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**Area of Expertise:** Emergency Medicine

**Title:** Can emergency department blood parameters predict coronary artery occlusion in acute myocardial infarction?

**Short title:** Coronary artery stenosis and hemogram parameters.

### **Abstract**

**Purpose:** The aim of this study is to assess the detectability of coronary artery stenosis in patients evaluated for acute myocardial infarction (AMI) in the emergency department and undergoing coronary angiography, based on blood parameters examined in the emergency setting.

**Materials and methods:** In our single-center prospective observational study, patients diagnosed with AMI in the Emergency Department between September 1 and October 31, 2023, and those who underwent coronary angiography by a single cardiologist were included. The blood parameters applied during routine assessment in the Emergency Department were recorded, and parameters with predictive effects based on the percentages of vessel stenosis after angiography were evaluated.

**Results:** A total of 64 patients (44 males and 20 females) who met the study criteria were included in our research. Following the evaluation based on the highest percentage of stenosis in any coronary artery after coronary angiography, patients were divided into two groups. Group 1 consisted of 15 patients with mild stenosis (stenosis <50%), and Group 2 comprised 49 patients with severe stenosis (70-99% stenosis). Group 2, a predominance of male gender was observed along with elevated Troponin-I (Tn-I) levels, and lower values of lymphocyte and platelet counts ( $p=0.010$ ,  $p=0.004$ ,  $p=0.042$ , and  $p=0.007$ , respectively).

**Conclusion:** In males, it has been observed that Tn-I levels are higher in association with coronary stenosis. Alongside atherosclerosis and thrombosis, inflammation may contribute to decreased platelet and lymphocyte counts in cases of severe stenosis. Further prospective, randomized controlled studies with larger sample sizes are needed to confirm these findings.

**Keywords:** Acute myocardial infarction, cardiac markers, whole blood count, coronary stenosis, coronary angiography.

**Makale başlığı:** Acil servis kan parametreleri akut miyokard infarktüsünde koroner arter oklüzyonunu öngörebilir mi?

**Kısa başlık:** Koroner arter stenozu ve hemogram parametreleri.

**Öz**

**Amaç:** Bu çalışmanın amacı acil serviste akut miyokard infarktüsü (AMİ) nedeni ile değerlendirilen ve koroner anjiyografi uygulanan hastaların koroner damar darlığının acilde bakılan kan parametreleri ile saptana bilirliliğini değerlendirmek.

**Gereç ve yöntem:** Tek merkez prospektif gözlemsel çalışmamızda 1 Eylül-31 Ekim 2023 tarihleri arasında acil serviste AMİ tanısı alan ve tek kardiyolog tarafından koroner anjiyografi yapılan hastalar dâhil edildi. Acil servis rutin değerlendirmede uygulanan kan parametreleri kayıt edildi ve anjiyografi sonrası damar darlık yüzdelerine göre prediktif etkisi olan parametreler değerlendirildi.

**Bulgular:** Araştırmamıza çalışma kriterlerini karşılayan toplam 64 hasta (44 erkek, 20 kadın) dâhil edildi. Koroner anjiyografi sonrası herhangi bir koroner arterde en yüksek darlık yüzdesine göre yapılan değerlendirme sonrası hastalar 2 gruba ayrıldı. Grup 1 hafif darlık (darlık <%50) saptanan 15 hasta ve grup 2 ciddi darlık (%70-99 darlık) tespit edilen 49 hastadan oluşmaktadır. Grup 2'de erkek cinsiyet baskınlığı ile Troponin-I (Tn-I) düzeyinin yüksek, lenfosit ve trombosit değerlerinin düşük olduğu görüldü (sırasıyla  $p=0,010$ ,  $p=0,004$ ,  $p=0,042$  ve  $p=0,007$ ).

**Sonuç:** Erkeklerde koroner darlığa bağlı olarak Tn-I düzeylerinin daha yüksek olduğu görülmüştür. Ateroskleroz ve trombozun yanı sıra, şiddetli darlık vakalarında iltihaplanma, trombosit ve lenfosit sayısının azalmasına katkıda bulunabilir. Bu bulguları doğrulamak için daha büyük örneklem büyüklüğüne sahip, ileriye dönük, randomize kontrollü çalışmalara ihtiyaç vardır.

**Anahtar kelimeler:** Akut miyokard infarktüsü, kardiyak belirteçler, tam kan sayımı, koroner darlık, koroner anjiyografi.

## Introduction

Acute myocardial infarction (AMI), commonly known as a heart attack, is a consequence of ischemic heart disease or coronary artery disease. It represents a clinical condition arising from the blockage of one or more coronary arteries by a vulnerable plaque, leading to the inadequate nourishment of the heart with blood [1]. Despite advances in prevention, diagnosis, and treatment strategies, it continues to be a leading cause of worldwide morbidity and mortality [2]. The diagnosis can be established with the presence of at least two characteristics among typical symptoms, a characteristic rise-fall pattern of a cardiac marker (such as creatine kinase MB (CK-MB) isoenzymes),

or preferably, the development of Q waves, in accordance with the consensus of the European Society of Cardiology and the American College of Cardiology [3].

Current marker technologies, particularly serum troponins, are capable of detecting very small amounts of myocardial necrosis (<1.0 g) when compared to patients without myocardial infarction in acute coronary syndrome [4]. In addition, CK-MB, a creatine kinase (CK) isoenzyme, serves as a standard marker for AMI. It begins to rise 4-9 hours after myocardial injury, reaching its peak within 24 hours, and returns to the normal range between 48-72 hours [5]. The pathophysiology of AMI involves a complex chain of reactions, including atheroma plaque rupture, platelet activation leading to aggregation, endothelial dysfunction, vasospasm, and revascularization [6]. The primary mechanism in the pathogenesis of AMI is thrombocyte hyperactivation and local platelet activation, with the progression rate of the atherosclerotic event determining the onset timing of symptoms [7, 8].

The aim of this study was to investigate the relationship between the percentage of coronary artery occlusion and cardiac enzymes, as well as hematological parameters, in patients diagnosed with acute myocardial infarction (AMI) upon admission to the emergency department who subsequently underwent coronary angiography.

## **Materials and methods**

This research constitutes a prospective observational study that obtained ethical approval from the Bandirma Onyedi Eylül University Health Sciences Non-Interventional Research Ethics Committee. The study adhered to the guidelines for observational studies outlined by STROBE ([www.strobestatment.org](http://www.strobestatment.org)).

We included patients diagnosed with non-ST-segment elevation myocardial infarction (NSTEMI) and Unstable angina pectoris (USAP) and undergoing coronary angiography by a single cardiologist at the Emergency Department of xxxxxxxx Training and Research Hospital between September 1 and October 31, 2023, in our study. The diagnosis and management of AMI, as well as the follow-up of coronary angiography procedures, were conducted as follows: Patients presenting to the emergency department underwent diagnostic evaluation by the attending physician, and those diagnosed with non-ST-segment elevation myocardial infarction (NSTEMI) following cardiology consultation were included in the study. Consultation assessments and coronary angiography procedures were performed by the same cardiologist for standardization purposes. We excluded patients referred from external centers, those without NSTEMI, individuals whose blood test results could not be analyzed in our emergency department, those with a history of previous bypass surgery or stent

placement, and patients presenting to the emergency department with coronary syndrome who could not undergo coronary angiography within the first 24 hours from the study. In Figure 1, the study design is illustrated in more detail using a flow chart.

After the patients' emergency admissions, electrocardiography, cardiac enzyme markers, and simultaneous hemogram data were recorded. Consultation with a same cardiologist was requested for patients suspected of having AMI. The procedure results of patients undergoing coronary angiography, consistently performed by the same physician using the same methodology and interpretation, were recorded. In coronary angiography, patients were categorized based on the percentage of stenosis in the Right coronary artery, Left Anterior Descending artery, Left Main Coronary Artery, and Circumflex arteries as follows: mild (<50%), moderate (50-70%), and severe (70-99%) according to the extent of vascular narrowing.

### **Statistical analysis**

The data acquired were recorded using the SPSS 20.0 version (Statistical Package for Social Sciences, Inc., Chicago, IL, USA) statistical program. The normal distribution of the data was evaluated through the Kolmogorov-Smirnov test. Descriptive statistics for continuous variables included standard deviation, mean, median, minimum, and maximum values, while categorical variables were represented using percentages and numbers. Student's t-test was applied to compare normally distributed data between two groups, and the Mann-Whitney U test was employed when the data deviated from a normal distribution. The Chi-square test or Fisher's exact test (used when Chi-square test assumptions were not met due to low expected cell counts) was utilized to compare categorical variables. The cut-off point was chosen based on the ROC (Receiver Operating Characteristic) curve analysis. A significance level of  $p < 0.05$  was considered statistically significant for all outcomes.

### **Results**

As shown in the flowchart (Figure 1), a total of 108 patients were evaluated by the same cardiologist. During the designated time frame, our research included a total of 64 patients, comprising 44 males and 20 females, who met the study criteria. The median age of the patients was 59.50 years, ranging from a minimum of 47 years to a maximum of 88 years. The results of the blood parameters at the time of admission for the patients are presented in Table 1.

In the assessment based on the highest percentage of stenosis in any coronary artery after coronary angiography, mild stenosis was observed in 15 patients (stenosis <50%) (Group 1), while severe stenosis (stenosis 70-99%) was detected in 49 patients

(Group 2). No patient with moderate (50-70%) stenosis was detected. Although the median age of Group 2 (61 years) was higher than Group 1 (51 years), no statistically significant difference was observed. When considering the gender distribution between the groups, a statistically significant higher prevalence of stenosis was observed in males ( $p=0.010$ ). Among the cardiac enzyme markers examined at the time of emergency admission, only Troponin-I (Tn-I) levels were found to be elevated in Group 2 ( $p=0.004$ ). No significant difference was observed among CK and CK-MB values (Respectively  $p=0.584$  and  $p=0.552$ ). Group-wise analysis of hematological parameters revealed that only lymphocyte and platelet (PLT) values were found to be higher in Group 1 (respectively,  $p=0.042$  and  $p=0.007$ ). The comparison of gender and blood parameters according to coronary artery stenosis percentage groups is presented in Table 2.

The ROC curve was plotted for Tn-I, lymphocyte, and PLT values regarding the severity of coronary artery stenosis. The area under the curve for Tn-I was 0.746 with a standard deviation (SD) of 0.06. The area under the curve was significantly higher than the diagnostic insignificance level of 0.05 ( $p=0.004$ ). The cutoff value for Tn-I in diagnosing severe coronary artery stenosis was 0.3 pg/ml. It was determined that this value had a sensitivity of 100% and specificity of 100% (Figure 2a). For lymphocyte and PLT values, the areas under the curve were 0.675 (SD=0.8) and 0.733 (SD=0.79), respectively. The areas under the curve were significantly higher than the diagnostic insignificance level of 0.05 ( $p=0.042$  and  $p=0.007$ , respectively). The cutoff value for lymphocyte in diagnosing severe coronary artery stenosis was  $4.02 \times 10^3/\mu\text{l}$ . It was found that having a value below this cutoff had a sensitivity of 98% and specificity of 60% for severe coronary stenosis (Figure 2b). The cutoff value for PLT in diagnosing severe coronary artery stenosis was  $367 \times 10^3/\mu\text{l}$ . It was determined that having a value below this cutoff had a sensitivity of 96% and specificity of 87% for severe coronary stenosis (Figure 2b).

## Discussion

AMI is responsible for approximately 7 million deaths worldwide annually, highlighting the importance of early identification of signs and symptoms, as well as the detection of specific serological markers for a prompt diagnosis and the initiation of potentially life-saving treatment [9]. The specificity of markers used in the diagnosis of AMI and ongoing research on new markers continue to be an active area in contemporary medical studies [9-12]. While studies are specifically focused on achieving a faster and more accurate diagnosis, there is limited research evaluating the correlation with vascular stenosis.

The clinical presentation of AMI involves complex reactions, including atheromatous plaque rupture in coronary arteries, platelet activation leading to thrombus formation, aggregation, endothelial dysfunction, vasospasm, and revascularization [7]. After the onset of atherosclerosis, continuous progression occurs, accompanied by inflammation. In this process, the formed elements of blood and inflammatory markers related to inflammation actively play a role. Particularly during the plaque rupture phase of atherosclerosis and consequently in the progression stages of this process, neutrophils, lymphocytes, and platelets actively participate [13]. Specifically, platelets actively play a role in plaque destabilization, rupture, and the coagulation cascade [13]. In early atherogenesis, the progression of lesions, and ultimately in the thrombotic complications of plaques, it has been shown that inflammatory pathways play a role, and decreased lymphocyte levels suppress the immune response [14]. The mechanism mentioned would lead to an expected positive correlation between the amount of thrombus formation and the PLT and lymphocyte values. Indeed, in our study, PLT and lymphocyte values were found to be lower in patients with severe coronary stenosis compared to those with mild stenosis. The literature contains findings consistent with the results of our study. A decrease in lymphocyte count has been reported to be associated with the progression of atherosclerosis and major cardiac complications [15, 16]. Similarly, Tangjitgamol et al. [17] found significantly low platelet levels in doctors with coronary artery disease. Yüksel et al. [18] also demonstrated that the average Platelet-to-Lymphocyte Ratio (PLR) in the severe atherosclerosis group was significantly higher compared to the mild atherosclerosis and control groups, supporting the mentioned pathophysiology. Liu et al. [19] have also provided evidence supporting the relationship between severe stenosis and the inflammatory process. In the literature, there are publications that express the opposite of this situation. Yücel and Amanvermez Şenarslan [20] investigated the relationship between the progression of atherosclerosis and hematological parameters in patients undergoing Coronary Artery Bypass Graft (CABG) surgery. In their study, they found that platelet counts increased in recurrent stenosis, while lymphocyte counts decreased. Ayaz et al. [21] reported that there was no statistically significant relationship between the severity of coronary artery disease and the number of vascular occlusions with platelet aggregation slope and % amplitude values. Patients monitored for AMI in the emergency department continue to be searched for new rapid markers. Although there is a relationship between coronary artery stenosis and the processes of platelet and inflammation, more detailed studies are needed.

## Study limitations

Our study has various limitations. Firstly, it is a single-center study with a small number of patients. Secondly, the inability to assess values such as HDL, Triglycerides, and Low-Density Lipoprotein, as well as comorbid additional diseases and other processes that may affect inflammation, before the procedure, is another limitation. However, values such as HDL, Triglyceride, and Low Density Lipoprotein could not be evaluated in patients who would undergo urgent angiography in the emergency department, as values such as HDL, Triglyceride, and Low Density Lipoprotein could not be studied, and previous or post-procedure values were not targeted for the acute situation in our study.

In conclusion, the severity of coronary artery occlusion in patients diagnosed with AMI in the emergency department can be predicted not only by cardiac enzyme markers such as Troponin I but also by using platelet and lymphocyte values. To generalize this condition, there is a need for multicenter randomized controlled prospective studies.

**Conflict of interest:** No conflict of interest was declared by the authors.

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**Ethics committee approval:** The study received approval from the Bandırma Onyedi Eylül University Health Sciences Non-Interventional Research Ethics Committee (approval date: 12.01.2023 and no: 2023-2).

#### **Authors contributions**

H.Y.B. Concept and design, data collection and processing, analysis and interpretation, literature review, writing, reviewing and revision. A.A. Concept and design, analysis and interpretation, literature review, writing, reviewing and revision, critical review A.B. Concept and design, data collection and processing, analysis and interpretation, literature review, writing, reviewing and revision.

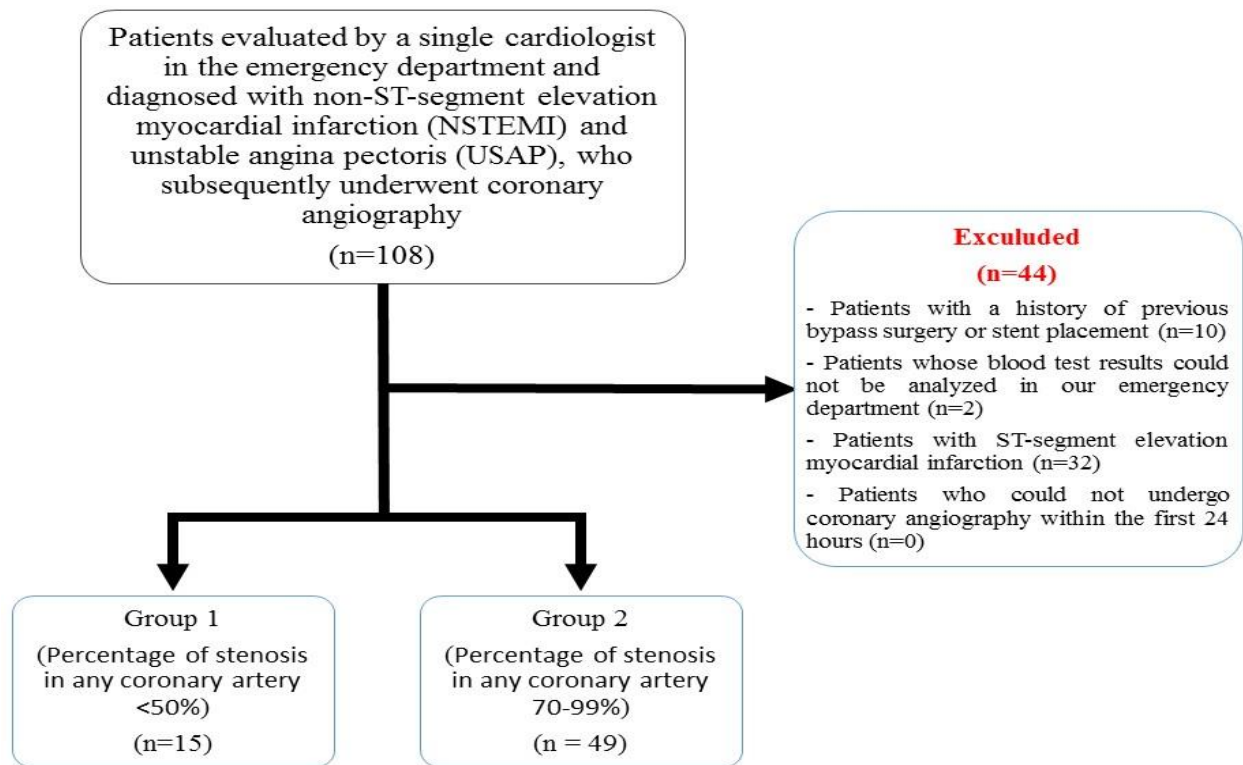


Figure 1. Flow chart the study design

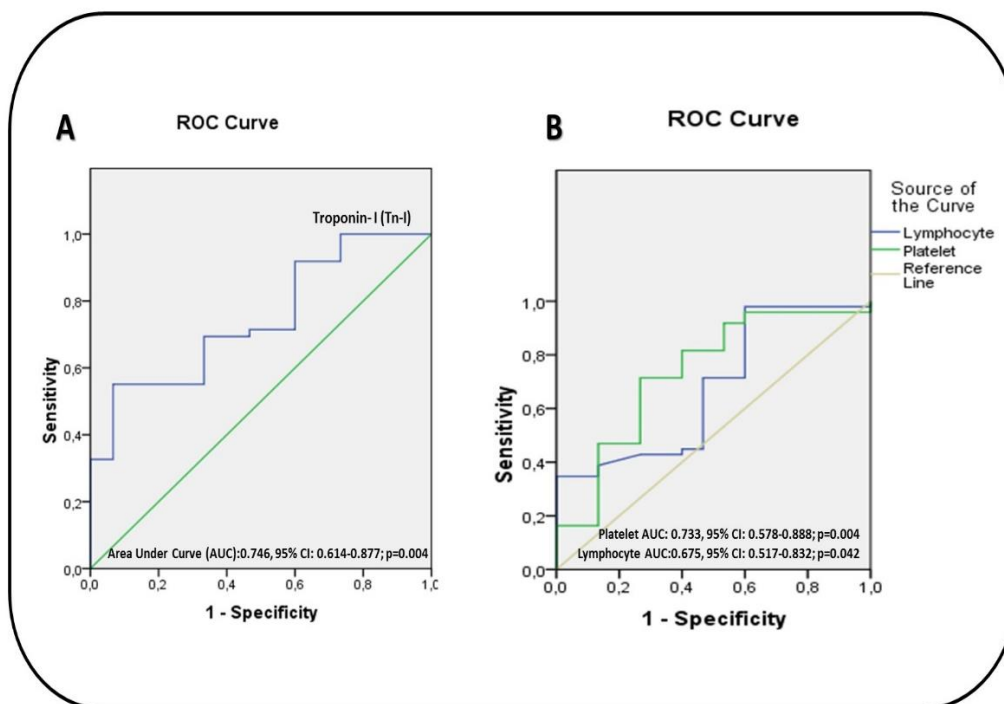


Figure 2. Diagnostic values of troponin-I, lymphocyte and platelet values and the severity of coronary artery stenosis

**Table 1.** Emergency department admission blood parameter results of the patients

Blood parameters	Median (IQR)
Troponin- I (Tn-I) (pg/ml)	153.80 (2746.5)
Creatine kinase (U/L)	126.50 (109)
Creatine kinase-myocardial band (CK- MB) (U/L)	26 (25)
CRP (mg/dl)	0.50 (0.89)
WBC ( $10^3$ /ul)	11.03 (3.99)
PLT ( $10^3$ /ul)	262 (80)
MPV (fl)	10.05 (0.90)
Neutrophil ( $10^3$ /ul)	6.71 (4.62)
Lymphocyte ( $10^3$ /ul)	2.20 (0.97)
NLR	3.22 (3.06)
PLR	111.38 (95.03)

IQR; Interquartile Range, CRP; C-Reaktif Protein, WBC; White Blood Cell, PLT; Platelet, MPV; Mean Platelet Volume,

NLR; Neutrophil Lymphocyte Ratio, PLR; Platelet Lymphocyte Ratio

**Table 2.** The comparison of gender and blood parameters according to coronary artery stenosis percentage groups

Blood parameters		Group 1 n=15	Group 2 n=49	<i>p</i>
Gender	Male n (%)	6 (40)	38 (77.6)	<b>0.010</b>
	Female n (%)	9 (60)	11 (22.4)	
Age (years) Median (IQR)		51 (21)	61 (19)	0.085
Troponin- I (Tn-I) (pg/ml) Median (IQR)		39.50 (179.3)	397.70 (2808.8)	<b>0.004</b>
Creatine kinase (U/L) Median (IQR)		137 (90)	120 (110)	0.584
Creatine kinase-myocardial band (CK- MB) (U/L) Median (IQR)		27 (25)	25 (30)	0.552
CRP (mg/dl) Median (IQR)		0.50 (1.60)	0.50 (0.89)	0.639
WBC ( $10^3$ /ul) Median (IQR)		11.33 (2.83)	9.89 (6.64)	0.617
PLT ( $10^3$ /ul) Median (IQR)		310 (107)	254 (64)	<b>0.007</b>
MPV (fl) Median (IQR)		10 (1.60)	10.10 (1.35)	0.994
Neutrophil ( $10^3$ /ul) Median (IQR)		6.60 (2.15)	6.71 (7.21)	0.981
Lymphocyte ( $10^3$ /ul) Median (IQR)		2.81 (2.50)	2.20 (1.14)	<b>0.042</b>
NLR Median (IQR)		2.72 (2.16)	3.43 (5.42)	0.062
PLR Median (IQR)		103.20 (77.38)	115.45 (96.80)	0.396

IQR; Interquartile Range, CRP; C-Reaktif Protein, WBC; White Blood Cell, PLT; Platelet, MPV; Mean Platelet Volume, NLR; Neutrophil Lymphocyte Ratio, PLR; Platelet Lymphocyte Ratio

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