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Systemic immune-inflammation index and high-sensitivity cardiac troponin T in acute coronary syndromes

Akut koroner sendromlarda sistemik immün-inflamasyon indeksi ve yüksek duyarlılıklı kardiyak troponin T

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ABSTRACT

Aim: Acute coronary syndromes (ACSs) are classified as ST-segment elevated myocardial infarction (STEMI), non-ST-segment elevated myocardial infarction (NSTEMI) and unstable angina pectoris (USAP). Cardiac troponins constitute the cornerstone biomarkers for the laboratory diagnosis of ACS. In this study, we aimed to investigate whether systemic immune-inflammation index (SII) is associated with peak cardiac troponin T (TnT) levels in ACS.
Methods: Consecutive patients with ACS whose coronary angiography was performed were included in the present study (n=397). Admission SII was determined as platelet count x neutrophil count/lymphocyte count. Serum levels of cardiac enzymes, including high-sensitivity TnT and creatine kinase-myocardial band (CK-MB), were measured at the time of admission and repeated daily during patients' hospital stay.
Results: Patients were categorized as namely STEMI (n=92) and NSTEMI/USAP (n=141). The findings obtained in this study showed that the median of SII levels was higher in STEMI than NSTEMI/USAP at a significant level. Correlation analysis of SII with various clinical and laboratory parameters demonstrated a significant correlation with C-reactive protein, peak CK-MB (r=0.52, p<0.001), peak TnT (r=0.49, p<0.001) and left ventricular ejection fraction (r= -0.48, p<0.001). Multivariate linear regression analysis identified age and log-SII (Beta Coefficient: 1.29, 95% Confidence Interval: 0.93-1.66, p<0.001) as independent predictors of peak TnT levels.
Conclusion: SII is an independent predictor of peak TnT levels and significantly correlates with peak CK-MB levels in patients with ACS. SII significantly and inversely correlates with left ventricular systolic functions.

Keywords: Acute coronary syndrome, inflammation, systemic immune-inflammation index, troponin

ÖZ

Amaç: Akut koroner sendromlar (AKS), ST-segment yükselmeli miyokard enfarktüsü (STEMI), non-ST-segment yükselmeli miyokard enfarktüsü (NSTEMI) ve kararsız angina pektoris (USAP) olarak sınıflandırılır. Kardiyak troponinler AKS laboratuvar tanısı için temel biyolojik belirteçleri oluşturur. Biz bu çalışmada sistemik immün-inflamasyon indeksinin (SII) AKS' de zirve kardiyak troponin T (TnT) seviyeleri ile ilişkisini araştırmayı amaçladık.
Yöntem: Koroner anjiyografi yapılan AKS hastaları ardışık olarak çalışmaya dahil edildi (n=397). Başvuru anındaki SII değeri, trombosit sayısı x nötrofil sayısı / lenfosit sayısı olarak belirlendi. Yüksek duyarlılıklı TnT ve kreatin kinaz-miyokardiyal bandı (CK-MB) içeren serum kardiyak enzim seviyeleri başvuru sırasında ölçüldü ve ölçümler hastaların hastanede kaldıkları süre boyunca günlük olarak tekrarlandı.
Bulgular: Hastalar STEMI (n = 92) ve NSTEMI/USAP (n = 141) olarak kategorize edildi. SII ortanca değerleri STEMI grubunda NSTEMI/USAP grubundan anlamlı düzeyde daha yüksekti. SII' nin çeşitli klinik ve laboratuvar parametreleriyle yapılan korelasyon analizinde C-reaktif protein, zirve CK-MB (r = 0.52, p <0.001), zirve TnT (r = 0.49, p <0.001) ve sol ventrikül ejeksiyon fraksiyonu (r =-0.48, p <0.001) ile anlamlı bir korelasyon gösterdiği tespit edildi. Çok değişkenli doğrusal regresyon analizi yaş ve log transforme-SII' yi (Beta Katsayısı:1.29, % 95 Güven Aralığı:0.93-1.66, p<0.001) zirve TnT seviyelerinin bağımsız prediktörleri olarak tanımladı.
Sonuç: SII zirve TnT seviyelerinin bağımsız bir öngörücüsüdür ve AKS hastalarında zirve CK-MB seviyeleriyle anlamlı seviyede korelasyon göstermektedir. Ayrıca, SII sol ventrikül sistolik fonksiyonlarıyla anlamlı seviyede ters korelasyon göstermektedir.

Anahtar Kelimeler: Akut koroner sendrom, inflamasyon, sistemik immün-inflamasyon indeksi, troponin.

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INTRODUCTION

Acute coronary syndromes (ACSs) are classified according to various clinical circumstances related to acute myocardial ischemia or infarction and encompass ST-segment elevated myocardial infarction (STEMI), non-ST-segment elevated myocardial infarction (NSTEMI) and unstable angina pectoris (USAP). Cardiac troponins, including troponin I (TnI) and troponin T (TnT), are the main regulatory proteins within the myocardium that are secreted into the circulation subsequent to myocardial damage. Thus, they constitute the cornerstone biomarkers for the laboratory diagnosis of ACS [1, 2]. Besides, elevations in troponin levels exhibit prognostic features, including mortality, adverse cardiovascular outcomes and infarct size, in patients with ACS [3-6].

The pathogenesis of ACS, which results in atherosclerotic plaque rupture and subsequent thrombosis, is multifactorial and involves complex and various cascades of local and systemic alterations of inflammation and immune system activity. Neutrophils, platelets and lymphocytes are the principal cellular components of this process [7]. Systemic immune inflammation index (SII), which brings together the counts of these cells, is a novel marker that represents the balance between inflammation and the immune system. The predictive capability and prognostication of SII have been proven in various cardiovascular situations, including coronary artery disease (CAD), aortic stenosis and contrast-induced nephropathy after percutaneous coronary intervention (PCI) [8-11]. However, to our knowledge, there are no data in the literature investigating the relationship between SII and biomarkers of myocardial damage, such as troponin in ACS. Accordingly, the present study sought to investigate whether SII was associated with peak TnT measurements in patients with ACS.

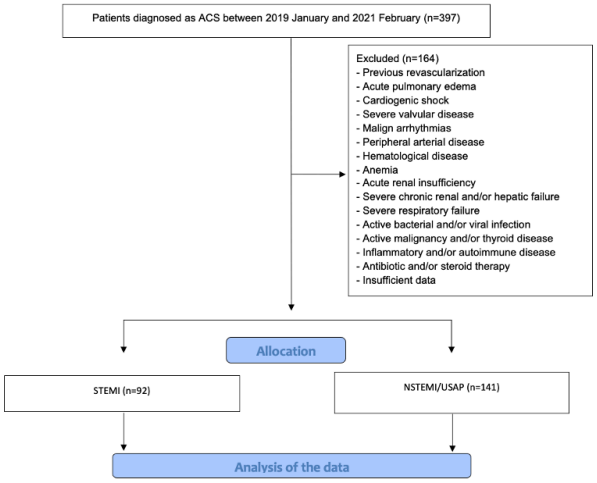
METHODS

Study Protocol and Participants

This study was designed in a retrospective and observational fashion and included 397 patients with ACS between January 2019 and February 2021. Consecutive ACS patients hospitalized in the cardiology department and underwent coronary angiography (CAG) participated in this study. Basal demographics and clinical characteristics, including medications, laboratory parameters and CAG data, were provided using an electronic database. The study protocol was approved by the local ethics committee (2017-KAEK-189_2021.02.10_11), and all study procedures were conducted in line with the Helsinki Declaration. Informed consent was waived due to the retrospective design of this study.

Previous coronary revascularization procedures, including PCI and coronary artery bypass graft (CABG), acute pulmonary edema, cardiogenic shock, severe valvular disease, presence of malign arrhythmias, peripheral arterial disease, active hematological disease, anemia, acute renal insufficiency, severe chronic renal and/or hepatic failure, severe respiratory failure, active bacterial and/or viral infection, active malignancy and/or thyroid disease, inflammatory and/or autoimmune disease, antibiotic and/or steroid therapy, were determined as exclusion criteria. Moreover, patients with insufficient data were excluded from this study. After the exclusion of 164 patients with the above criteria, 233 patients were allocated into STEMI (n=92) and NSTEMI/USAP (n=141) groups and included in statistical analyses (Figure 1).

Figure 1. Flow-chart diagram of the study.



ACS, acute coronary syndrome; NSTEMI, Non-ST segment elevation myocardial infarction; STEMI, ST segment elevation myocardial infarction; USAP, unstable angina pectoris.

Definitions

The diagnosis of ACS was performed according to current guidelines using anamnesis, electrocardiography (ECG), imaging methods and troponin levels. Patients with new-onset symptoms suggestive of ischemia, such as chest discomfort or pain and persistent ST-segment elevation on ECG, were diagnosed as STEMI [12]. Patients with new-onset symptoms suggestive of ischemia, no persistent ST-segment elevation on ECG and accompanying cardiac troponin increase greater than the upper limit of normal level were diagnosed as NSTEMI, whereas patients with new-onset symptoms suggestive of ischemia, no persistent ST-segment elevation on ECG without cardiac troponin increase were diagnosed as USAP [13]. Previous diagnosis of arterial hypertension (HT) with or without drug usage or mean office blood pressure measurements ≥140/90 mmHg at multiple measurements was described as arterial HT. Diabetes mellitus (DM) was described as fasting plasma glucose level ≥126 mg/dL in multiple tests or glucose level ≥200 mg/dL at any test or usage of antidiabetic therapies. Smoking was described as current smoking in the last six months. Hyperlipidemia was diagnosed as basal cholesterol measurement above 200 mg/dl and/or low-density lipoprotein (LDL) cholesterol measurement above 130 mg/dl or usage of hypolipidemic agents.

Laboratory Measurements

Peripheral venous blood sampling was performed from a large antecubital vein at the time of hospital admission, and measurements were made immediately. Total complete blood count test was administered using an automated blood cell counter (Sysmex XN-1000, Kobe, Japan) and admission SII levels were calculated as platelet count x neutrophil count/lymphocyte count [8]. Blood chemistry parameters, including cholesterol panel, were evaluated using standard methods.

C-reactive protein (CRP) levels were determined using the turbidimetric method (Roche Cobas 6000 c501) (normal reference values 0.15-5 mg/L) at admission. Serum levels of cardiac enzymes, including high-sensitivity TnT (Roche Cobas 6000 e601) (99th percentile 14 ng/L) and creatine kinase-myocardial band (CK-MB) (Roche Cobas 6000 c501) (99th percentile 6.73 ng/mL for men and 3.77 ng/mL for women), were measured using an electrochemiluminescence immunoassay method at the time of admission and repeated daily during patients' hospital stay. Reference values were calculated with a coefficient of variation <10% [14, 15].

Procedures and Medications

According to the physician's preferred access site, CAG was carried out through the standard Judkins technique (Allura Xper FD10, Philips Healthcare, the Netherlands) using femoral or radial route. Conventional coronary angiography images were recorded in multiple projections for all coronary arteries and PCI procedures were carried out immediately after diagnostic CAG when appropriate. During CAG and PCI procedures, the operator was free to decide revascularization type and technique, such as bare metal or drug-eluting stent implantation and bifurcation or provisional technique, choice of antithrombotic and anticoagulant therapy, and glycoprotein IIb/IIIa receptor antagonist administration. During their hospitalization times, all patients were followed up and treated in line with the recommendations of the international guidelines.

Two-dimensional transthoracic echocardiography (Philips Logic Affiniti 50G, Philips, Amsterdam, the Netherlands) was performed on patients at the left lateral decubitus position during their hospital stay. Left ventricular ejection fraction (LVEF) was calculated using Simpson's method. All echocardiographic procedures were in line with the recommendations of the American Society of Echocardiography [16].

Statistical Analysis

All statistical tests were exerted using IBM SPSS Statistics for Macintosh, Version 24.0 (IBM Corp., Armonk, New York, USA). The distribution pattern of numerical variables was tested by the One-sample Kolmogorov-Smirnov test. Afterwards, independent two samples t-test was applied to normally distributed numerical data, and the results were given as mean and standard deviation. The Mann-Whitney U test was applied for the abnormally distributed numerical data, and results were given as median with interquartile range

(percentiles 25th and 75th). Categorical variables were tested using Chi-square test or Fisher Exact test. Logarithmic transformations were applied to abnormally distributed data to yield an approximately normal distribution. The correlation of SII with various parameters was tested by Spearman's correlation analysis. Afterwards, the correlation between log-SII and log-peak TnT was tested using Pearson's correlation analysis.

Variables associated with peak TnT levels were investigated using univariate and multivariate linear regression analyses and the results were given with beta coefficient and 95% confidence interval (CI). Variables, which could be related to peak TnT levels, such as age, gender, DM, HT, LDL, log-creatinine, log-CRP and log-SII, were included in univariate analyses. The variables that reached a p-value below 0.1 in univariate tests were included in the multivariate model. A two-sided p-value below 0.05 was determined as statistically significant for all tests.

RESULTS

There remained 233 patients with ACS with 61±11 years old and percentage of male gender 74% after exclusion criteria were applied. Afterwards, patients were classified as STEMI (n=92) and NSTEMI/USAP (n=141). Baseline demographics and previous medications were comparable between the groups except for HT, hyperlipidemia and antiplatelet therapy. The number of diseased vessels was similar, whereas LVEF was significantly decreased in STEMI patients compared to NSTEMI/USAP patients (p<0.001). Culprit coronary artery and treatment of choice, including medical therapy, CABG and PCI, also significantly differed among groups (p<0.001 for both) (Table 1).

Regarding the laboratory parameters, there was no difference between groups regarding glucose, hemoglobin, blood urea nitrogen, creatinine, gamma-glutamyl transferase and total bilirubin levels, whereas aspartate aminotransferase, alanine aminotransferase and lactate dehydrogenase (LDH) levels were higher in STEMI patients at a significant level. On the contrary, total cholesterol and triglyceride measurements were significantly increased in NSTEMI/USAP group. Admission CRP levels were comparable among the two groups. Peak CK-MB and TnT levels were significantly higher in the STEMI group (p<0.001 for both). Besides, white blood cell and neutrophil counts were significantly elevated, and lymphocyte count was significantly decreased in STEMI patients. There was no difference among groups concerning platelet and monocyte counts. The median of SII levels was higher in STEMI group patients compared to NSTEMI/USAP group (1241, 646, p<0.001, respectively) (Table 2).

Table 1. Baseline demographic and clinical characteristics of the study population

Variables	All (n= 233)	STEMI (n=92)	NSTEMI/ USAP (n=141)	P value
Age	61±11	61±10	61±11	.955
Gender, male	173 (74%)	67 (73%)	106 (75%)	.688
Body mass index, kg/m2	29±5	30±5	29±5	.832
Smoking	86 (42%)	39 (48%)	47 (38%)	.160
Diabetes mellitus	96 (41%)	37 (40%)	59 (42%)	.805
Hypertension	111 (48%)	34 (37%)	77 (55%)	.008
Hyperlipidemia	139 (61%)	48 (53%)	91 (%67)	.032
Previous medications				
Beta-blocker	33 (14%)	10 (11%)	23 (16%)	.244
Calcium channel blocker	34 (15%)	16 (17%)	18 (13%)	.328
RAAS blocker	62 (27%)	22 (24%)	40 (29%)	.433
Antiplatelet	43 (19%)	9 (10%)	34 (24%)	.006
Statins	26 (11%)	8 (9%)	18 (13%)	.355
Oral antidiabetic	64 (27%)	21 (23%)	43 (31%)	.200
Insulin	21 (9%)	9 (10%)	12 (9%)	.740
Number of diseased vessels	1.6±0.9	1.7±0.7	1.6±1.0	.471
Left ventricle ejection fraction, % *	52±10	44±6	54±9	<.001
Culprit coronary artery				<.001
Left anterior descending artery	111 (54%)	42 (46%)	69 (62%)	
Circumflex artery	35 (17%)	10 (11%)	25 (22%)	
Right coronary artery	56 (27%)	40 (44%)	16 (14%)	
Intermediate artery	1 (1%)	0	1 (1%)	
Left main coronary artery	1 (1%)	0	1 (1%)	
Treatment procedure				<.001
Medical therapy	39 (17%)	1 (1%)	38 (27%)	
Coronary artery bypass grafting	27 (12%)	0	27 (19%)	
Percutaneous coronary intervention	166 (72%)	91 (99%)	(54%)	

NSTEMI, Non-ST-segment elevation myocardial infarction; RAAS, renin-angiotensin-aldosterone system; STEMI, ST-segment elevation myocardial infarction; USAP, unstable angina pectoris.* Left ventricular ejection fraction data was present in 98 patients.

Correlation analysis of SII with various clinical and laboratory parameters demonstrated a significant correlation with CRP (r=0.15, p=0.03), peak CK-MB (r=0.52, p<0.001), peak TnT (r=0.49, p<0.001), LDH, high-density lipoprotein, LVEF (r= -0.48, p<0.001) and number of diseased vessels (Table 3). Correlation analysis between log-SII and log-peak TnT levels also yielded a positive and significant correlation (r=0.44, p<0.001) (Figure 2).

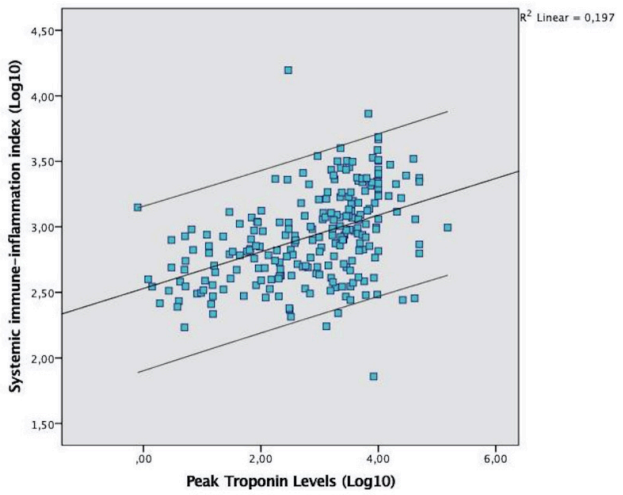


Figure 2. Correlation between the log-systemic immune-inflammation index and log-peak troponin T levels.

Linear regression analyses, including univariate and multivariate tests, showed that age, LDL, log-CRP and log-SII were associated with peak TnT in univariate analyses. In multivariate analyses, age and log-SII (Beta Coefficient: 1.29, 95 CI%:0.93-1.66, p<0.001) remained as independent predictors of peak TnT levels (Table 4).

DISCUSSION

Our results emphasize that SII is independently associated with peak TnT levels and significantly correlates with diverse markers of myocardial injury, such as peak CK-MB in ACS patients. Moreover, SII significantly and inversely correlates with left ventricular systolic functions. To our knowledge, this is the first study in the literature demonstrating an association between SII and markers of myocardial injury in an ACS patient population.

Atherosclerotic plaque formation with local and systemic activation of inflammation and immune system related cells are considered the main pathophysiological steps for ACS occurrence [7]. Neutrophils infiltrate into endothelial tissue, activate vascular inflammation and plaque erosion by secreting inflammatory mediators, which subsequently cause, atherothrombosis [17]. Lymphocytes reflect immune system activity and the number of lymphocytes decreases in ACS due to systemic stress [18]. Furthermore, lymphopenia is known to be linked with worse outcomes in CAD [19]. In general, leukocytosis, neutrophilia, and lymphopenia are thought of as a body response to systemic stress and related to worse prognosis, specifically in situations where inflammatory activity plays a major role, such as ACS [18]. On the other hand, platelets participate in all stages of inflammation and the atherothrombotic process by mediating leukocyte and progenitor cell recruitment into vascular injury sites and by secreting chemokines and cytokines that mediate vascular inflammation [20].

The pathophysiological contribution of these cell types in ACS and alterations in their counts have led the researchers to develop new biomarkers that reflect the inflammatory activity. These biomarkers are primarily derived from hematological parameters, such as neutrophil, platelet and/or lymphocyte cell counts. For example, neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are well-defined inflammation-related biomarkers which are easily derived from a complete blood count examination and their associations with adverse cardiovascular outcomes were already demonstrated [21-23]. On the other hand, SII includes neutrophils, platelets and lymphocytes and identifies the balance of inflammation and immune system. The prognostic advantage of SII on NLR and PLR has been well-documented in cancer patients [24, 25]. Furthermore, the findings in a current study suggest that SII can predict functionally significant CAD better than NLR and PLR [9]. Accordingly, we hypothesized that SII is associated with peak TnT levels as a reflection of the extent of myocardial injury in ACS. Our findings have demonstrated that SII is an independent predictor of peak TnT levels and significantly correlates with peak CK-MB levels. Moreover, SII significantly and inversely has correlated with left ventricular systolic functions. In our analyses, SII as an inflammation-related

marker has also correlated with CRP levels.

Table 2. Laboratory findings of the study population

Variables	All (n= 233)	STEMI (n=92)	NSTEMI/ USAP (n=141)	p value
Glucose, mg/dL	158±85	167±84	152±86	.191
Hemoglobin, g/dL	14.2±1.8	14.2±1.8	14.2±1.7	.908
Blood urea nitrogen, mg/dL	16±6	16±6	16±5	.488
Creatinine, mg/dL	0.80 (0.70-0.93)	0.80 (0.70-0.90)	0.80 (0.70-0.96)	.580
Aspartate aminotransferase, U/L	29 (18-65)	63 (29-108)	22 (16-33)	<.001
Alanine aminotransferase, U/L	26±18	30±22	24±14	.014
Gamma-glutamyl transferase, U/L	22 (16-31)	21 (15-28)	22 (16-34)	.273
Lactate dehydrogenase, U/L	293±193	381±257	234±97	<.001
Total bilirubin, mg/dL	0.4 (0.3-0.6)	0.5 (0.3-0.6)	0.4 (0.3-0.6)	.597
Total cholesterol, mg/dL	191±42	183±39	195±43	.029
Low-density lipoprotein, mg/dL	119±37	119±36	119±38	.988
High-density lipoprotein, mg/dL	40±9	40±10	40±9	.923
Triglyceride, mg/dL	123 (83-210)	95 (70-144)	167 (100-237)	<.001
C-reactive protein, mg/L	4.0 (2.0-9.6)	4.3 (2.0-11.1)	4.0 (2.0-9.3)	.525
Peak creatine kinase-MB, ng/mL	35 (8-99)	102 (52-221)	13 (4-39)	<.001
Peak troponin T, ng/L	1566 (127-4592)	4645 (2802-9674)	283 (32-1548)	<.001
White blood cells, x 103	10.2±3.1	11.6±3.4	9.2±2.5	<.001
Neutrophils, x 103	7.2±2.9	8.8±3.0	6.2±2.4	<.001
Lymphocytes, x 103	1.9 (1.3-2.7)	1.6 (1.1-2.4)	2.0 (1.5-2.7)	.001
Platelets, x 103	243±59	244±66	242±55	.871
Monocytes, x103	0.6±0.3	0.7±0.3	0.6±0.2	.246
Systemic immune-inflammation index, x103	834 (467-1506)	1241 (665-2234)	646 (397-1080)	<.001

MB, myocardial band; NSTEMI, Non-ST-segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction; USAP, unstable angina pectoris.

Cardiac troponins are widely utilized for the diagnosis of ACS. In addition to being an ideal diagnostic marker, troponin measurements also provide prognostic benefits, such as estimation of infarct size after ACS. For example, a recent cardiac magnetic resonance imaging study showed that high-sensitivity TnT accurately predicts systolic function impairment in patients six months after first STEMI [14]. Similarly, TnI measurement at 72 hours after primary PCI strongly correlated with infarct size at five and 30 days and independently predicted adverse clinical events in STEMI patients [26]. At this point, it is reasonable to question the contribution of inflammation to myocardial damage in ACS. Evidence coming from a previous study indicates that an increase in troponin levels is independently associated with elevated CRP levels in NSTEMI [15]. Admission white blood cell and neutrophil counts were strongly related to infarct size in anterior STEMI [27]. Furthermore, NLR was linked with myocardial damage assessed using CK-MB measurements and systolic dysfunction detected through echocardiographic calculations in patients with ACS [28]. In another study, NLR negatively correlated with LVEF measurements and independently predicted systolic dysfunction in NSTEMI patients [29]. Consistent with these findings, we found that SII, which is an inflammation and immune system related marker, independently predicted peak TnT levels and inversely correlated with LVEF in patients with ACS.

Table 3. Correlation analysis of systemic immune-inflammation index with various parameters

	Systemic immune-inflammation index	
	r coefficient	p-value
Age	0.10	.109
C-reactive protein	0.15	.038
Peak creatine kinase-MB	0.52	<.001
Peak troponin T	0.49	<.001
Lactate dehydrogenase	0.54	<.001
Low-density lipoprotein	0.06	.387
High-density lipoprotein	0.14	.034
Left ventricle ejection fraction *	-0.48	<.001
Number of diseased vessels	0.22	.001

r coefficient= Spearman's rho, MB, myocardial band. * Left ventricular ejection fraction data was present in 98 patients.

Table 4. Univariate and multivariate linear regression analysis for variables associated with peak troponin levels

Variables	Peak Troponin Levels			
	Univariate		Multivariate	
	Beta Coefficient (95% CI Lower/ Upper)	p-value	Beta Coefficient (95% CI, Lower/ Upper)	p-value
Age	0.02 (0.01/0.03)	.003	0.01 (0.01/0.03)	.018
Gender	-0.09 (-0.42/0.24)	.607	..	..
Diabetes mellitus	-0.10 (-0.39/0.19)	.497	..	..
Hypertension	-0.12 (-0.41/0.16)	.394	..	..
Creatinine (Log10)	-0.89 (-2.3/0.5)	.208	..	..
Low-density lipoprotein	0.01 (-0.01/0.01)	.028	0.01 (-0.03/0.01)	.944
C-reactive protein (Log10)	0.30 (0.03/0.57)	.030	0.12 (-0.12/0.36)	.338
SII (Log10)	1.41 (1.04/1.78)	<.001	1.29 (0.93/1.66)	<.001

Multivariate Model's Adjusted R2= 0.234, p-value <.001, CI, confidence interval; SII, Systemic immune-inflammation index.

Although cardiac troponins are the surrogate markers of ACS diagnosis, it should be mentioned that they may not be specific to the etiology of ACS in every circumstance, and it is unclear whether troponins are secreted entirely from the infarcted myocardium or ischemic and/or failing cardiomyocytes also secrete troponin [14]. CK-MB is less cardiac-specific when compared to troponin, but previous data suggest that peak CK-MB is an independent predictor of LV functions and one-year mortality after primary PCI in patients with STEMI [30]. In our analysis, we found a significant correlation between SII and peak CK-MB levels. Considering as a whole, our results may provide pathophysiological insights into myocardial damage in ACS and contribute to biomarker investigations from a diverse perspective. Because both inflammation and the immune system play significant roles in the pathogenesis of ACS, SII, which is a marker that identifies the balance between the inflammation and immune system at a systemic level, may yield superior benefits when compared to other biomarkers and/or evaluation modalities. Moreover, it is a cheap and non-invasive test that is derived easily through a complete blood count examination. The utility of SII deserves to be investigated in various cardiovascular conditions.

Our study has several limitations that need to be underlined. A small number of patients, single-center design and retrospective nature of this study should be acknowledged. Although cardiac enzyme measurements were performed regularly, the lack of specified fixed time points and variations between blood sampling might have yielded a misrepresentation in true peak levels. Lack of echocardiographic data in some patients may be associated with selection bias which needs to be debated in well-designed future prospective studies. Besides, it is incomprehensible from the present data whether left ventricular systolic dysfunction is present before the ACS or it is a consequence of ACS. Furthermore, utilizing follow-up SII and CRP levels instead of only admission levels could provide more beneficial results. Thus, our observational and retrospective analysis should be considered hypothesis-generating only.

In conclusion, SII is independently associated with peak TnT levels and significantly correlates with peak CK-MB levels in ACS patients. Moreover, SII significantly and inversely correlates with left ventricular systolic functions.

Conflict of Interest: The author declares no conflict of interest related to this article.

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Ethics Committee Approval: Ethics committee approval (2017-KAEK-189_2021.02.10_11) was obtained from the ethics committee of hospital (Yozgat Bozok University, Clinical research Ethic Committee, 10.02.2021).

Peer-review: Externally and internally peer reviewed.

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