clinical endpoints in treatment of STEMI [1-3].

The main purpose of p-PCI is to open occluded coronary artery urgently in order to slow progression of myocardial infarction, by providing sufficient blood flow to threatened myocardium. However, despite a patent infarct-related artery with restored blood circulation, some patients still suffer poor short and long-term outcomes. Therefore, prediction of short and long-term outcomes in patients with successfully restored coronary flow by p-PCI and clarification of related factors may be important in improving the prognosis of high risk individuals in STEMI.

During STEMI, there are many routinely evaluated hematological and biochemical parameters besides the cardiac enzymes. The prognostic role of these parameters in patients with restored blood flow has not adequately been determined.

In this study, we investigated relationship of several hematological and biochemical parameters besides the cardiac enzymes with 30-day outcomes in patients with TIMI-3 flow following successful p-PCI.

Methods

Study Population

This study, having prospective observational cohort study design, was conducted in the cardiology clinics at Rize Education and Research Hospital and Dr. Siyami Ersek Cardiovascular and Thoracic Surgery Center. Two hundred patients with STEMI and no history of prior MI, who underwent p-PCI and have been restored TIMI-3 flow, were enrolled between 1 January and 31 December 2011 consecutively. All patients were examined by an experienced cardiologist immediately after hospitalization. The study was performed in accordance with the principles stated in the Declaration of Helsinki and approved by the local Ethics Committees of Rize University, Faculty of Medicine and Dr. Siyami Ersek Cardiovascular and Thoracic Surgery Center.

Clinical characteristics, which consisted of multiple descriptors from each patient's history and physical examination, were collected by physicians from cardiology clinics of each patient and were stored in the database of coronary angiography laboratory at each institute. We recorded the baseline characteristics, which include hypertension, diabetes mellitus, smoking status, family history for coronary artery disease and lipid parameters. Killip score and TIMI risk score was also calculated and used for risk stratification [4, 5].

Coronary angiography and primary PCI

All of the patients received 300 mg aspirin and 600 mg clopidogrel prior to the procedure. At the start of the procedure, 5000-10.000 IU (adjusted according to weight) intravenous heparin was administered. Coronary stenting directly, or followed by balloon angioplasty, was performed where eligible. Glycoprotein IIb–IIIa inhibitor (tirofiban) was administered at the preference of the operator. After the procedure, patients were followed in the intensive coronary unit (ICU) until stabilization. All of the patients were treated according to the recommendations of ACC/AHA Guidelines for the Management of Patients with ST-Elevation Myocardial Infarction [6].

Selective coronary angiography was performed urgently at the angiography laboratory using Standard Judkins technique through the femoral artery. Multiple views were obtained in all patients, with visualization of the left anterior descending and left circumflex coronary in at least 4 views, and the right coronary artery in at least 2 views. The TIMI (Thrombolysis In Myocardial Infarction) Flow Grade was used to scale coronary flow [7]. TIMI grade 3 flow at the intervened coronary artery with a residual stenosis of <20% was considered successful PCI. Two invasive cardiologists who were blinded to the patients' identities, electrocardiogram (ECG) and echocardiography findings and outcomes analyzed every case.

Table 1: Baseline and follow-up parameters of study population.

Parameters	MACE		p value
N = 200	Absence (173)	Presence (27)	
Age (yrs)	58 ± 12	60 ± 13	0.691
Gender (male)	87%	70%	**0.029**
BMI (kg/m²)	27 ± 4	29 ± 4	0.120
Hypertension	34%	56%	**0.032**
Diabetes mellitus	16%	26%	0.215
Smoking	67%	48%	0.154
Hyperlipidemia	10%	11%	0.911
Family history of CAD	20%	7%	0.123
Heart rate (bpm)	78 ± 16	84 ± 16	0.058
Systolic blood pressure (mmHg)	126 ± 23	124 ± 29	0.928
Diastolic blood pressure (mmHg)	78 ± 14	75 ± 20	0.590
Plasma blood glucose (mg/dL) (*Adm.*)	147 ± 62	169 ± 111	0.175
Creatinine (mg/dL)	1.0 ± 0.3	1.1 ± 0.5	0.158
GGT activity, U/L	32 ± 23	54 ± 53	**0.001**
AST, U/L	96 ± 111	135 ± 144	0.160
ALT, U/L	43 ± 41	121 ± 172	**0.004**
LDH, U/L	409 ± 264	497 ± 316	0.241
Total cholesterol (mg/dL)	185 ± 42	181 ± 45	0.917
LDL (mg/dL)	119 ± 35	119 ± 40	0.657
HDL (mg/dL)	40 ± 10	37 ± 8	0.348
Triglyceride (mg/dL)	130 ± 2	121 ± 73	0.393
Leukocytes (10^3/mm²)	11.2 ± 3.6	13.2 ± 4.9	**0.037**
Neutrophils (10^3/mm²)	8.5 ± 5.8	9.4 ± 4.8	0.259
Lymphocyte (10^3/mm²)	2.2 ± 1.0	2.7 ± 1.7	0.315
Monocyte (/mm²)	664 ± 292	969 ± 560	**0.002**
Hemoglobin (mg/dL)	13.8 ± 1.5	13.6 ± 2.0	0.587
RDW	14.9 ± 1.4	14.7 ± 1.0	0.699
Platelet count (x10^3/mm²)	262 ± 74	241 ± 67	0.099
MPV, fL	8.3 ± 1.4	9.2 ± 2.1	**0.033**
PDW	16.0 ± 2.7	16.9 ± 2.3	0.090
hsCRP, mg/L	0.84 ± 1.04	2.42 ± 4.7	**<0.001**
CK-MB (U/L) (*Adm.*)	45 ± 58	68 ± 90	0.372
CK-MB (U/L) (*peak*)	197 ± 110	196 ± 124	0.900
LVEF on admission, %	47.4 ± 9.1	42.4 ± 9.2	**0.008**
Pain to balloon time (*minutes*)	227 ± 162	376 ± 459	0.485
Killip score	0.7 ± 0.7	1.1 ± 1.1	0.053
Total ST elevation on *Pre-PCI* ECG (mm)	12 ± 11	12 ± 7	0.843
ST segment resolution %	61 ± 34	62 ± 23	0.703
TIMI flow grade	2.9 ± 0.3	2.9 ± 0.4	0.630
LAD/CX/RCA%	54 / 35 / 11	52 / 26 / 22	0.252
TIMI risk score	3.2±2.2	4.3±2.6	**0.025**
Anterior MI	49%	56%	0.499
Glycoprotein IIb/IIIa antagonist	57%	59%	0.799
Previous medications			
ACEi/ARB	16%	22%	0.389
Beta Blocker	7%	19%	**0.045**
Statin	6%	7%	0.741
Aspirin	15%	33%	**0.015**
CCB	5%	7%	0.640
Nitrate	2%	7%	0.079
Discharge medications			
ACEi/ARB	95%	82%	**0.006**
Beta Blocker	91%	85%	0.370
Statin	98%	89%	**0.008**
Aspirin	100%	100%	1.000
Clopidogrel	100%	100%	1.000
Nitrate	48%	59%	0.275
Follow-up			
MACE, n (%)	27 (13.5)		
Death, n (%)	7 (3.5)		
CVE, n (%)	0 (0)		
TVR, n (%)	17 (8.5)		
Re-MI, n (%)	14 (7)		

Adm., admission; BMI, body mass index; CAD, coronary arterial disease GGT, gamma-glutamyl transferase; ALT, Alanine aminotransferase; AST, aspartate aminotransferase; LDH, lactate dehydrogenase; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; RDW, red blood cell distribution width; MPV, mean platelet volume; PDW, platelet distribution width; hsCRP, high-sensitivity C-reactive protein; CK-MB, Creatine Kinase isoenzyme MB; LVEF, left ventricular ejection fraction; PCI, Percutaneous coronary intervention; TIMI, thrombolysis in myocardial infarction; left anterior descending (LAD), circumflex (Cx) and right (RCA) coronary arteries; MI, myocardial infarction; ACEi, angiotensin converting enzyme inhibitors; ARB, Angiotensin II receptor blockers; CCB, calcium channel blockers; MACE, major advanced cardiovascular events; CVE, Cerebrovascular event; TVR, target vessel revascularization.

Laboratory measurements

Cardiac biomarkers levels including creatine kinase (CK), creatine kinase-MB fraction (CK-MB) and Troponin-I and inflammatory markers including leukocytes were measured at our emergency department and used in the analyses as admission values. The lipid samples were drawn by venipuncture to perform routine blood chemistry after fasting for at least 8 hours. Glucose, creatinine, and lipid profile were determined by standard methods. White blood cell (WBC, leukocyte) counts were obtained from an automated cell counter (Coulter Gen-S, COULTER Corp, Miami, USA). Admission blood samples were centrifuged immediately and serum specimens for high-sensitivity CRP (hsCRP) were frozen and stored at −20°C before analysis. Serum levels of hsCRP were determined by the immunoturbidimetric method performed on the Abbott auto-analyzer (Architect C1600, Abbott,

USA).

Exclusion criterion

Patients with chronic hepatic or cholestatic disease, chronic renal failure, prior CABG, prior MI and valve operation, hematological disorders and known malignancy were excluded from the study. In addition, patients who refused to sign the informed consent form or p-PCI was not included in the study.

ECG

A 12-lead surface ECG was obtained from all patients in the supine position immediately after their admission to the emergency care unit (ECU). The 12-lead ECG (Nihon Kohden - cardiofax S ECG-1250K, filter range 0.5 Hz to 150 Hz, AC filter 60 Hz, 25 mm/s, 10 mm/mV) was analyzed by two independent clinicians who were blinded to study design and data. A repeat ECG was obtained 60 minutes after p-PCI.

STEMI was defined according to the universal definition of MI [8] as typical rise and fall of the cardiac biomarker troponin I (TnI) with at least one value above the 99th percentile of the upper reference limit in patients presenting with symptoms of ischemia together with new ST elevation at the J-point in two contiguous leads with the cutoff points: 0.2 mV in men or 0.15 mV in women in leads V2-V3 and/or 0.1 mV in other leads or new left bundle-branch block. A special ruler was used to measure the difference (in millimeters) between isoelectric line and ST-segment elevation at 20 milliseconds after the J-point. The diagnosis of acute STEMI was also confirmed by demonstrating the culprit lesion by coronary angiography.

Jeopardized myocardium was determined by the sum of ST elevations (in mm) on each ST elevated derivation on pre and post PCI ECGs (Total ST elevation score). Percentage of total ST resolution was calculated by the following formula: (Sum of ST elevations on Pre-PCI ECG) - (Sum of ST elevations on Post-PCI ECG) / (Sum of ST elevations on Pre-PCI ECG) x 100 [9].

Clinical follow-up and study end points

All patients were followed for 30 days from the time of application. The primary endpoint of the study was defined as composite of death, fatal and non-fatal MI, target vessel revascularization and cerebrovascular event. In hospital re-infarction was defined as recurrent chest pain lasting more than 30 min, associated with new Q waves or recurrent ST-segment elevation ≥0.1mV in at least two contiguous leads and a re-elevation of creatine kinase-MB to at least twice the upper limit of the normal value and/or more than 50% above the previous value after index procedure [10]. TVR was described as repeat percutaneous intervention or surgical bypass grafting of any segment of the target vessel. The target vessel was defined as the whole major coronary artery proximal and distal to the target lesion including all branches [11]. A two-dimensional echocardiogram was performed in-hospital before discharge for the evaluation of left ventricle ejection fraction (LVEF) by using modified Simpson's technique. All the patients were questioned for primary endpoints after 30 days by telephone.

Statistical analysis

Continuous variables were given as mean ± standard deviation; categorical variables were defined as percentages. Continuous variables were compared by Student t test and the $\chi 2$ test was used for the categorical variables between two groups. The Spearman's correlation coefficient was used for correlation analyses. Logistic regression analysis was used for multivariate analysis of independent variables. All tests of significance were two-tailed. Statistical significance was defined as $P < 0.05$. The SPSS statistical software (SPSS 15.0 for windows, Inc., Chicago, IL, USA) was used for all statistical calculations.

Table 2: Effects of various variables on 30-day outcomes in univariate and multivariate logistic regression analyses.

Variables	Unadjusted OR	95% CI	P value	Adjusted OR*	95% CI	P value
TIMI risk score	1.211	1.026-1.429	**0.023**			
Gender (male)	0.364	0.143-0.928	**0.034**			
Hypertension,+	2.415	1.062-5.493	**0.035**	3.010	1.081-8.384	**0.035**
Heart rate (bpm)	1.022	0.996-1.049	0.094			
ALT, U/L	1.010	1.004-1.016	**0.001**	1.010	1.003-1.018	**0.008**
Monocyte (/mm³)	1.002	1.001-1.003	**<0.001**	1.002	1.001-1.004	**0.005**
MPV, fL	1.340	1.074-1.673	**0.010**	1.334	0.960-1.853	0.086
LVEF%	0.941	0.898-0.986	**0.011**	0.926	0.875-0.981	**0.008**
ACEi/ARB,+	0.213	0.064-0.710	**0.012**			
Statin,+	0.141	0.027-0.740	**0.021**			
GGT activity, U/L	1.017	1.006-1.029	**0.004**			
hsCRP (mg/dL)	1.275	1.064-1.529	**0.009**			

**Logistic regression analyses with Backward: LR method was used for multivariate analysis of independent variables including gender, HT, heart rate, ALT, monocyte count, MPV, LVEF, ACEi/ARB and statin use, GGT and CRP which had a p value <0.1 in univariate analysis. After exclusion of irrelevant variables from model, logistic analysis with enter method were performed with remain significant variables and then obtained results were presented.*

Results

The baseline clinical characteristics are presented in Table 1. The study population consisted of 200 patients with STEMI who underwent p-PCI. The patients who experienced any MACE component during follow-up demonstrated higher rate of hypertension ($P = 0.032$), increased liver enzymes (GGT activity: $P = 0.001$ and ALT levels: $P = 0.004$), hematological markers (leukocyte and monocyte count: $P = 0.037$ and $P = 0.002$, respectively, and MPV value: $P = 0.033$), increased hsCRP levels ($P < 0.001$), lower LVEF% ($P = 0.008$) and a higher TIMI risk score ($P = 0.025$) in comparison to patients without MACE.

Increased levels of ALT, hsCRP, GGT activity, monocyte count, MPV; higher TIMI risk score, depressed left ventricular ejection fraction, and low ACE/ARB and statin usage were predictors for MACE (Table 2). In our study, ALT levels correlated to N/L ratio ($r = 0.263$, $P < 0.001$), admission CK-MB ($r = 0.524$, $P < 0.001$), peak CK-MB ($r = 0.313$, $P < 0.001$), hsCRP ($r = 0.148$, $P = 0.044$), pain to balloon time ($r = 0.222$, $P = 0.002$) and TIMI risk score ($r = 0.162$, $P = 0.022$).

Only ALT level (OR: 1.010, 95% CI: 1.003 - 1.018, $P = 0.008$), monocyte count (OR: 1.002, 95% CI: 1.001 - 1.004, $P = 0.005$), hypertension (OR: 3.010, 95% CI: 1.081 - 8.384, $P = 0.035$) and lower LVEF% (OR: 0.926, 95% CI: 0.875 - 0.981, $P = 0.008$) were the independent predictors of MACE in multivariate logistic regression analysis.

When we investigated specific determinants of MACE components, death and TVR were mainly related to increased ALT and monocytes, but re-MI was related only ALT level (Table 3).

Discussion

In this study, we demonstrated that increased concentrations of ALT, monocyte at admission, hypertension and low EF independently predict of 1-month MACE in patients with STEMI followed successful p-PCI with well-restored coronary flow. Despite being statistically dependent, admission values of GGT, hsCRP, MPV and female gender were also higher in patients with MACE. Additionally, patients whom did not receive ACE/ARB and statin treatments were more prone to MACE. One important aspect of our study is that we included only patients with good coronary flow; therefore, our results may have a value in classifying patients even though they seem at lower risk and guiding clinical treatment.

We revealed a strong relationship between monocyte count, death and TVR in subgroup analyses of MACE. In addition, there was a trend for increased re-infarction in patients with higher monocyte counts, although not reaching significance. Monocytes have a very important role in mediating inflammation during myocardial infarction. The different subtypes of monocytes might have different actions [12, 13]. Monocytes differentiate into macrophages, becoming as a source of cytokines and growth factors that regulate extracellular matrix metabolism, after

recruitment to the infarction tissue [14, 15]. During healing process, ventricular geometry and function alters considerably [16, 17]. Optimum healing after MI requires a coordinated process, balancing debris removal and repair of the myocardial extracellular matrix. Excessive inflammation and eventually adverse remodeling can both cause heart failure [18-20]. Moreover, recent studies revealed detrimental effects of monocytes and macrophages in microvascular damage after reperfusion in patients with STEMI and stent restenosis [21, 22]. Monocytes, in addition to fundamental effects in inflammation, may influence platelets causing reactivation [23, 24]. We think that, monocytes increase MACE due to both increased inflammation, remodeling and platelet reactivation. Although a statistically insignificant tendency, observation of higher MPV values in patients with MACE may support this hypothesis.

ALT is mainly located in hepatocytes and renal tubular epithelium, however some activity is present in skeletal and cardiac muscle [25]. Surprisingly, admission ALT values independently predicted all endpoints and combined MACE. The mechanism of this relationship is not totally clarified. Lazzeri et al. identified admission ALT concentration as a predictor of in-hospital mortality in non-diabetic patients, in a group of 1000 STEMI patients following mechanical reperfusion [26]. A recent study demonstrated an association between increased liver enzymes and mortality, congestive heart failure, shock, or stroke 30 days after STEMI [27]. Similar to our study, ALT displayed a strong correlation with infarct size assessed by enzyme levels in both of these previous studies. In addition, ALT also correlated to hsCRP, admission and peak CK-MB, paint to balloon time and TIMI risk score in our study. Nevertheless, the association of ALT with re-MI and TVR may suggest possible different mechanisms except infarct related pathways.

Another source of ALT might be liver due to acute hepatic congestion or relative hypotension associated with larger infarction. Accordingly, unlike chronic heart failure, which mainly shows cholestatic pattern of liver enzyme elevation, acute heart failure and ischemic hepatitis most often result in elevated transaminases [28-31]. The pathophysiological procedure regarding elevated ALT levels, increased TVR, re-infarction and mortality is still hypothetic. We think that further studies are needed to clarify this relationship. Another potential explanation is that elevated liver enzymes including ALT and GGT are associated with the metabolic syndrome via non-alcoholic fatty liver disease. This hypothesis may be supported by that although AST is known as a more related parameter to myocardial necrosis than ALT; it was not an independent parameter for MACE in-patient with well-perfused myocardium.

The relationship between CRP and cardiac mortality in patients with acute myocardial infarction, have been demonstrated by previous many studies[32-34]. Despite, being high in MACE group, hsCRP was not an independent variable for the study outcomes in our study. Possible explanations for this may be that CRP is a nonspecific marker or lack of an adequately numbered study population to demonstrate possible independent relation. In both situations, our study supports that monocyte and ALT are more important than CRP in this patient population.

Gamma-glutamyl transferase (GGT), the enzyme responsible for the extracellular catabolism of glutathione, has a role in oxidation of LDL cholesterol within the atherosclerotic plaque and progression of atherosclerosis[35-37]. GGT activity has been demonstrated to be an independent risk factor for myocardial infarction (MI) and cardiac death in patients with documented coronary artery disease (CAD)[38-41]. Recent studies have revealed the prognostic importance of GGT in patients undergoing mechanical revascularization for STEMI [42, 43]. However, in our study group, although GGT was significantly increased in MACE group, it was not a statistically significant predictor of MACE independent of other parameters.

Table 3: The distribution of independent predictors according to MACE components.

Parameters	Death		P value
	Absence	Presence	
Hypertension,+	36%	71%	0.055
ALT, U/L	49 ± 58	189 ± 266	<0.001
Monocyte (/mm3)	685 ± 312	1265 ± 802	<0.001
LVEF%	47 ± 9	40 ± 8	0.077
	TVR		P value
Hypertension,+	37%	41%	0.709
ALT, U/L	49 ± 69	106 ± 134	0.004
Monocyte (/mm3)	677 ± 343	999 ± 350	<0.001
LVEF%	47 ± 9	44 ± 8	0.140
	Re-MI		P value
Hypertension,+	36%	50%	0.296
ALT, U/L	49 ± 69	107 ± 146	0.007
Monocyte (/mm3)	694 ± 344	875 ± 471	0.076
LVEF%	47 ± 9	43 ± 11	0.074

ALT, Alanine aminotransferase; LVEF, left ventricular ejection fraction; MI, myocardial infarction; TVR, target vessel revascularization.

Mean platelet volume (MPV), a marker for platelet reactivity, has been shown to be predictive of unfavorable outcomes among survivors of STEMI [44]. In our study, MPV was also higher in patients with MACE, but with only a tendency to predict to MACE. In our opinion, platelet reactivity is also important for this patient population, but relatively small sample size of our study may have prevented to represent its possible independent relation.

As a result, even though successfully re-perfused by primary PCI, the patients with high admission levels of ALT and monocyte may be prone to an increased cardiovascular morbidity and mortality; therefore may be targeted to gain more benefit with intensive therapy such as antiplatelet, anticoagulant, ACEi/ARB and statins.

Study limitations: Our study population, involving 200 patients, is rather small. Although we excluded known chronic hepatic or cholestatic disease, we may not exactly state that elevated ALT is due to MI, not a previous disorder like nonalcoholic fatty liver disease. Moreover, we only included patients with successful reperfusion and TIMI-3 flow, thus our results do not apply to all patients with STEMI.

Conclusion: We found that elevated liver enzymes as determined by serum Alanine aminotransferase level and monocyte count as well as hypertension and lower LVEF independently predicted 30-day outcomes in patients with successfully restored coronary flow following primary PCI. These parameters may provide new aspects, to identify the pathophysiology and prognosis of acute vascular events, which in turn may facilitate discovery of new treatment modalities.

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